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DRUG ERUPTIONS*

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THE first duty of a doctor is *primum non cere i.e.*, not do harm. Several drugs often produce skin eruptions in sensitive patients.

Drug eruptions of dermatitis medicamentosa is often recognized by their sudden appearance, bright colour, and symmetric wide-spread distribution.

The manifestations of drug eruptions are protean and are often bizarre. The various types of lesions are listed below :—

(1) Maculopapular lesions may be morbilliform, erythematous, pruritic, wide spread and often symmetrical ; these have been noted in arsenical poisoning with belladonna, barbitone and sulphonamides ; (2) urticarial rashes including angioneurotic œdema occurring after penicillin injections ; (3) vesiculo-bullous lesions following the administration of sulphonamides ; (4) pustular lesions produced by bromides ; and (5) purpuric rashes occurring after barbiturates and thiocyanates.

A. Certain dermatological patterns have been noticed with certain drugs :—*e.g.*, (1) Erythema nodosum after sulphones ; (2) granuloma after iodides or bromides ; (3) exfoliative dermatitis after arsenic ; (4) dyshidrosis may occur after iodides and (5) erythema multiformæ after penicillin.

B. Drug eruptions may mimic skin diseases :—*e.g.*, (1) Lichen planus-like lesions after atebrin ; (2) seborrhœic dermatitis, after gold ; (3) acne lesions after A.C.T.H. ; (4) erysipelas-like lesions after amidopyrine ; and (5) pemphigus-like ones after sulphonamides and bromides.

C. Drugs may activate latent viral infection :—*e.g.*, Herpes zoster occurring after radiomimetic compounds.

D. Pigmentation and depigmentations *e.g.*, Raindrop pigmentation after arsenic and vitiligo after thiouracil.

E. Fixed drug eruptions.—These are interesting and highly specific cutaneous eruptions which persist or recur at the same sites consistently. When phenolphthalein is taken, erythema, œdema, and bullae may form and leave finally an area of hyper-pigmentation. After subsequent intakes of phenolphthalein, the skin lesions appear at the site of hyper-pigmentation.

Aspirin, barbiturates, aureomycin, and Dilantin may produce fixed drug eruptions.

F. Along with drug eruptions other manifestation may occur in dermatitis medicamentosa :—(1) *Central nervous system* producing drug fever ; psychosis or psychoneurosis ; (2) *Blood*:

*Specially contributed to the ANTISEPTIC

anæmia + leukopænia; (3) *Kidneys*: albuminuria; (4) *Mucous membranes*: stomatitis, gingival hypertrophy as in dilantin toxicity; and (5) *Respiratory system*: asthmatic paroxysms.

G. Some commonly used drugs produce cutaneous manifestations :—

Antibiotics.—(1) Penicillin produces a medley of cutaneous manifestations: (*a*) maculo-papular; (*b*) vesiculobullous; (*c*) urticarial; and (*d*) purpuric.

Other antibiotics produce comparatively lesser sensitivity *e.g.*, with broad spectrum antibiotics, there may be stomatitis and pruritis ani.

Sulphonamides may produce—(1) Pruritus; (2) morbilliform rashes; (3) erythema nodosum; and (4) pemphigoid eruptions. Drug eruptions can be treated with BAL which is useful in heavy metal poisoning.

Antihistamines and prednisolone help in other types of drug eruptions.

SAFE CIGARETTES?

On the theory that cigarettes cause an increased incidence of lung cancer by a nonspecific effect, Kotin and Falk believe current attempts to produce carcinogen-free cigarettes are not sensible unless the aim is also to make a smoke-free cigarette. The authors believe that cigarette smoke adversely affects the epithelial lining of the respiratory tract so that ciliary action is impaired, mucus flow is slowed, retention of carcinogenic particulate matter is facilitated and cellular permeability increased.

These effects are common to those resulting from various infections and the industrial contamination of the atmosphere. While a reduction in lung cancer may be properly anticipated as a result of reduction in cigarette smoking, this report suggests "the reduction in lung cancer would be of a low order of magnitude in the absence of the removal of the remaining sources of irritants and carcinogenic agents from the respiratory environment."—(*Cancer, 13* : 250, 1960. via *G.P.*, July, 1960).

CORTISONE ULCERS

The adrenal has an important role in the genesis of peptic ulceration. This has been postulated for years on the basis of animal experimentation and the observations in the human of increased incidence of peptic ulceration on corticoid therapy. Gray collected data on 1,361 patients on adrenal steroid maintenance therapy. Peptic ulcer was found in 7·1% as compared with a reported annual incidence of spontaneous development of ulcer of 0·15 to 0·38% in the general population. In a collected series of 363 patients with Addison's disease, chronic peptic ulcer was found in only three patients. Ulcers developed in a significant number of both the Addison's disease and adrenalectomized patients given 25 mg. of cortisone daily for several years. Gray postulates that the adrenal hormone must be present for normal gastric secretion and excess corticoid hormone may sensitize the gastric mucosa to ulcerogenic influences it could otherwise withstand.—(*Gastroenterology, 37*: 412, via *G.P.*, July '60).

CARBAZOCHROME SALICYLATE*
IN THE TREATMENT OF PULMONARY HÆMORRHAGE

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PULMONARY hæmorrhage is a symptom which needs immediate attention and treatment even before a diagnosis is made. The course of hæmorrhage is unpredictable. The commonest cause in our country is pulmonary tuberculosis.

Various drugs are in use for emergency treatment to arrest the hæmorrhage; the drugs used have no specific action on the cause of hæmorrhage. Calcium preparations, Vit. C, Vit. K, Coagulen Ciba, Congo-red have all been used by physicians. Thrombokinase preparations made from animal tissues are quite popular, *e.g.*, Clauden prepared from animal lung tissue. These drugs influence the bleeding, and clotting times. If the bleeding and clotting times are determined in cases of pulmonary hæmorrhage, most cases do not show any alteration and so it is difficult to understand how these drugs are useful. Recently a new hæmostatic agent has been made available *i.e.*, Carbazochrome salicylate (Stadren) chemically known as Adrenochrome-monosemicarbazone. It is an oxidation product of adrenalin. It has no action on the autonomic nervous system, pulse, blood-pressure, bleeding time and clotting time. It is rapidly absorbed when given orally or by intramuscular injection. Toxicity is absent. It acts by increasing the elastic tissue tone in the wall of the capillaries. This was proved experimentally in the cheek pouch of hamsters, when carbazochrome prevented hæmorrhages inspite of snake-venom. It maintains normal capillary permeability and promotes capillary retraction. It has no vasoconstrictor action. Thus it is useful in all conditions characterized by a hæmorrhagic diathesis.

I propose in this article to deal only with the action of the drug in pulmonary hæmorrhage.

Material and methods.—All the cases were admitted to the Tuberculosis department of the Civil Hospital, Ahmedabad. A detailed history of the duration and severity of hæmoptysis was recorded. Four schedules of drugs were administered at random without any conscious selection of any schedule: *viz.*:—(1) Clauden alone; (2) Clauden + coagulants like Cal. gluconate, Vit. C and Vit. K; (3) Stadren alone; and (4) Stadren + coagulants like Cal. gluconate, Vit. C and Vit. K.

Clauden was administered daily in doses of 10 cc. *i.v.*

Stadren was administered daily in doses of 2 cc. *i.m.*

* Stadren supplied by the Minlex Laboratories.

Specially contributed to the ANTISEPTIC.

These drug schedules were intended to assess the comparative values of the usefulness of the drugs. The cases were followed daily and the colour and quantity of blood and the severity of hæmoptysis were noted. Bright-red was taken as fresh hæmoptysis, while dark coffee-coloured blood was taken as old. Hæmoptysis was considered to have stopped when fresh blood was not seen, also when no blood was seen. In a few cases additional measures like blood-transfusion and pneumoperitoneum were employed when the hæmoptysis became profuse and uncontrollable. In a few cases bleeding and clotting times were ascertained before and after the treatment to assess the effect of the drugs. Sputum and radiological examinations were then made to confirm the diagnosis. The total number of cases treated was 45 ; but the results could be studied in only 43 cases.

Results.—A detailed analysis of the cases studied under various schedules will be found in the statements that follow. Radiological extent is mentioned as 1 + to 6+. It is equivalent to one radiological zone *i.e.*, upper zone=area above the lower margin of the anterior end of 2nd rib=1+. Thus 3 radiological zones on each side make a total of 6 zones. 'Mild' hæmoptysis refers to where blood was present in traces and 'Severe' refers to profuse frank blood in bouts. The rest were considered 'Moderate.'

Table I

Showing results under Schedule (1) *i.e.*, Clauden alone :

Case No.	Age	Sex	Radiological extent of disease	Severity of hæmoptysis	Duration of hæmoptysis before treatment (In days)	Duration after treatment (In days)	Additional measures
4	20	M	4+	Moderate	4	2	Recurrence
9	50	M	6+	Mild	4	30	
11	50	M	6+	Moderate	2	2	
23	28	M	2+	,,	2	5	
25	25	M	3+	,,	2	5	
27	35	M	6+	Severe	2	7	
28	20	M	4+	Moderate	2	3	P.P.
32	25	M	2+	,,	1	15	,,
33	28	M	4+	,,	4	3	
34	25	F	3+	,,	1	2	
39	32	M	2+	Mild	1	3	
11			42+		25	77	
Average 1			3·8		2·2	7	

Mild 2 cases 16·5 days
Moderate 8 ,, 4·8 ,,
Severe 1 case 7 ,,
} Average duration in days.

Table II

Showing results under Schedule (2) Clauden + Coagulants like Cal., Vit. C and Vit. K.

Case No.	Age	Sex	Radiological extent of disease	Severity of hæmoptysis	Duration of hæmoptysis before treatment (In days)	Duration after treatment (In days)	Additional measures
1	23	M	6+	Moderate	2	1	
2	28	M	6+	,,	1	5	
3	40	M	4+	,,	10	10	
5	28	M	6+	,,	4	4	
6	36	M	1+	,,	Few hrs.	1	
7	32	M	3+	Severe	1	5	
13	35	M	2+	Mild	2	3	
15	30	M	2+	Moderate	11	11	Bl. transfusion + P.P.
16	36	M	2+	Severe	16	12	P.P.
19	47	M	2+	Moderate	3	4	P.P. & recurrence
20	28	M	6+	Severe	15	6	
11			40+		66	62	
Average 1			3·6+		6	5·6	

Mild 1 case 3
Moderate 7 cases 5·1
Severe 3 ,, 7·6
} Average duration in days.

Table III

Showing results under Schedule (3) — Stadren alone :

22	23	M	2+	Moderate	1	4	
24	20	M	6+	,,	2	5	
26	25	M	3+	,,	1	5	
29	45	M	6+	,,	1	4	
30	40	M	4+	,,	1	7	
31	37	M	6+	,,	3	10	
35	20	M	4+	,,	1	1	
36	50	M	3+	Severe	3	3	Headache, body ache, bradycardia 56/min.
37	25	F	6+	,,	1	12	Headache, bodyache
38	25	M	6+	,,	3	7	
10			46+		17	58	
Average			4·5		1·7	5·8	

Mild Nil
Moderate 7 5·1
Severe 3 7·3
} Average duration in days.

TABLE IV

Showing results under Schedule (4) Stadren + Coagulants: like Cal., Vit. C and Vit. K.

Case No.	Age	Sex	Radiological extent of disease	Severity of Hæmoptysis	Duration of hæmoptysis before treatment (In days)	Duration after treatment (In days)	Additional measures
8	20	M	4+	Severe	5	4	B. transfusion
12	32	M	6+	Moderate	2	4	
17	26	M	4+	Severe	2	7	
18	26	M	1+	Moderate	10	3	
21	40	M	4+	,,	2	6	P.P.+Blood
40	50	M	2+	,,	2	3	
41	20	F	1+	,,	1	4	
42	32	M	4+	Mild	1	2	
43	24	M	3+	Moderate	1	3	
44	20	M	1+	Severe	2	10	Bl. transfusion
45	28	M	3+	Mild	1	6	
11			33+		29	52	
Average 1			3+		2·8	4·7	

Mild	2	4
Moderate	6	3·8
Severe	5	7

Average duration in days.

TABLE V

Showing the average duration of hæmoptysis after various schedules (In days)

Schedule	1	2	3	4
Days	7	5·6	5·8	4·7

TABLE VI

Showing the relation between the schedules, severity of hæmoptysis and its duration in days after treatment

Severity	1	2	3	4
Mild	16·5	3	Nil	4
Moderate	4·6	5·1	5·1	3·8
Severe	7	7·6	7·3	7

TABLE VII

Showing the relation between the average radiological extent, schedule and duration in days

	Schedule	Average extent	Average duration	Duration per unit zone
1+2 = 2·69	1	3·8+	7	1·84
	2	3·6+	5·6	1·55
3+4 = 1·41	3	4·5+	5·8	1·26
	4	3+	4·7	1·56

The total number of cases treated was 43, and the total duration of hæmoptysis was 249 days, giving an average duration per patient of 5·76 days.

The average duration of cases treated with Clauden including coagulants, Sch. 1 and 2 was 6·3 days; and with Stadren including coagulants, Sch. 3 and 4 was 5·25 days.

The average duration of cases treated without coagulants, Sch. 1 and 3 was 6·4 days, and cases treated with the coagulants Sch. 1 and 4 was 5·1 days.

TABLE VIII

Showing the bleeding and clotting times before and after treatment

Case No.	Schedule	Bleeding time in minutes		Clotting time in minutes	
		Before treatment	After treatment	Before treatment	After treatment
22	3	3·45	1·50	6·20	9·20
23	1	1·55	2·50	5·5	4·35
25	1	2·15	2·50	5·5	6·15
26	3	1·2	1·50	4·5	5·60
27	1	1·5	2·5	4·37	5·20
28	1	1·10	2·15	5·30	5·20
29	3	1·15	1·15	0·30	6·5
30	3	1·25	1·45	4·9	5·4
33	1	1·10	1·2	4·18	3·40
36	3	1·6	1·2	2·40	2·50
37	3	1·4	1·3	2·35	2·20
38	3	1·40	1·12	3·40	3·10

Discussion.—From the data presented in the above tables the following conclusions appear to be justifiable :—

1. The average duration of hæmoptysis was least (4·7 days) with schedule 4, *i.e.*, Stadren with coagulants.

2. Whatever the severity of the hæmoptysis the average duration was least with Schedule 4, *i.e.*, Stadren with coagulants. Mild cases are not taken into consideration because of the small number (*See* Table VI, p. 142).

3. The average duration of hæmoptysis was least with Stadren group (Schedules 3 and 4) when the average radiological extent was considered. The average duration per unit zone was 1·41 days with 3 and 4 *i.e.*, Stadren group while it was 1·69 days with Sch. 1 and 2 *i.e.*, Clauden group.

4. The average duration of hæmoptysis per patient considering all patients together was 5·76 days. But schedule 3, had a duration of 4·7 days *i.e.*, less than the average.

5. The average duration was less in the Stadren cases *i.e.*, Schedules 3 and 4, 5·25 days while it was 6·3 days with Clauden cases (Sch. 1 and 2).

6. The average duration was 6·4 days with coagulants; thus coagulants like Cal., Vit. C and Vit. K are of some value in checking hæmorrhage.

7. There were 2 cases of recurrence of hæmoptysis with Clauden group (1 and 2) while there were none with Stadren group (3 and 4).

8. Additional measures like blood transfusion and pneumoperitoneum had to be used in 6 cases with Clauden group (1 and 2) and in 4 cases with Stadren group (3 and 4).

Two cases of allergic symptoms were noted with Stadren none were noted with Clauden.

10. There was no appreciable effect on bleeding and clotting times either with Stadren or Clauden.

Stadren is a drug which in this study, proved superior to other drugs in the sense that the hæmoptysis was checked earlier irrespective of the duration and severity of the hæmoptysis, radiological extent of disease. The previous reports that the drug had no action on blood-pressure, pulse-rate and bleeding and clotting times are confirmed in this study. The drug is practically non-toxic as only 2 cases had mild allergic reactions in a total of 21 cases. The drug is easier to administer *i.e.*, by the intramuscular route and so can be given by the nurse even before the doctor arrives.

I would like to make it clear that the number of cases in this trial is small and extended trials will be necessary before definite conclusions of value can be drawn. Stadren is not a master-drug which has solved our problems of controlling hæmorrhage. Additional measures like blood-transfusion, pneumothorax or pneumoperitonium or surgical intervention must also be used as and when necessary. The drug however shows promising results and I would suggest that if Stadren is used along with coagulants, hæmorrhages can be controlled earlier and the drug may even be life-saving.

Summary.—1. 43 cases were studied using different schedules as detailed in the article.

2. The average duration of hæmoptysis was least when Stadren and coagulants were used irrespective of the severity and duration of the hæmoptysis and of the radiological extent of the disease.

3. The addition of coagulants like Cal., Vit. C and Vit. K, definitely helped in reducing the average duration of the hæmoptysis.

4. Stadren is non-toxic, and has no action on blood-pressure, pulse-rate and the bleeding and clotting times.

I wish to express my grateful thanks to Dr. Gopal K. Karandikar, Dean, B. J. Medical College and Civil Hospital, Ahmedabad, for his valuable suggestions. My thanks are also due to Dr. T. L. Patel, Asstt. Hon. Tuberculosis Specialist, Dr. Francis, Dr. Kulkarni, Dr. Desai and the Ward Master Mr. Joshi for their help in carrying out this study in the Dept. of Tuberculosis and Chest diseases of the Civil Hospital, Ahmedabad. I am also thankful to Messrs Milnex Laboratories for a liberal supply of the drug Stadren used in this clinical study.

Cases and Comments

REPORT ON A CASE OF NEGLECTED TRANSVERSE LIE

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Mrs. M. K., a Muslim primipara, full term, of moderate stature and good health was seen by me with transverse presentation, the fœtal left hand projecting outside the vulva. She had had intermittent pains for a fortnight in the lower abdomen, simulating those of labour. Real labour pains however, set in on 17th May 1960, early in the night. After a few bouts, the attending *dhais* found a fœtal part protruding from the vagina, which they afterwards recognized as the left hand, by the hand-shake method. Unable to deliver the baby, they sought my help.

I first tried internal version by pushing the head upwards and bringing the breech down by traction. As the uterus was contracting powerfully and the fœtus had got impacted, I had to abandon my attempts at version and traction.

Destructive methods had therefore to be resorted to, and the permission of the guardians was obtained. There were no facilities for giving anæsthesia and I had therefore to deliver the fœtal contents as best as possible, with the physical assistance of three *dhais*, who assisted by holding, fanning and comforting the patient with soothing words, while I was engaged in bringing out the fœtal viscera and organs one by one. After evacuating the bladder and bowels, and swabbing the vulval parts with antiseptic lotion, I gave her an injection of $^{1}/_{100}$ grain of atropine sulphate. I then tried to reach the neck of the fœtus which was high up in the right flank and could not be got down in any way; nor the breech which was also high up in the left flank with the trunk curved in the pelvis.

As there was no hope of getting at the head, I pulled down the prolapsed hand and proceeded to eviscerate the fœtus, through the cleavage made in the fœtal axilla under the prolapsed limb by cutting the 4th, 5th and 6th ribs with blunt scissors.

A part of the thoracic wall was removed for perspective advantage. I then, got the heart and lungs out and pulled the prolapsed limb in order to bring down the head in which I did not succeed. Then I ruptured the diaphragm and brought out the whole of the intestines with the liver; the trunk of the fœtus then got collapsed and with suitable traction on the cut end of the thorax, the trunk was bent following the breech in view. Then I applied the breech hook and brought down the breech along with the legs which were delivered abruptly and the head

followed. The placenta was removed in tact after proper uterine squeeze. There was not even a single injury to the maternal parts either internal or external. The vagina and vulva were washed with dettol 1% solution and a vaginal pad applied with sanitary napkins. There was profuse visible post-partum hæmorrhage, just after the birth of the placenta. I gave an injection Neogynergen 1 cc. *i.m. stat* and Mist. Ergot ʒ i *t.d.s.* A.T. serum 3000 *i.u. i.m. stat* and Injection of Penicillin G sodium 10 lacs units once a day for six consecutive days. Sulphamezathine 0·7 gm. tab. 2 tabs. thrice daily for 6 (six) 'days.

On the first day she was given pure milk diet with complete rest in bed. After the manœuvres, she had a few bouts of vomiting which subsided soon. She then made an uneventful recovery.

FAILURE IN TEMPERATURE REGULATION DURING PROGRESSIVE DEHYDRATION

Hertzman and Ferguson of the Department of Physiology, St. Louis University School of Medicine, St. Louis, state: "Dehydration raises the thermal threshold for sweating, heat storage correspondingly increases, and each increment in body temperature provides additional stimulation to the regulatory mechanism whose reactivity is diminishing. An increasingly precarious equilibrium is almost attained between heat exchanges with the environment and heat production in the body, but at the expense of progressively higher body temperatures. In this sense, dehydration elicits failure in temperature regulation during exposure to heat.

The evaporation of water on the body's surface is the only mechanism available for the transfer of metabolic heat to the environment when the latter is hotter than the subject. A slight deficit in evaporation must result in a corresponding storage of heat. Circulatory changes may follow this event and may influence the distribution of heat in the body and the extent of thermal heterogeneity; but cannot prevent heat storage under these circumstances. They are inclined, therefore, to discount peripheral circulatory failure as directly responsible for the rising body temperatures in a dehydrating subject exposed to a hot climate, particularly in our experiments in which the indexes of cutaneous blood-flows suggested levels that were several times greater than in the comfortable subject.

If normal resting subjects were kept hydrated, they maintained their total and regional sweating rates without evidence of "fatigue" of sweating and without a rise in body temperatures during a continuous exposure for 32 hours to 43·3°C.

Dehydrating subjects lost weight at the rate of 0·5% per hour of exposure in the same conditions; their body temperatures rose 0·1°C. per hour, but total evaporative heat-loss changed very little despite the increase in body-temperatures. Calculations indicated that the rise in the latter was due to a slightly inadequate sweating, which in turn was attributed to a rising thermal threshold for sweating.

Regional sweating rates, particularly on the head and upper parts of the body, varied widely during the exposure of the dehydrating subjects. Rates on the lower extremity tended to fall as the exposure continued.

Cutaneous conductances, thermal circulatory indices, and the pad pulses in the finger and toe changed very little. There was no evidence of peripheral circulatory failure in these experiments. Its direct influence in accounting for heat storage was discounted.

RECURRENT DIPHTHERIA IN A FULLY IMMUNIZED CHILD (Report of a Case)

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K. A., a 2 year-old male child was first inoculated by me with 0·5 cc. of triple antigen of a standard make when he was 6 months old. After a month he was given 1 cc. of antigen which was repeated a month later. Thus the child was fully immunized against tetanus, whooping cough and diphtheria.

When the child was 14 months old, I was asked to treat for fever fluctuating between 101°F and 104°F. The pulse was 120/mt. and the respiration was hurried. He had running in the nose and sore eyes. The tonsils were congested and enlarged. The chest was clear. He was given Inj. Streptopenicillin (plain) daily for three days with no improvement. On the third day, the child had marked dysphagia and became dyspnœic. On the fourth day, a membrane which bled on touch appeared in the right tonsil which gradually spread on to the left one. The suspician of diphtheria came to my mind in a flash. In order to confirm my suspicion, a senior colleague was consulted. The child was immediately given a loading dose of 40,000 units of Diphtheria antitoxin followed by 20,000 units a day for three more days. The temperature came down to 97°F. on the second day and the membrane disappeared on the third day and the child was then perfectly all right.

Second attack:—When 20 months old, the child had fever of 104°F. with a little chill this time, running in the nose and sore eyes. Pulse was 130/mt. and the respiration was hurried. Injection Streptopenicillin plain was given daily for three days followed by injection Quinine Bi-hydrochloride 2·5 grs. with no effect. On the fourth day I found a membrane on the right tonsillar region making its headway towards the left. Dysphagia and dyspnœa were then marked. I was compelled to give Diphtheria antitoxin, 20,000 units on the first day followed by 10,000 units daily for two more days. The whole picture had now cleared.

Third attack:—This came on exactly six months after the second one. Thinking it to be a case of acute tonsillitis, antibiotics were given for the first three days, followed by injection of Terramycin 100 mg. daily for two more days but with no effect. A membrane appeared on the fifth day in a similar fashion; 20,000 units of Diphtheria antitoxin were immediately injected. This time there was not prompt response. Next day, 40,000 units were administered followed by 20,000 units for 2 days more. The throat became clear on the third day and

there was remarkable clinical improvement. Microscopic examination of a smear revealed B. diphtheriæ.

Discussion.—Here is the case of a normally healthy child fully immunized against diphtheria. In spite of this, he got the first attack six months after the last inoculation. Since then the child was getting regular recurrences every six months as narrated above. Other children in the same family were not affected at all. The disease responded only to Diphtheria antitoxin during all the attacks.

Is it likely that there is reservoir in a nest harbouring B. diphtheriæ in the tonsillar crypts of the child? Does the disease recrudesce when the child's resistance gets low, or does the virulence of the organism increase? This child has now been advised to undergo tonsillectomy after prior administration of Diphtheria antitoxin and antibiotics.

A reference was made to a leading manufacturing firm regarding the possibility of such recurrences of Diphtheria in an immunized child. The following quotations from leading Medical Journals were cited in reply. These will interest my readers.

Attacks of diphtheria after the use of the toxoid have been very rarely reported, but if the infection is severe or extremely virulent, production may fail. The disease runs a milder course in the inoculated.

This has been admirably discussed in a Medical memorandum reporting "Fatal diphtheria in the fully immunized child" (*British Medical Journal*, January 23, 1960, P. 251), which says:—

"The low incidence and mortality rate of diphtheria in the fully immunized community has been well described. There were 51 cases of diphtheria in England and Wales in 1956 (*Ministry of Health*, 1957), of which 40 occurred in nonimmunized patients. There were three deaths, one of which was that of an immunized child aged 2 years. *The Ministry of Health* (1956) recorded 10 deaths out of a total of 123 cases of diphtheria in children under 15. Five deaths out of 26 cases occurred in the 1–4 age group, four of which had never been immunized and the other child had had only one dose of the antigen."

Another quotation from the *Journal of the American Medical Association* of March 5, 1955 says:—

"It should be borne in mind that there is no disease against which absolute immunity can be achieved. This fact was sharply brought into focus with the report of an epidemic of smallpox among our Armed Forces in Korea. This experience showed that adequate exposure could break down resistance even after multiple vaccinations against smallpox. The potency of the vaccine and the methods of administration were also taken into consideration."

Acknowledgement.—I am thankful to Dr. D. H. Mehta, M.B., B.S., for the joint consultation during the first and the third attacks. My thanks are also due to Dr. M.V. Soneji, M.B., B.S., for his helpful guidance and kind help in tracing the bacilli in the stained smear. I am also thankful to Messrs. Glaxo Laboratories, Bombay for the above valuable information.

The Antiseptic

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Editorials

THE EIGHTH MADRAS STATE OPHTHALMIC CONFERENCE

(A Momentous Session)

INAUGURATING the Eighth Madras State Ophthalmic Conference at Vellore on the 16th of December 1960, Shri Dr. C. V. RAMAN, the eminent scientist and Nobel-Prize winner, said that the common endeavour on the part of scientists all over the world in the pursuit of truth and acquisition of knowledge had in its own way helped to emphasize the brotherhood of man. In the field of scientific research specialization had also its own uses and particularly in the field of ophthalmology, it could be of immense help. In his brilliant address, Dr. RAMAN dealt chiefly with his recent research in the field of "the perception of light and colour and the physiology of vision." He described in detail the functioning of the human eye with reference to the retina. For the human being there was nothing so precious as the organ of vision, which was fundamental. "The human eye can see and distinguish nearly 250 different colours in the spectrum and it can also perceive incredibly feeble light."

The picture that has emerged as a result of his recent researches in this field has brought about a new approach to the subject of vision and it could open up new possibilities for the ophthalmologists as well.

Sri Dr. Y. K. C. PANDIT of Bombay who presided over the Conference stressed the need for training the best ophthalmologists to meet the problem of eye diseases in the country. He said well-organized and planned camps under superior management with better results of scientific research would work out only a partial solution of the problem. A sectional improvement in the prevention of blindness might be noted with the genuine efforts our Government is making in the direction of self-sufficiency in food, water-supply and nutrition, but that will not solve the problem completely. Myopia amongst school-going children is on the increase. Besides this, Eales's disease, detachment of retina, and injuries to the eyes took a heavy toll amongst the younger generation.

"The approach to ophthalmic problems" said Dr. PANDIT, "should be a planned one. A fair solution would be to have a team of experts forming an Advisory Board comprising seniors and juniors. It would then be possible to co-ordinate schemes; it would also do away with the present practices of trimming, truncating and altering of schemes beyond recognition at various levels."

It is now more than six years that the Trachoma Control Project was launched under the joint auspices of the World Health Organization and the Indian Council of Medical Research. It no doubt involves considerable laborious field work for which organizational arrangements are necessary; but the public in general and ophthalmologists in particular, have yet no definite information of its achievements. Even the map showing the incidence of Trachoma is not yet complete. A study should therefore, be carried out in Trachoma-free zones of the country to assess the reason for the immunity, that the residents in those areas enjoy.

Dr. PANDIT also said the Government and philanthropists felt that the "eye-camps" were the answer to the problem of the blind, but he was sure that they were only adding man-made blindness to the existing population of the blind."

Sri Dr. T. M. KUMARASWAMI, Convenor of the Conference, also drew attention to the many deficiencies in the country's ophthalmological services. which have been with us for quite a long time; it may come as a revelation to many that India has the largest number of blind or near-blind persons in the world. Homes for the blind, such as exist in the State capitals, are no answer to this tremendous challenge which can be met only by a more intensive and extensive organization of preventive and curative measures. No other public health problem has perhaps been so sadly neglected, but the reason may well be that the resources of medical science in India have failed to measure up to the magnitude of the problem. There are no well-equipped research laboratories, and adequate attention is not being paid to elementary precautions such as proper scientific illumination of class rooms and of workshops and other institutions employing labour. These have all combined to condemn large numbers of people to perpetual darkness. In his very instructive address on the "*Role of Heredity in Ophthalmic Affections*", Dr. M. S. MEHKRI of Bangalore referred to the hundred and more common hereditary eye diseases and said "quite a big percentage of blindness in our country is of the avoidable type and to this category belong those who are blind due to hereditary diseases. There are no myope schools in India and the children affected with progressive myopia are compelled to attend schools meant for normal healthy children, read books

printed in types meant for normal eyes and use benches and desks meant for children with normal vision."

We are convinced that while the establishment of research institutes and the extension of curative treatment may be long-term measures, at least the contributory causes to eye diseases, such as ill-lit class-rooms and badly printed books, need to be tackled *immediately* if the threatened increase in total and partial blindness is to be arrested.

We think it would be proper in this context to refer also to the observations made by Dr. MEHKRI while presiding over the All India Ophthalmic Conference at Agra last year, stressing the urgency and importance of a proper All-India Survey of blindness in our country, and the desirability of instituting such a survey at the same time as the All-India-Census is being taken. As Dr. MEHKRI then said the census of 1961 affords a valuable opportunity to get this most useful and important information by merely including three or four simple queries, so that areas with a high incidence of blindness can be visited later by ophthalmologists and further studies made. By and large, these vital problems of eye diseases and blindness in India appear to require tackling along two important lines *viz.*, to prevent people from being exploited by quacks, and to induce them to seek expert advice in the early stages of visual trouble. Also it is essential that all general practitioners are made to undergo a refresher course in the subject and that ample facilities are provided for the specialists to keep themselves abreast of the results of the progressive researches made abroad from time to time. The establishment of proper eye clinics under qualified medical supervision in villages, where trachoma and cataract claim a heavy forfeit, is also an urgent requirement.

PÆDIATRIC PROBLEMS OF INDIA

ADDRESSING a meeting of national and international experts who met at Delhi on 6-1-1961, under the auspices of the Medical Forum set by the Union Ministry of Health, Sri Dr. S.T. ACHAR, Director of the Pædiatrics Institute at Madras, and a well-known authority on pædiatrics in India, stressed the need for consolidating and improving under-graduate teaching in pædiatrics with sufficient staff for it in all the medical colleges, in order to provide for basic health services for the children, both well and ill. In his lucid historical survey of the development of pædiatrics in the world particularly during the past few decades, he pointed out that generally in the well-developed countries during the last 100 years there were *three* major phases of development:—(1) founding of children's curative services;

dispensaries, and hospital beds; (2) establishment of infant and pre-school welfare clinics; and (3) the development of academic pædiatrics with departments of child-health in the universities, interlinking the curative and preventive aspects with research organizations in the larger hospitals." These three phases had followed each other in a chronological sequence in countries like the U.S.A., England, the European countries, and also in the young continent of Australia during the last 150 years, along with the development of economic prosperity, material wealth and the various sciences. Russia compressed these three stages into a simultaneous phase in a much shorter span following the political, economic and industrial awakening. China was attempting to do likewise. "In India modern concepts underlining the fact that the child-patient was a separate entity and not a small-scale adult patient, reinforced the appreciation of the need for stepping up of the teaching of pædiatrics to the under-graduates by opening pædiatric departments in the medical colleges manned by pædiatricians, as well as a rapid expansion in numbers and equipment of the maternity and child-health centres in India." The useful role of the primary health-centres, which are being established all over the country in looking after the health of the children who form nearly 40 per cent of the population in India, is being recognized gradually. During recent years pædiatric wings are being opened in Indian hospitals. Only half of the medical colleges are said to have pædiatric departments. Even granting that all of them start such wings and give instruction in pædiatrics, as part of the medical degree course, the availability of trained personnel in the rural areas, where the majority of the children are growing up, is extremely doubtful.

If it is the case, as pointed out by Dr. Achar, that the pre-school children constitute the most vulnerable group, it is necessary to establish a large number of pre-school welfare clinics particularly in rural areas, as has been done in the West. This may not however, be practicable in India for some time to come, but we think that primary health-centres now being set up in the community development areas can be utilized for the purpose, if only trained personnel can be found to man them.

The improvement of under-graduate teaching in pædiatrics is of the greatest importance, if basic health-services for children are to be rendered whether as general practitioners, maternity health officers or medical officers in hospitals. Pædiatric specialists with post-graduate training and experience will alone be able to serve as teachers, to train such personnel.

The present situation in India with its 100 million child population and with a high incidence of various children's diseases, like diarrhœa, diphtheria, whooping cough, typhoid,

and tuberculosis, certainly warrants a consolidation of the resources in this matter of providing adequate personnel.

Dealing with the research on pædiatric problems which is necessary for improving child-welfare in India, Dr. Achar dwelt on various base-line researches on pædiatric problems like nutrition, weight studies etc., which have been in progress over the past two decades in India, and urged that we should learn from the experience of the more developed countries by applying their scientific approach and know-how to the solution of our problems here in India. We are glad to note however, that he warned against launching on a project of blindly copying some of their modern movements, like "the investigation of metabolic disorders or congenital malformations or psycho-therapeutics etc., which developments in these countries stemmed from an almost achieved conquest of the communicable diseases and malnutrition there." These latter conditions claim priority here in India. In the highly developed countries of the world notably in the United Kingdom their improved pædiatric service has greatly reduced infant mortality dramatically and has also led to a remarkable improvement in the health and general physique of their children and adolescents. We gather from the reports of the School Medical Officers in Great Britain, their school children of today are healthier, taller and generally of better physique than the children of 10 or 20 years ago. This may be directly attributed to the recognition by the State that special medical care, both preventive and curative, is essential to the welfare of growing children and to the establishment of a competent School Health Service to provide that care effectively. Milk at the rate of one-third of a pint is given *free* to all children who wish to have it and a School Meals Service provides a daily dinner planned on a high nutritional standard at a subsidized price to nearly half the pupils in schools run by local education authorities.

The recently introduced Mid-day Meals Scheme in this State is no doubt a useful though small beginning in this direction, but on the medical front, the facilities available are negligible, in relation to the need. Thus, we are yet to have anything like an organized and efficiently functioning system of school medical inspection, correction of defects and a compulsory programme of follow-up for children from 5 to 15 years of age. The medical care and follow-up of the young is in fact a science in its own right and so deserves to be given top priority in the Third Five Year Plan.

JOINT CONFERENCE OF THE ALL INDIA ASSOCIATIONS OF PHYSICIANS AT MADRAS, 1961

THE Annual Joint Conference of the All India Associations of Physicians belonging to the several disciplines of Medical Science was inaugurated by Sri BISHNURAM MEDHI, Governor of Madras, at the Rajaji Hall, Madras, on the 13th of January 1961. About 300 delegates from all over India attended the Conference and among them were also Prof. I. G. W. HILL from Scotland and Dr. HARRY PENNS of the Delhi Chest Institute. It was a Conference of the Association of the Physicians of India, the Cardiological Society of India, the Neurological Society of India, the Indian Association for Chest Diseases, the Indian Society of Hæmatology, and the Indian Society of Gastroenterology. These societies held business meetings and scientific sessions, independently and jointly, on the 14th, 15th and 16th January 1961. Several interesting and instructive papers relating to the respective specialities were presented and symposia also held, in which many of the delegates took part.

Shri Dr. RATNAVELU SUBRAHMANIAM's address as Chairman of the Reception Committee was very illuminating and thought-provoking, as it forcibly brought out certain pressing problems of the day in proper perspective and at the same time contained very useful and practical suggestions to solve them. Thus, in regard to the most urgent problem of the lack of medical personnel in the country to meet which the Central and State Governments have been adopting and contemplating various measures, *e.g.*, the opening of new medical colleges, Dr. SUBRAHMANIAM very rightly pointed out that the teaching staff for these colleges are drawn from the retired personnel of the neighbouring States—people with ripe teaching and research experience, and that the criticisms levelled against the employing of retired men are improper and unjust for they were doing excellent work, which he (Dr. SUBRAHMANIAM) could vouch for, from personal knowledge. The time of these retired men who are still physically fit and mentally quite alert, is being usefully spent and their talent and rich experience are being wisely utilized. It would be a pity that such excellent material should be allowed to lie dorment or go to waste without being utilized for producing more, younger and capable medical men to supply the want. Dr. SUBRAHMANIAM's suggestion to this end, and at the same time to obviate interested criticisms against retired men being re-employed, is that it should be made a universal rule that the age of retirement, should be 60 and not 55, as the younger men could not then complain of their prospects being blocked for they too can certainly look forward to a longer lease of official career.

To-day we find that our country is being ruled wisely and well by statesmen, ninety per cent of whom are past 60 and

some nearer 70 than sixty. Surely State-administration is a much harder and more strenuous task than teaching or doctoring.

"The opening up of more medical colleges is not a real solution," said Dr. SUBRAHMANIAM, "when more medical graduates are urgently required by the country. Going through the results of many medical colleges, one is surprised that only 10 to 20% of students pass through the entire course without a failure." He attributed this to the disproportion in the ratio between the teacher and the taught, as compared with the western institutions. Efficient checks on the attendance and day to day progress of the students are very essential to ensure systematic and regular studies and application among the students. Coming from a teacher of medicine of nearly 20 years' standing, this aspect of the medical student's career is entitled to serious consideration, particularly because he is all in favour of conducting a series of periodical tests and clinical examinations, and we believe, with penalties for non-attendance and poor performances.

Apart from the above reason adduced by Dr. SUBRAHMANIAM for the numerous failures, we have a shrewd feeling that admissions to the medical course should be made by stricter and more rational methods than obtain at present. This matter has recently been discussed frequently at various levels and the concensus of informed opinion would appear to be that instead of a strict adherence to definite principles based on merit and aptitude, other considerations, which in effect run counter to the desirable modes of selection, come into play with the result that during recent years, students who cannot cope with the arduous medical studies enter the college and are unable to leave it with the degree in anything under six or seven or even 8 years. "To-day," Dr. SUBRAHMANIAM said, "50% of the examiners are drawn from outside the Home University and there is therefore, no scope for any teacher to exercise any favouritism."

We agree that it is false economy to have more medical colleges with a higher percentage of failures which, in turn, is a national waste apart from the loss of money and time to the parents and students.

Dr. SUBRAHMANIAM then referred to the appeal that is being made by persons at the top-most and also at lower levels that medical men should willingly go to the villages; he said that it was not found to be a feasible proposition to have a doctor for every village, even in U.S.A. and other western countries and it must therefore, be still more difficult in the under-developed countries of the world. According to him the correct solution will be to have a group of 5 or 6 doctors at the taluk level,

supply them with a field ambulance and ask them to go round the villages twice or thrice a week. The conditions of service and scales of remuneration will have to be very greatly improved and they should be provided with adequate modern equipment, medical stores and ancillary staff, if any real good work is to be turned out. Education facilities for their children must be guaranteed in adjoining taluk centres, and any extra cost involved in so doing must be met at State level.

In his inaugural address Sri BISHNURAM MEDHI, Governor of Madras, expressed the hope that the conference would find out ways and means of effectively co-operating with the Government in the execution of various schemes adumbrated in the successive Five-Year Plans to give medical relief and provide amenities for public health in rural areas.

Sri Dr. A. LAKSHMANASWAMI MUDALIAR, Vice-Chancellor of the Madras University, in his very lucid and eloquent presidential address to the conference said it was his conviction that ere long "India should be in a position to have all the facilities necessary for any branch of medicine to progress. While for mere post-graduate education one should not go to other countries, there is a stage when post-graduates and others *must* visit the countries where highly specialized work is being conducted." We quite agree that there should be in every State at least one highly specialized institution to foster research and post-graduate education.

The modern armamentarium available to the medical profession was such that side by side with the treatment that might be given by the general practitioner, he should have the opportunity of referring his cases to the specialists concerned. Dr. LAKSHMANASWAMI MUDALIAR struck a note of warning against the modern tendency to greater and greater specialization in narrower fields of practice. Narrow specialization might overlook the fundamentals of the general concept of the patient as a whole; while adequate opportunities should be given to those who were competent to take to post-graduate studies, a certain number of years of study was absolutely essential before the person concerned was given the status of a specialist in the particular subject.

Dr. LAKSHMANASWAMI MUDALIAR said in conclusion that too often the opinion of the medical profession was ignored because it was supposed to be tainted with self-interest and other unfortunate trends. The members of the medical profession have no ideologies except service to humanity. That noble aspiration of the medical profession shall be handed down from generation to generation, so that it might be said that among the many professions that must necessarily be practised, medicine would continue to be the noblest of them all.

The Conference held separate sittings to receive and discuss the papers presented on various subjects of interest and we are glad that this Conference of the joint association of the different societies that met at Madras, had its beginnings here 13 years ago under the distinguished presidency of the late lamented Dr. M. R. GURUSWAMY MUDALIAR, to whose foresight the present combined deliberations of different societies, are largely due.

We offer our heartiest good wishes for the continued success of the joint conferences of these societies of India's talented men in the years to come.

Special Feature

NEWS-LETTER FROM THE UNITED STATES

ALTHOUGH there appears to be no end to undiscovered frontiers in medicine, we are fortunate to be living in an age when many major problems have been solved. A pleasant result of this is that we are able to devote more time to the finer details of medical care and patient comfort. *A new adhesive tape is proving successful for closing wounds in place of stitches*, according to T. Golden and co-workers reporting at the 14th Clinical Meeting of the American Medical Association in Washington, D. C. The new tape was used successfully on 300 patients during the past 18 months for closing all sorts of wounds and incisions in every location of the body. The wounds healed completely and without complications, and the functional and cosmetic results were good. Although previous attempts had been made to develop such an adhesive tape, there was always a drawback, such as irritative complications and slipping or creeping. This new tape has shown a high degree of adhesions and no skin irritation. Its use should simplify post-operative management and reduce the number of complications from wound healing.

Prolonged daily anticonvulsant therapy of children with one epileptic seizure was considered effective and safe not only for preventing a second seizure, but also for preventing the fear of another seizure. Children with simple febrile convulsions are not considered suitable for this type of therapy. S. Livingston reporting in the September 10 issue of the *Journal of the American Medical Association* (*174*: 135, 1960) points out that the longer a patient has had convulsions, the harder it is to control them. Therefore, he has been *administering Dilantin in full dosage to any child with one true epileptic seizure*. Treatment is continued for at least four years, at which time the dosage schedule is gradually reduced and finally discontinued over a period of one or two years. The author has seen no addiction to anticonvulsant medication in children, and feels that this therapeutic approach has a valid place in the management of epilepsy.

A simplified method of replacing fluids in burn victims has been reported by J. F. Eagle and co-workers in the November 19 issue of the *Journal of the American Medical Association* (*174*: 1589, 1960). A single formula replaces water, protein, and electrolytes when administered intravenously during the first 48 hours after the burn has occurred. Use of this new formula on 28 patients with burns covering 15 per cent or more of the body shows that the formula does not influence over-all mortality rates, but does seem to reduce the number of deaths during the first 48 hours. The main advantage is simplicity of administration, a particularly valuable asset in the event of disasters when inexperinced personnel sometimes must be used. The only factor that

needs adjustment to suit a particular patient is the rate of administration, which depends on the size of the patient and the extent of the burn.

A new sympathomimetic bronchodilator, Caytine, has proved useful for treating bronchial asthma and emphysema in adults. D. B. Frankel reports in the September issue of *Clinical Medicine* (*7*: 1793, 1960) on results of a modified double-blind study using the drug prophylactically in children. Four groups of children were studied, ranging in age from 4 to 18 years. The first group was given Caytine three or four times daily as a prophylaxis against asthmatic attacks. The second group was given placebos under the same circumstances. The third group received Caytine at the beginning of an attack to abort a full-blown episode, and the fourth group was given placebos under the same conditions as the third group. Results of the study indicate that *Caytine is an effective drug for preventing asthmatic attacks as well as for controlling acute asthmatic distress.* There was a marked difference between the control groups and those receiving the drug. The author concludes that Caytine is a valuable addition to the armamentarium of physicians treating patients with allergies, and that if side effects occur, they are mild and few in number.

A new method of rehabilitating a clubfoot that has been surgically corrected was described by M. B. Furlong and G. W. Lawn at the 14th Clinical Meeting of the American Medical Association in Washington, D.C. The new method involves the use of an open cast following surgery. This cast permits the foot to be moved by reflex stimulation. With this technique an infant is forced to exercise his leg and foot muscles 100 to 200 times per day. This treatment is carried out for nine months and the result is that leg muscles develop with normal strength and balance. Dr. Furlong believes that this type of exercise produces little or no tendency for the clubfoot to recur, a problem believed to be the result of a muscular imbalance which invariably accompanies the anatomical deformity.

In patients who have had subtotal gastrectomy, fat absorption may be a problem. This is thought to be caused by increased cholinesterase activity of the pancreas which, in turn, causes inadequate secretion of pancreatic juice into the intestine. According to a report in the November 22 issue of the *University of California Clip Sheet* (*36*: 1, 1960), the consumption of dry white wine more than doubles the absorption of fat in these patients. Studies are now being conducted to see whether the addition of moderate amounts of wine to the diet of these patients might improve their long-term nutrition.

SECONDARY CHRONIC RHEUMATOID ARTHRITIS

In contrast to Anglo-American usage, which recognizes only two sharply defined conditions, rheumatic fever and rheumatoid arthritis, German-speaking doctors often refer to secondary chronic polyarthritis as a distinct disease. Strictly this includes only those cases which have developed from rheumatic fever, an occurrence that is extremely rare (about 3·5%). Many of these cases represent, in fact, either the healing stage or imperfect resolution of an attenuated form of rheumatic fever (usually uncomplicated by cardiac lesions) or a subacute form of rheumatoid arthritis. The value of serological methods in doubtful cases is pointed out and illustrated by case-histories. The antistreptolysin titre is a measure of rheumatic fever, while the Rose-Waaler-test, the latex fixation and the rapid latex fixation tests are pointers to rheumatoid arthritis. Even though the occurrence of atypical forms prevents rigid classifications it would be best to drop the term "secondary chronic polyarthritis" altogether or at the most reserve it for exceptional cases.—(*Med. Klin., 54:* (1959), 625, via *Germ. Med. Monthly*, July, 1960.

GLEANINGS FROM THE MEDICAL PRESS

MEDICINE & THERAPEUTICS

The use of cortisone in the treatment of typhoid fever.—(*J. Egypt. Med. Assoc.*, *43* : 5, 1960).

Gamal Nor-el-Din and Wagih Yasseen of the Abbassiah Fever Hospital, have used cortisone and hydrocortisone in the treatment of typhoid fever since 1954. The number of cases in which these drugs were used exceeded 300 of whom 50 cases were put under strict personal observation. Cortisone and hydrocortisone were the drugs mainly used but later prednisone and prednisolone were used in some cases.

Cortisone was limited only to severe cases of typhoid which showed marked toxæmia, such as apathy, convulsions, vasomotor cardiac failure. All cases with positive blood culture were selected to ensure diagnosis. In all these cases the toxæmia was rapidly aborted, a marked drop of temperature occurred within 24 to 48 hours in most of them. The patients felt general improvement, regained their appetite and great amelioration of their symptoms occurred. Some cases who were so moribund and hopeless showed striking and impressive improvement. Chloramphenicol was given in every case with cortisone in the usual course for 7 to 10 days. Cortisone was also given to some patients who showed those toxic symptoms from the start of the disease or when those symptoms appeared later in its course. Cortisone was also given when a large dose of chloramphenicol such as 150 mg. per kg. body weight daily had to be administered in order to avoid a possible harmful effect resulting from such a dose. Actually the old fashioned method of giving a big initial loading dose of 3 g. of chloramphenicol is now abandoned due to its danger. However we noticed that some patients were allergic or sensitive to chloramphenicol even when given in ordinary doses of 30 to 50 mg. per kg. body weight daily. They may develop marked vasomotor shock, marked fall of blood-pressure and other signs and symptoms of peripheral circulatory failure. Previous administration of cortisone was found by us to save the patient the harmful and not uncommonly fatal manifestations.

Another group of mild cases of typhoid failed to respond to chloramphenicol given in the routine doses which we follow. In this group cortisone addition to the treatment had in several patients cut the course of the disease and saved the patient from the risk of exhaustion due to the long illness and its complications.

The doses of cortisone for adults were 200 to 300 mg. daily given for a period of 2 days. On the third day half this dose was given, and the drug continued in the same dose in the fourth day. In some cases we noticed that the response to the drug was dramatic; the temperature fell down to 36°C or less within a few hours, usually "12 hours" after the start of cortisone In these cases the drug should be continued with smaller doses which did not exceed a daily dose of 100 mg. or less according to the degree of response.

In most cases the temperature fell by crisis within 24 hours and never rose again. In some cases it came down gradually in 2 to 3 days but continued in subfebrile level for a few more days. In some cases the toxæmia was markedly abated while the temperature might continue in the usual course. In these cases the value of cortisone is only manifested on the general toxæmic symptoms.

Cortisone administration is not without danger. Its administration is not advisable in the third week of the disease or late second week, because it may mask the signs and symptoms of peritonitis after intestinal perforation which usually occurs in the third week. It may enhance

the spread of peritonitis and may lead to the aggravation of the condition of the patient. Cortisone is supposed to enhance the formation of peptic ulcers and this may delay the healing of the already formed intestinal ulcers. Cortisone inhibits the formation of fibroblasts and delays the production of granulation tissue. A number of cases of peritonitis treated with combined chemotherapy and cortisone showed a rapid disappearance of toxicity and marked improvement of the symptoms.

The beneficial action of cortisone in cases of typhoid has not been adequately explained, We suggest that its action is due to the fact that it may enhance the activity of the reticulo-endothelial system which forms part of the defensive mechanism of the body against infection.

The use of butazolidine in the treatment of typhoid fever was also tried by us in a series of 10 cases. The dose recommended was 2 gm. daily given as 0·5 g. every six hours; chloramphenicol was used as in the usual routine. Results similar to cortisone but rather inferior were obtained by us. The use of butazolidine came to our mind because it was assumed that its value in rheumatic conditions was due to the fact that it liberates cortisone-like substances in the body. After publishing this observation in the annual report of Abbassia Fever Hospital of 1955, a few articles were published by other authors stating the value of this drug. The use of this drug should however, be carefully controlled as it may affect the bone-marrow in an adverse way and may lead to leucopænia especially in toxic patients.

Hæmorrhagic varicella pneumonia.—(*Ann. Int. Med.*, September, 1960).

It is not generally appreciated that chickenpox, usually a benign disease in adults, may run a very severe course, or may be fatal. In recent years, papers have been published in radiologic journals describing the appearance of varicella pneumonitis in severe cases of chickenpox in adults. Other papers and communications have indicated the adrenal steroid therapy may be deleterious in varicella pneumonitis. A case is presented by Drs. Esswein and DiDomenico, M.D., of Portsmouth, New Hampshire to (1) document further the small number of cases of hæmorrhagic pneumonitis due to varicella; (2) report the apparent improvement with cortisone therapy; and (3) emphasize the radiologic appearance of varicella pneumonitis.

Review of the literature indicates that the first implication of the varicella virus in the ætiology of pneumonitis was by Waring *et al* in 1942. In 1956 Southard reviewed the severe cases of varicella pneumonia and presented a synthetic "typical severe adult case." The case herein presented appears to be more severe than her "typical case" because of marked cyanosis and hæmoptysis. In addition, there was probably gastrointestinal bleeding, as evidenced by the severe abdominal pain, tenderness and black stools which were guaiac-positive. However, it is possible that the patient swallowed some of the hæmorrhagic sputum.

Treatment with cortisone in the present case was followed by prompt remission; however, it is not known whether this was coincidental or whether the corticosteroid played a role in the rapid improvement.

Because the patient appeared to be *in extremis*, it was felt that the use of corticosteroid was indicated. As may be noted in the case report, the signs and symptoms cleared rapidly within the course of 12 hours after the initiation of this therapy. This would appear to us to be in contrast to the course in the five cases reported by Southard, which showed clearing of symptoms by lysis despite all therapy. It is suggested that the hæmorrhagic lesions in the lungs, skin and gastrointestinal tract may well represent generalized vasculitis, or an immunovascular phenomenon secondary to varicella infection and the improvement noted may have been entirely coincidental.

The oxyhæmoglobin dissociation curve in anæmia.—(*Ann. Internal Med.*, February, 1960).

The primary function of hæmoglobin is the transport of oxygen from the lungs to the tissues. Anæmia compromises this transport mechanism and exposes the tissues to the dangers of hypoxia. The fact that patients with slowly developing anæmia are frequently symptom-free with low levels of circulating hæmoglobin strongly suggests that efficient compensatory mechanisms are available to provide an adequate supply of oxygen to the tissues. There are two generally recognized compensatory mechanisms: a reduced tissue oxygen tension, which results in more nearly complete extraction of oxygen from the blood, and an increased cardiac output.

The affinity of hæmoglobin for oxygen has been studied in 23 anæmic patients with normal, adult-type hæmoglobin. The *in vivo* oxyhæmoglobin dissociation curve of each patient was out-lined by determining the oxygen tension, oxygen saturation and *p*H of blood while the patient breathed different concentrations of oxygen.

A reduction in the affinity of hæmoglobin for oxygen in the form of a rightward displacement of the dissociation-curve was demonstrated in patients with hæmoglobin levels below 9 g. per 100 ml. The displacement was moderate in patients with hæmoglobin levels between 6·5 and 9·0 g. per 100 ml., and more marked in those with less than 6·5 g. per 100 ml. The dissociation-curve had shifted back toward its normal position in those patients with severe anæmia who were restudied after their hæmoglobin content had been raised. The reduced affinity for oxygen in patients with hæmoglobinopathies appeared to be a property of the abnormal hæmoglobin, and did not seem to be related to the severity of the anæmia.

Magnesium deficiency.–(*Editorial, Ann. Int. Med.*, September, 1960).

Magnesium deficiency arising spontaneously in cattle has been well known for three decades. It has repeatedly been produced experimentally and studied extensively in animals, particularly in rats. In man, however, it has been infrequently recognized, and until recently its manifestations as distinguished from those of other associated deficiencies had not been clearly established.

Magnesium is widely distributed in food, in both plants and animals, and almost any human diet amply supplies the need under ordinary circumstances. A greatly increased requirement, however, or progressive depletion in conjunction with an inadequate intake may cause outspoken symptoms of deficiency.

Magnesium is widely distributed in the body, the total quantity, a little over 20 grammes in an average subject, being exceeded only by that of the electrolytes, sodium, potassium and calcium. A little over half of the magnesium is in bone, and of the balance, according to Shohl, about 9·5 g. are within the cells and 0·5 g. in the extracellular fluids, including the blood-plasma. Next to potassium, magnesium is the most abundant intracellular electrolyte, and it is essential for the activity of many intracellular enzymes of vital importance.

During the past decade more adequate studies have been made and the manifestations of magnesium deficiency more clearly defined, although the earlier clinical descriptions have been largely confirmed. Initial symptoms are often nervousness and agitation, ataxia, tremor and muscular twitching which may progress to choreiform or more rarely athetoid movements. There may be facial or carpopedal spasm with positive Chvostek and Trousseau signs, like the tetany of hypocalcæmia, which indeed may coexist. It is distinguishable by a normal blood calcium level and by the fact that calcium given intravenously does not check the disturbance and may aggravate it. With this, mental disturbances are usual—delirium, confusion, hal-

lucinations, sometimes with great excitement and violent behaviour, followed later by stupor and coma in the severest cases, particularly in cirrhotics, with generalized convulsions which may be fatal if neglected. There may be a state of hyperexcitability in which convulsions can be precipitated by trivial external stimuli such as a loud hissing sound.

These disturbances can usually be controlled by the timely administration of magnesium sulphate parenterally, usually given intramuscularly in 50% solution, 1 to 2 grammes four times a day for several days. The effect is not immediate, however, even if given intravenously. There is usually an interval of at least several hours and sometimes two to four days before the disturbances are substantially relieved. This supports the view that the significant trouble is intracellular, probably a need for more intracellular magnesium even though no definite deficiency within the cells has been demonstrated. It has also been suggested that a disturbance of the ratio of the intracellular to extracellular concentration of magnesium is at fault. Even after magnesium is immediately available, some little time is evidently required to make the necessary readjustments.

Magnesium, unlike calcium, is readily absorbed from the digestive tract without the assistance of any hormone, and oral administration would usually suffice. Other deficiencies should not be neglected, but the administration of large amounts of potassium or calcium to relieve deficiencies of these electrolytes is likely to aggravate symptoms of magnesium deficiency if the latter is neglected. In case of vomiting or in patients receiving large amounts of fluid parenterally, many such crises could probably be avoided by adding magnesium to the usual infusions or by administering it intramuscularly.

The treatment of virus diseases.—(*The Practitioner*, October, 1960).

Lymphogranuloma venereum:—Although sulphonamides are known to exert a beneficial effect on the course of lymphogranuloma venereum, antibiotics are more effective. Wright and his co-workers (1948) were among the first to demonstrate the high degree of therapeutic activity of chlortetracycline in this disease. Other studies have confirmed these observations. Chloramphenicol has also been shown to be useful. Erythromycin has been found to produce good results but is not as active as chlortetracycline, oxytetracycline, or chloramphenicol. Most recently, it has been suggested that triacetyloleandomycin has a place in the therapy of lymphogranuloma venereum. This recommendation is based on only one report, however, and requires confirmation, in attempting to develop the most effective therapy for the acute and chronic stages of this disease. Loughlin and his colleagues (1958-59) gave patients chloramphenicol and human gamma globulin together. They noted that the administration of 2 to 10 ml. of globulin plus 1 g. of the antibiotic per day produced better clinical results than chloramphenicol alone or, for that matter, an antimicrobial agent given singly, in the control of the advanced secondary or tertiary lesions of lymphogranuloma venereum. They also remarked on the fact that considerably shorter courses of therapy, using smaller quantities of the antimicrobial compound, were possible when it was given together with gamma globulin. The data available at the moment indicate that the tetracycline compounds are effective in the treatment of lymphogranuloma venereum and probably represent the first choice in therapy.

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OBSTETRICS & GYNÆCOLOGY

Cancer of breast in pregnancy.—(Michael J. Jordan, M.D., *J.A.M.A.*, 1-10-1960).

The treatment of carcinoma of the breast discovered during the third trimester of pregnancy should not vary from the treatment of carcinoma of the breast discovered at any other time. The curative treatment of carcinoma of the breast is local radical attack on the primary tumour and its regional lymph-node spread. Success depends on complete removal of the cancer and of its local spread before general metastases have become established.

In the average operable group, about one-half of the patients show metastasis in the axillary lymph nodes and one-fourth in the internal mammary nodes. The internal mammary nodes are involved more frequently when the primary lesion occurs in the medial, or more central, portion of the breast. In 1951, Urban at the Memorial Centre for Cancer and Allied Diseases, devised an original and more complete operation—radical mastectomy with internal mammary chain resection, in order to remove the primary breast cancer together with its primary lymph-node depots, namely, the axillary as well as internal mammary nodes.

Supplemental X-ray therapy after radical mastectomy and lymph-node dissection should be given on an individual basis, depending on the presence or absence of positive findings in the lymph nodes. As far as the management of the pregnancy is concerned, I believe that, if the size of the baby and the condition of the cervix permit it, induction should be performed any time after the 36th week of gestation.

Variations in malignancy of cancers of uterine cervix.—(*J. Obst. and Gynaec., Br. Emp.*, June, 1960).

Any series of cancers of the uterine cervix represents a complex of tumours of widely different behaviour patterns as regards rate of growth, invasiveness, and disseminating properties, and this variation in behaviour is emphasized when the cases are grouped on the basis of duration of symptoms. All 924 cases of cancer of the uterine cervix observed at the Cardiff Royal infirmary during the years 1940-1954 are classified into 4 groups according to the reported length of time elapsing from the patient's noticing the first symptom to the day treatment was begun. A modified Stockholm technique of radium irradiation was used in 894 (or 97%) of the women, and in 38 of these surgery was used as an adjunctive procedure. Roentgen irradiation was not used as a primary form of treatment. In 30 patients the disease was so extensive that treatment was deemed inadvisable. Survival after radium therapy was not significantly affected by the age of the individual or by the histological grade of the tumour. The outlook was determined almost exclusively by 2 factors: the rate of tumour-growth and the extent of the disease when first seen. Therapy achieved its best results in the cancers which grew relatively slowly. These more favourable tumours did not present any distinctive pathology and the results of this investigation are consistent with the view that the slow-growing cancers are seen in women who possess a high degree of natural resistance to the disease.

Acute leukæmia and pregnancy.—(*Ann. Int. Med.*, October, 1960).

During the last five years, Frenkel and Meyers of Ann Arbor, Michigan, have encountered eight pregnant women with acute leukæmia. With the rising incidence of acute leukæmia, and the potentiality of prolonging life with the antileukæmic agents, the problem can be expected to assume increasing importance. The cases reported emphasize the incidence and complexity of the problem, and offer a rationale for management.

The effect of pregnancy on the survival and longevity of leukæmic patients has been controversial. Some authors feel that pregnancy has a definitely deleterious effect and shortens life-expectancy. That this concept is still current in some quarters is evidenced by Miasnikov's recent article in the Russian literature reporting three cases of leukæmia and pregnancy, two chronic and the third a case of acute chloroma, in which he felt pregnancy aggravated the leukæmia. The survival time of his patients was short, but it should be noted that none

received specific antileukæmic therapy. *His conclusion is: that "termindtion of pregnancy is indicated in leukaemia at as early a stage as possible." The more common current feeling*, and one to which we subscribe, *is that pregnancy exerts no specific effect per se* on the course of the acute leukæmia, except in so far as early gestation imposes an obstacle to vigorous treatment of the leukæmia. Birge *et al* in 1949 described a case of acute leukæmia where a spontaneous remission of 21 months' duration occurred, with the onset of the remission during pregnancy. However, increased fœtal mortality and abnormality in acute leukæmia are well recognized.

With the advent of specific antileukæmic therapy the treatment of pregnant leukæmia patients has undergone many changes. The management of such patients can be divided into *two facets*. The *first*, and generally simplest, is that of the obstetric care. This should be in the nature of the good obstetric principles applicable to any pregnancy. Since evidence is lacking that pregnancy has a deleterious effect on acute leukæmia, and since, as Allen has noted, the stress of interruption of the pregnancy can be just as great as the stress of parturition, no indication exists for the interruption of the pregnancy. However, the obstetrician must be alert to the possible need for emergency cæsarean section in these patients in the event of rapid deterioration or death prior to delivery.

Effective management of the leukæmia requires the close co-operation of the patient and frequent follow-up by the physician. Routine supportive measures, such as blood and antibiotics, should be employed as needed. The question of specific antileukæmic therapy is perhaps somewhat more controversial. Dameshek states that "one's therapeutic efforts should be limited to relatively gentle procedures, such as the use of transfusions, the administration of relatively small doses of prednisone (we have used 20 to 50 mg. daily), antibiotics, and other symptomatic care. Other authors express similar sentiments. It is our observation, however, that specific antileukæmic therapy is beneficial and can be initiated safely after the first trimester of gestation.

Reversible refractory anæmia in pregnancy.—(*J.A.M.A.*, October 1, 1960).

The purpose of this report by Kyser and Danforth of Evanston, Illinois is to present a case of primary refractory anæmia occurring during pregnancy, in which the hæmatological findings returned to normal after delivery. The pregnancy was allowed to go almost to term, with the survival of both mother and child.

Primary refractory anæmia (aplastic anæmia) is rare in pregnancy, and the diagnosis is difficult. Only 17 previous cases have been reported, and only six patients survived. In the present case the patient, a 26-year-old primigravida, was found in the course of an office examination to be anæmic, and subsequent examinations showed that the anæmia had become more severe despite ordinary antianæmic treatment. After transfusions of whole blood and of platelets and a trial of induced labour, a healthy 3,300 gm. baby was delivered by cæsarean section. The post-operative course of the mother was uneventful, and her hæmogram returned gradually to normal. The authors believe that therapeutic abortion is *not* indicated in this condition if facilities for dealing with the anæmia and with possible complications are adequate.

"Anti-vitamin" suspect in causing congenital malformation and death in infant.—(*N.Y.S.J. Med.*, 15-6-1960).

A dramatic case has been reported in which a pregnant woman's consumption of an "anti-vitamin" seems to have caused the malformation and quick death of the child she bore months later.

As summarized in *Nutrition Reviews*, a twenty-seven-year-old mother with six living and normal children succeeded in buying a supply of a potent vitamin B "antagonist," aminopterin, from her druggist. The powerful drug has been used experimentally to kill

t fœtuses and, with humans, has metimes been administered to in- uce therapeutic abortions.

Beginning the self-prescribed regi- en at about the beginning of the ird month of pregnancy, the woman as soon thereafter quite sick, "show- g symptoms compatible with minopterin poisoning." Treated at e hospital with vitamin B and liver xtract, she recovered and, months ter, went on to a full-term delivery. Weighing less than 3 pounds, her hild was seriously malformed and nly survived twenty-nine hours. In vestigating the case, medical resear- hers found no evidence of birth ab- ormalities in either of the parents' milies. They also noted that the alformations of the short-lived child howed a very close physical corres- ondence to a typical nine-week mbryo—thus recalling the time when e mother began to dose herself with e "anti-vitamin."

The case, according to *Nutrition eviews*, indicates that a nutritional insult" to an unborn baby, if of appropriate intensity and timing, ay be followed by the development f congenital anomalies." The young oman's tragedy also makes clear the portance of consulting a physi- ian before embarking upon any rastic nutritional regimen, whether evere reducing diets or risky addi- ives.

pilt milk mastitis.–(*The Medical Jour- al of Australia*, 8-10-1960).

The breast condition discussed in his paper is most commonly known s plasma cell mastitis (Ewing) or ammary duct ectasia (Haagensen). imilar (or closely allied) lesions have een described in the literature, under wide variety of names. Of the ames offering, we believe that spilt ilk mastitis comes closest to descri- ing both the clinical and pathologi- al picture in most cases. The dis- ase occurs in women, usually middle- ged and parous, who may suffer a eeting inflammation of one breast. ooner or later a lump appears, which imics cancer so closely that needless radical operation may be performed.

1. Three parous women, not pregnant or lactating, presented with lesions near the nipple. Two had lumps, one had inflammation with an area of induration.

2. At operation, all the patients had lesions characterized by dilated ducts containing secretion.

3. Pathological examination showed that the dilated ducts contained amorphous and crystalline fatty material. In two of the lesions there was notable inflammatory fibrosis. Evidence of escape of duct contents into the tissues was found.

4. These lesions represent three stages of a disease process which is due to accumulation of secretion in the ducts with subsequeut escape.

5. In any stage the clinical and gross appearance may simulate some form of carcinoma.

6. A clinical diagnosis should be attempted and confirmed at biopsy.

7. Excision of lesional tissue is advised.

8. The name spilt milk mastitis is preferred.

Treatment of metrorrhagia by infusion of black coffee.—(*London Medical Record* from *New Orleans M. and S.J.*, *7*: 1130, June, 1880).

Dr. Despres (Abeille Medicate) recommends the use of this method, which he says has succeeded with him already in three severe cases. The first was a case of metrorrhagia following confinement, which had resisted all the ordinary methods. The second was a case of a metrorrhagia due to anæmia. It had equally resisted all treatment. The third case was observed in a young woman, aged 26, subject to metrorrhagia, recurring every fifteen days and lasting eight days at a time. Rest in bed and cold compresses had not produced any result. Despres gave from three to six cups of strong coffee daily. In this dose, it produced agitation, sleeplessness, sometimes even a sort of intoxication.

of the 135 patients who underwent further studies, 92 were found to be free from glaucoma, and 43 were found to have the disease. Thus, a total of 86 (1·7%) of 5,000 patients had glaucoma. The first step in the study of those who, on routine testing, had a pressure above 25 mm. Hg. was to repeat the test. Then gonioscopy was done to determine whether the corneoscleral angle is of the wide or the narrow type. If the angle is narrow, a mydriatic test is performed, unless the pressure is very high. If the angle is wide, or the mydriatic test is negative, a water drinking test is done. The authors believe that routine tonometry should be performed as part of the eye examination of every patient over the age of 40.

BOOKS RECEIVED

Tourist Annual of Kashmir Today—The Editor, "Kashmir Today," Government of J. & K., Srinagar.

The Clinical Apprentice—By J. M. NAISH, M.D., M.R.C.P., and J. APPLEY, M.D., M.R.C.P. 2nd edition. M/s. John Wright & Sons Ltd., The Stonebridge Press, Bath Road, Bristol-4.

Emergencies in General Practice—By J. R. GOYAL, M.B., B.S. Third edition. M/s. Medical Review of Reviews, P.O. Box No. 1160, Burn Bastion Road, Delhi.

Cancer in Childhood and Youth—By SIGISMUND PELLER, M.D., F.R.S.H. M/s. John Wright & Sons Ltd., The Stonebridge Press, Bath Road, Bristol-4.

Supplement to Materia Medica—M/s. Medical Digest, Girgaum, Bombay-4.

Special Number on Management of Cardiac Diseases—Vol. 4. No. 12. M/s. Current Technical Literature Co. Pr. Ltd., India House, Opp. G.P.O., Post Box No. 1374, Bombay-1.

Modern Trends in Cardiology—By A. MORGAN JONES. M/s. Butterworth & Co. (Publishers) Ltd., 4 & 5, Bell Yard, London, W.C. 2.

REVIEWS OF BOOKS

Medical Annual–Edited by R. BODLEY SCOTT and R. MILNES WALKER, 78th year, 1960, published by M/s. John Wright and Sons Ltd., The Stonebridge Press, Bath Road, Bristol-4.

The Medical Annual as is well known is a collection of articles written by various authors. It is published every year and has always devoted its pages to the advances in every branch of Medicine and Surgery during that particular year. The outstanding feature of the present edition is the presentation of a number of special articles. They are on "Auscultation of the Heart," the present status of bone-marrow transplantation in the human, the use of profound hypothermia in cardiac surgery and surgery in the treatment of peptic ulcer. The transplantation of bone-marrow in human beings has opened out a new vista in the treatment of aplastic anæmia and leukæmia, which were hitherto considered difficult to treat. Similarly the use of profound hypothermia shows immense promise in the future of cardiac surgery and perfection of this technique should make it possible for cardiac surgeons to discard the circulatory mechanism like the heart lung machines which are now used during operation on the heart. In addition to these special articles there are references made to the advances in every branch of medicine. It is not possible to review all the various subjects dealt with. However, particular mention should be made of certain features. The effect of polio-vaccination in the prevention of the diseases and the use of living vaccines is very well described. Very interesting is the chapter on the treatment of diabetes mellitus and its complications especially that relating to blindness. The latest methods of surgical treatment in Parkinson's disease have been described. The section on radio-therapy includes a description of the recent advances in super-voltage radiation and its effect on malignant diseases. The place of certain radio-sensitizers in this therapy has also been discussed. There is a separate chapter on venereal diseases which describes the advances made in the treatment of all venereal conditions. The book contains an index of the various Textbook publications in the different branches of medicine, as also 9 separate indexes for the subject matter of the book. The book is an outstanding publication and should find its rightful place in the library of every medical practitioner.

PREPARATIONS AND INVENTIONS

Farmamalt (Farmavin)—Palatable Multivitamin Nutritive tonic.

FARMAMALT is a judicial combination of Vitamins A, D and B_1. It also contains Iron in high assimilable form and flavoured in a base containing Malt Extract. Each 30 ml. contains Vitamin A 15000 *i.u.*, Vitamin D_2 I.P. 2500 *i.u.*, Vitamin B_1 I.P. 3 mg; Saccharated Iron Carbonate B.P.C. 0 375 g and Malt Extract I.P. 8 g.

FARMAMALT is also indicated as a general tonic during convalescence after illnesses like Influenza, pneumonia, typhoid and other diseases. It is available in Jars of 450 g.

Multivitamin Tablets (Farmavin)—Judicial combination of essential Vitamins present in MULTIVITAMIN TABLETS marketed by Farmavin Laboratories Private Ltd., Bombay has singled out this product to be a drug of choice by the Medical Profession. It is not always important what it contains, but it is vital in what proportion these Vitamins are present in a product. The haphazard quantum of Vitamins present in a product often does more harm than good to its consumers. This point is stated to have been kept in view in the manufacture of Farmavin MULTIVITAMIN TABLETS. Each tablet contains Vitamin A 1000 *i.u.*; Vitamin D_2 I.P. 100 *i.u.*,; Vitamin B_1 I.P. 1 mg.; Vitamin B_2 I.P. 1 mg.; Vitamin C I.P. 5 mg.; Nicotinamide I.P. 2·5 mg.

In tropical countries like India such products are bound to lose potency on storage. This factor has also not been neglected and Farmavin MULTIVITAMIN TABLETS are fortified with extra quantity of these vitamins. It is stated to have prophylactic and curative value in Vitamin deficiency disease.

Farmiron Tablets (Farmavin)—No drug is more useful in the treatment of microcytic anæmias than Iron Salt. FARMIRON TABLET is a combination of Iron with Vitamin B^1.

No Iron salt is more easily assimilable than Ferrous fumarate. FARMIRON TABLETS marketed by Farmavin Laboratories Private Ltd., Bombay is said to contain Ferrous fumarate. Each tablet of FARMIRON contains Ferrous fumarate 0·2 g., Vitamin B_1 USP 3 mg.

It is indicated in the treatment of Iron deficiency anæmias. It is claimed that the timely administration of FARMIRON TABLETS will save many lives. Available in bottles of 40 and 250 tablets.

Madribon (Sulphadimethoxine)—Roche has introduced a new long-acting, low-dosage sulphonamide. It is marketed under the above trade name.

The most outstanding property of MADRIBON is claimed to be that therapeutic blood levels are maintained for at least 24 hours after each dose.

Unlike other sulphonamides, which are excreted either in free or acetylated form, MADRIBON is found in the urine primarily as the highly-soluble glucuronide conjugate, which also retains some antibacterial properties. The high solubility of glucuronide minimizes the possibility of crystalluria or kidney damage. This product is reported to have undergone extensive clinical trials in the United States

DERMATOLOGY

The treatment of tropical diseases.—(*The Practitioner*, Oct., 1960).

Leprosy:—Dapsone has continued to prove of wide application in the treatment of all forms of leprosy but the course of treatment is very long and, unless the drug is used in very small doses initially (*e.g.*, 25 mg. to 100 mg. twice weekly), allergic reactions and other side-effects may seriously hamper its use and necessitate its temporary suspension and then the use of solapsone intramuscularly or thiambutosine (*Ciba* 1906), a diphenylthiourea compound, 2 g. daily. A combination of streptomycin and isoniazid ('strepto-hydrazid') has proved of value in patients intolerant of sulphones, especially if buccal lesions are present.

A promising adjuvant to treatment has been the introduction of diethyldithiolisophthalate, known as ditophal ('etisul'). This drug is administered by the daily inunction of 5 g. (6 ml.). Many lepromatous patients show a rapid and heartening improvement. As, however, drug resistance develops after a few weeks if ditophal is used by itself, the present proposal is to use the drug in combination with dapsone and thiambutosine, perhaps preceded by a short course of dapsone alone. It is hoped that the introduction of ditophal will prove to be a major advance in shortening the period of infectivity of lepromatous patients and in giving the patient welcome encouragement at the start of a long period of treatment. The search continues for drugs to reduce still further the total length of treatment.

A clinical evaluation and toxicity study of griseofulvin.—(*New York State J. Med.*, 15-4-1960).

The effectiveness of orally administered griseofulvin in many types of superficial fungus infections of the skin, scalp, and nails is now well established. We have more than justified the initial enthusiasm for an effective antibiotic to treat fungus infections which can be given systemically. Some of the problems which must be answered now are: (1) what disease states are responsive to griseofulvin, (2) anticipated toxicity, (3) optimal effective dosage, and (4) the possible development of resistant strains.

One hundred and thirty-three patients with proved fungus infections of the skin, scalp, and nails were treated with varying doses of griseofulvin for a period sufficient to evaluate the response to therapy.

Dosages were adjusted on three schedules. Most patients were treated with 250 mg. of griseofulvin four times a day. A sizable group was given 3 g. a day for four days and was then observed for therapeutic response. A third group received 2 g. a day for a prolonged period in an effort to evaluate the effect of this dosage on the sperm count. Complete blood counts and urinalyses were done in about one third of the patients treated. Sperm counts were done on 24 patients every two weeks for a three-month period.

Sixty-four patients with various dermatoses not considered at present to be mycotic were treated with griseofulvin. The dosage varied from 250 mg. four times a day to 500 mg. four times a day.

The clinical trial with griseofulvin demonstrates this to be an effective drug when given orally in a dose of 250 mg. four times a day for superficial fungus infections of the skin, scalp, and fingernails. Fungus infections of the toenails are much slower to respond to continuous treatment. Griseofulvin is *not* effective in moniliasis or in tinea versicolor. Recurrences of infection after apparent clinical cure suggest that topical therapy *plus* the systemic use of griseofulvin is the ideal approach for systemic fungus infections of the skin. The incidence of toxic reactions to griseofulvin was very low in this series of patients treated.

Griseofulvin topical dusting powder used in conjunction with systemic griseofulvin has since been found quite effective in preventing recurrences in tinea cruris and epidermophytosis.

OPHTHALMOLOGY

Retinal detachment.—(*Editorial*, *J.A.M.A.*, 18-6-1960).

Although the ophthalmologist plays the leading role in the treatment of retinal detachment, *the family physician may have to make important decisions*. He may have to decide whether an elderly patient can endure long general anæsthesia and confinement to bed with a minimum of movement. He may have to evaluate the emotional reserve in a patient already apprehensive and depressed by sudden blindness. He may have to participate in long-term post-operative care. He will be better able to co-operate if he has a general idea of the complex problems involved. Robert Fink's recent explanation provides a brief synopsis of the pathogenesis and current treatment. About 50% of all detachments occur in near-sighted people; another 20% develop within three years after cataract extraction, not as a result of poor surgical technique or complications but because the changes in the lens are part of a dystrophic eye condition. Clinically, 10% of detachments result from trauma. Although children who have congenital retinal weakness may be victims, detachments occur usually in the 50-to-60 year age group.

An important ætiological factor is the vitreous which fills the cavity of the eye. The vitreous, a viscous fluid, contains collagen fibrils which are attached to the retina. Pathological changes in vitreous, which may develop for various reasons, cause it to shrink in size, and its elastic collagen fibrils then put tension on the delicate sensory portion of the retina. Thus, tears may occur in spots that have been weakened by inflammation, trauma, or ther causes. Serous fluid seeps through the holes, and the normal movements of the eye force the fluid behind the retina, ballooning it forward.

This tugging on the retina by the shrunken vitreous brings on the patient's initial complaint, that of flashing lights. Next he may observe floating black specks caused by small clumps of blood in the vitreous. Shortly, he may notice a "curtain" across his vision, which indicates that the retina has detached. The patient should be put to bed to see if the fluid beneath the retina will be absorbed and to permit the retina to settle back against the choroid. If the detachment is relatively small, with no evidence of vitreous traction, and if the retina settles back during bed-rest, diathermy alone may be sufficient treatment.

The ophthalmologist must search for all tears in the retina and seal them off. However, if there is evidence of a strong vitreous pull, diathermy alone will not suffice, and more complex surgery such as scleral resection, a scleral-buckling operation, or a vitreous implant may be considered. The later methods of handling the more severe detachments are said to have increased the chance of success, but nearly one-fourth of all operations for detachment still end in failure.

The post-operative period is trying for the specialist and the patient. Intraocular hæmorrhage, infection, and further retinal shrinking sometimes occur. The family physician too must be on the alert for possible systemic complications.

Routine tonometry in 5,000 patients for detection of early glaucoma.—(J. E. L. Bendor-Samuel, W. May and H. Reed, *Brit. M. J.*, *1*: 853–855, March 19, 1960, via *J.A.M.A.*, 18-6-1960).

It has been routine practice in the eye department of the Winnipeg Clinic during the last 4 years to measure the intraocular pressure of every patient above the age of 40 years, nurses having been trained to perform this simple test. Among 5,000 patients 43 (0·9%) were found to have clinical signs of glaucoma, but 217 (4·3%) were found to have a pressure above 25 mm. Hg. is one or both eyes, but no other clinical sign of glaucoma. These 217 patients were advised to undergo further investigation; 82 failed to report for further tests, but

and many European countries, and to have proved very effective in all infections due to sulphonamide-sensitive organisms.

MADRIBON is available in the form of Tablets 0·5 g. in packings of 10 and 250 at Rs. 4.50 and Rs. 80.00 respectively.

NEWS AND NOTES

A 100-bed Mental Hospital for Orissa

The Government of Orissa has decided to construct a hospital for the treatment of mental patients, before the end of the Second Plan period. The Health Minister of Orissa, Dr. R.P. Misra, visited the Mental Hospitals at Madras and Bangalore in December last to study the working of those hospitals and obtained detailed information about the set up, equipment etc. It is learnt that this hospital will be designed to accommodate 100 patients at a cost of Rs. 11 lakhs.

Army Service for Government Doctors in Andhra

The Andhra Pradesh Government is actively considering a proposal to depute doctors of the Assistant Surgeon's cadre in the State Government service for serving in the Army for three years.

Sri P.V.G. Raju, Medical and Health Minister, said the proposal had been accepted by the Army authorities.

The idea was to make service in the Army compulsory for Assistant Surgeons in the State Government service after some time.

It was proposed to offer some inducement by way of seniority in service and eligibility for promotion to those Assistant Surgeons who volunteer to serve in the Army. All those Assistant Surgeons serving in the Army for three years would be given double increments. Service in the Army for three years would be deemed as equivalent to six year's service under the State Government.

N.C.C. training would be made compulsory for students in medical colleges in the State from the next academic year. Admission to medical colleges would be restricted to those who are found fit for N.C.C. training in future.

It was also proposed to associate the Army or N.C.C. authorities in the selection of candidates for admission to medical colleges from the next academic year. The idea is that the N.C.C. training received by medical college students will stand them in good stead when service in the Army is made compulsory for Assistant Surgeons in the State Government service.

Training for the Deaf
Centre Likely for Andhra

Mr. Shrimali, Minister of Education informed the Rajya Sabha today that the Government proposed to set up a training centre for the adult deaf in Andhra Pradesh.

The Minister said the scheme had not made much progress till now because of various difficulties. However, officials of the Ministry recently visited Hyderabad and had discussions with the Andhra Government which had welcomed the proposal. A final decision would be taken shortly.

A New Medical College for Kerala

The Kerala Government has decided to appoint a committee of experts to recommend a site for the location of the third Medical College to be started in the State during the Third Five-Year Plan.

Claims for the location of the college have been made by Trichur, Ernakulam, Kottayam and Alleppy. But the choice is reported to have narrowed to Trichur and Kottayam.

The Travancore and Malabar areas of the State already have Medical Colleges at Trivandrum and Kozhikode. Trichur had been asking for a medical college, in the private or public sector, ever since 1954 and presses its claim for the third medical college.

Bile pigment :—Bilirubin in urine can be detected by various [illegible] Iodi[illegible]

FALLACIES IN QUALITATIVE BIOCHEMICAL TESTS*

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THE clinicians welcome only such biochemical findings as are acceptable, while the rest are ignored. Biochemical investigations often yield important clues for proper diagnosis when clinical findings may fail.

The correct interpretation of the results obtained in biochemical investigations is however, a very important factor. If the interpretation is not correct, discrepancies between clinical and biochemical investigations are bound to occur.

The object of this paper is to show that under various circumstances and conditions many qualitative biochemical tests may permit of false inferences and if not properly interpreted by an experienced clinical biochemist, or an able clinician, biochemical investigations may be of little or no value. Several authors have suggested various modifications in qualitative urine analysis, but have not even hinted about possible fallacies in many biochemical tests. Some of the fallacies in the routine qualitative biochemical tests of urine will therefore be discussed.

Colour of urine.—Sometimes, the colour of urine furnishes an important clue in the diagnosis of an obscure case. The commonest abnormality is a red colour in the urine[1]. In the female, contamination of the specimen by menstrual blood must first be excluded, in order to ascertain whether the colour is due to hæmaturia. Red urine may be due also to the presence of porphyrine[2]. When drugs[3] like aloes, senna, phenolphthalein, analgesics, antipyrine, etc. are administered in large doses, the urine becomes red in an alkaline medium. The anticoagulant phenylindanedione sometimes results in the passage of pink urine and in this case, it is of particular interest to differentiate hæmaturia[4]. The red pigment of beetroot, and the eosin in sweets may cause the urine to be red.

Tests for occult blood in urine.—A number of chemical tests *e.g.*, Benzidine[5], Phenadione, and orthotoluidin, have been suggested for the detection of occult blood in fæces, and urine. The most sensitive test for occult blood in urine is the orthotoluidin test.

Presence of Iodites[6] usually gives a positive reaction in the benzidine and guaiacum tests. This may be mistaken for hæmoglobin as both reactants survive boiling previous to testing. Benzidine test is not so sensitive as the orthotoluidin test and guaiacum test is even less.

* Specially contributed to the ANTISEPTIC.

The concentration of benzidine plays a very important part in the benzidine test. When the fæces of patients on normal diet and without any gastric or intestinal trouble is tested with benzidine of more than 0·5% concentration, a false positive reaction may be observed. There is great confusion as to whether medication with iron interferes or not with the benzidine test. Medicinal iron preparations do not give a typical positive reaction although they may do so with guaiacum. It is quite possible that in a very sensitive person, iron may irritate the gastric or intestinal mucosa but it is unlikely that this will lead to bleeding, sufficient to yield a positive reaction in the test. Regarding spectroscopic examination of blood in urine, the spectroscopic bands of hæmoglobin in urine cannot be detected on some occasions owing to the presence of hæmoglobin in minute quantities[7].

Proteinuria.—Normal urine does not generally give a positive reaction to any of the protein tests, though it is excreted normally in quantities of 30 to 200 mg. per day in the urine[8].

Protein may be present in the urine of normal persons after severe exercise, after a high protein diet, or as a result of a temporary impairment of the renal circulation when a person stands erect (*e.g.*, postural proteinuria)[9]. Normal albuminuria occurs occasionally in young subjects. Proteinuria occurs after a bath, leading to a constriction of the renal blood vessels and anoxia. Proteinuria is frequently associated with pregnancy, probably as a result of pressure interfering with the return of blood in the renal veins.

The female's urine may often show the presence of protein. Secretions and discharges from the vagina and admixture of semen may also add protein to the urine and positive results may be had in the tests for protein[9].

Benedict's qualitative test for detection of glucose in urine :—Benedict's qualitative test for the detection of glucose in urine is negative for normal urine, although a very small amount of glucose passes in normal urine. Benedict's qualitative test in the absence of glucose may be positive.

The presence of vitamin C, glucuronic acid, pentose, lactose, galactose, etc. in the urine may show a reduction of the Benedict's solution. Galactosuria should be suspected if Benedict's qualitative test is positive in the urine of a marantic baby. Lactose is the reducing non-fermenting sugar found in the later stages of pregnancy, and is always present in early puerperium and during lactation.

Chloroform in urine used as preservative interferes with the detection of glucose since it reduces Fehling's solution. If more formalin is added for the preservation of urine, it may give positive results with Benedict's solution in the absence of reducing sugars or glucose[10].

Bile-pigment :—Bilirubin in urine can be detected by various tests *e.g.*, Fouchet's tests, Gmelin's tests, Iodine tests and methylblue tests. Methylblue tests are generally used in many pathological laboratories. The ictotest tablet of Ame's & Comp. Ltd. gives reliable results for the presence of bilirubin in urine. The Gmelin's and iodine tests depend on the oxidation or bilirubin into biliverdin. They are unsatisfactory to perform, and not of great value. The methylblue test has no significance for the detection of bilirubin.

Urobilinogen.—The excretion of urobilinogen in urine is altered in hepatic biliary and other pathological conditions. Qualitative and quantitative measurement of urine and fæcal urobilinogen may be of value in diagnosis when serial estimations are made for assessing progress in treatment. Urobilinogen is detected by the red colour which it gives with Ehrlich's aldehyde re-agent—p-dimethyl-amino benzaldehyde[11].

This reagent should not be confused with Ehrlich's diazo-reagent used for Van den Bergh tests. Ehrlich's aldehyde reagent gives a red colour with porphobilinogen (insoluble in chloroform). The presence of Indole, Indican and unidentified chromogen in the urine may also show a red colour with Ehrlich's aldehyde reagent. Tests for urobilinogen should be done on fresh urine, as otherwise some of the urobilinogen may get converted into urobilin, which does not give a colour with the reagent. Accurate quantitative estimation of urinary urobilinogen is difficult, because of the presence of other chromogens.

Hey's sulphur-test :—This test for the presence of bile-salts is insensitive, and of no practical value and so is not as useful clinically as that for bile-pigment.

Test for Indican in urine :—Indican excretion increases in urine during intestinal obstruction, typhoid, bacterial decomposition of tissue proteins, in gangrene, and in empyema[14]. For the detection of indican in urine Jaffe's test is usually done. This test is unreliable, because the concentration of oxidizing agents is very important in this test. In the absence of an oxidizing agent the blue colour will not develop. In the presence of an excess of an oxidizing agent, the colour will be destroyed. Concentration of HCl has varying oxidizing properties according to the extent of decomposition that has taken place due to exposure to light. The yellowish specimen that contains oxides of chlorines is usually sufficiently active to give the indigo reaction without the addition of hydrogen peroxide[12]. Many constituents in urine interfere with the test by combining with the liberated indoxyl.

Rothera's test for acetone in urine :—Rothera's test for acetone in urine is well known. Normal urine rich in organic

sulphide (thiol) gives an immediate but transient red colour, with the reagent[13].

This must not be confused with ketone reaction which lasts for a few hours. Rothera's test in urine is positive in the presence of creatinine or metaproteins and is distinctly positive in the urine of patients who have been given a phenolphthalein-containing purgative[15].

Methaemoglobin :—Blood and urine specimens are often sent for detection of methæmoglobin, but the spectroscopic bands seen by the ordinary spectroscope are not very convincing as they look like those of oxyhæmoglobin; methæmoglobin bands in plasma should be well seen when the blood is very much saturated with methæmoglobin, otherwise the methæmoglobin bands in blood are very difficult to detect by the ordinary spectroscope[16].

If an acid urine containing hæmoglobin has been in the patient's bladder for a long enough time the spectrum of methæ-moglobin may be detected in the urine instead of hæmoglobin. The combined spectra are found in fresh urine if hæmoglobin has been converted to methæmoglobin in the patient's bladder prior to hæmolysis, as in nitrobenzene poisoning. The urine containing hæmoglobin in very acidic media kept for some time will show methæmoglobin bands and not the hæmoglobin bands.

To sum up, it will be tragic indeed, if the results of bio-chemical tests are not intelligently interpreted and made to help in diagnosis.

Failure of proper interpretation of biochemical findings may not only mislead clinicians but also give room to some to think of biochemistry as a collection of recipes; as Dr. Arthur Jorden rightly said, "The unfortunate habit of referring to chemical pathology as biochemistry has led some to think of biochemistry as a collection of recipes suitable for a cook-book, and this confused thinking has led at times to a neglect of the important medical aspect of the subject."[17]

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A FEW ASPECTS OF RADIO-ISOTOPES*

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Two thousand years ago Democritus of Greece first conceived the idea that matter was composed of invisible and indes-tructible particles called "atoms." Today nucleonics is an outgrowth of this ancient concept. About 50 years ago, Becquerrel of France discovered the radio-active properties of uraniun. With the discovery of Radium in 1898 by the Curies, and Mme. Curie's isolation of the first pure salt of radium in 1902, a new major therapeutic weapon became available. Radium and X-rays were the sole sources of radio-activity available till 1934, when radiation was first discovered. By the end of 1935 there were about a hundred artificial radio-isotopes. By 1947 more than 500 came to be known—at least one for each of the elements of atomic numbers from 1 to 96 (inclusive). But of more than a thousand five hundred isotopes known today, about nine hundred are radio-active.

The atom is composed of a nucleus (which is positively charged), surrounded by a certain number of electrons which are negatively charged. The electrons are equal in number to the positive charges on the nucleus. Under certain conditions the positively charged protons and neutrons (having no charge) change places and are considered as two-stages of the same particle—the *nucleon*. The number of positive charges, *i.e.*, the number of protons is known as "Nuclear charge number" or the commonly called *atom number*. The total number of nucleons (both protons and nucleons) is called the *mass number*. This specification of the two numbers defines the atomic species (Nuclide).

Each element has its own atomic number and all nuclides having the same atomic number (and a different *mass number*) are called *isotopes* of the corresponding element. Usually the *atomic number* and *mass number* are written respectively *below* and *above* the chemical symbol of the element and to the left of it. Thus ^{1}H, ^{2}H, ^{3}H indicate the three isotopes of hydrogen. The nucleus of the first (ordinary hydrogen) consists of only one proton, that of the second (also called Deuterium or heavy hydrogen) of a proton and neutron and that of the third (also known as Tritum) comprises of a proton and two neutrons. Usually the atomic number is usually omitted and the isotopes are written as ^{1}H, ^{2}H, ^{3}H.

It is now possible to transform a nuclide into a different one by means of nuclear reaction. When nuclear reactions modify only the *mass number* (and not the *atomic number*) a different

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(thiol) gives an immediate but transient red colour, [illegible] the reagent[13].

This must not be confused with ketone reaction which lasts for a few hours. Rothera's test in urine is positive in the presence of creatinine or metaproteins and is distinctly positive in the urine of patients who have been given a phenolphthalein-containing purgative[15].

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To sum up, it will be tragic indeed, if the results of biochemical tests are not intelligently interpreted and made to help in diagnosis.

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otope of the same element is obtained. If, instead, the *atomic umber* is altered as isotope of a different element is formed. In his way even nuclide non-existing in nature—("artificial isopes")—of the various natural elements can be produced. sotopes may be of two kinds :—(1) the unstable isotopes, whose nuclei spontaneously disintegrate. This spontaneous disintegration of an atomic nucleus is always accompanied by the emission of radiations which is commonly called radio-active disintegration or transformation and the unstable nuclides are also called radio-active isotopes or radio-isotopes or radio-nuclides.

A certain number of natural radio-isotopes occur and they are the isotopes of the elements of atomic number 84 and upwards (among which are Polonium, Radium, Thorium and Uranium) while those having less *atomic numbers* are exclusively represented in nature by (2) the stable nuclides (with rare exceptions of extremely little practical importance). Some consist of a single stable nuclide (mono-nuclide elements) for example :—Natural gold is 100% composed of ^{197}Au, iodine of the isotopes ^{127}I and arsenic of the isotopes ^{75}As, many others are formed of a mixture of stable isotopes in constant proportions such as :—

(1) Natural oxygen consists of 99·757% isotopes ^{16}O; 0·039% of ^{17}O and 0·204% of ^{18}O. (2) Chlorine consists of 75·4% isotopes of ^{35}Cl and 24·6% of ^{37}Cl.

By means of nuclear reactions, it has been possible to produce elements (radio-active) non-existent in nature of atomic numbers superior to that of uranium (so called the new trans-uranic elements) and isotopes (always radio-active) which do not exist in nature, of all the stable and natural elements. In this way ^{196}Au, ^{198}Au, ^{199}Au, have been produced from gold and similarly ^{14}O, ^{15}O and ^{19}O are obtained from oxygen.

The expression, artificial radio-active isotopes, refers precisely to the unstable nuclides, non-existent in nature and which are produced by nuclear reaction. All the isotopes whether natural or artificial, stable or unstable of the *same* element have identical chemical properties and cannot be separated by means of chemical methods, but only, by processes (technically very delicate) which make use of some small difference in physical or chemico-physical behaviour, bound up with difference in *mass* of the *atoms*. Mass spectrograph is used to analyse the composition of an isotopic mixture. The presence of a radio-active isotope in a sample of an element can be very simply shown by its radio-activity, but in no way does it alter the properties of the elements.

A *tagged compound* is a chemical compound in whose molecule certain atoms are substituted by atoms of the radio-active isotopes of the same element.

Measurement of radio-activity :—The radio-active atoms are unstable atoms, where an essential change by conversion of a neutron to a proton or *vice versa* occurs resulting in the emission of one or more types of radiation. All elements whose atomic numbers are greater than 82 are radio-active while those with atomic numbers less than 82 are naturally radio-active forms which decay very slowly and these are slightly radio-active. The preparation of the artificially radio-active isotopes of a large number of elements started in 1936. The three usual types of radiations of these radio-active isotopes are :—*alpha*, *beta* and *gamma*.

(1) The *alpha* radiations are known as '*alpha particles*,' which are rapidly moving helium nuclei and consist of two protons and two neutrons. These are given off only by the radio-active isotope of *atomic number* greater than 61 ; (2) *Beta* radiations are called '*beta rays*,' which are simply rapidly moving electrons and (3) *Gamma* radiations are called '*gamma rays*' which are electromagnetic waves essentially equivalent to those produced by a high-energy X-ray generator.

Regarding penetrability, *gamma rays* are the most powerful and *alpha* particles are the least. The radiation decreases rapidly with the time. The radio-active decay constant is referred to as λ. The time required for a radio-isotope to decrease to 50% of its original activity is known as "*half life*." The radio-activity of uranium is detected by the blackening of a photographic emulsion. For very weak samples, the instrument known as Geiger-Muller counter is used.

Units of measurement :—(1) The *Curie* is $2{\cdot}22 \times 10^{12}$ disintegrations per minute ; (2) the *Rutherford* is one million disintegrations per second ; (3) for *gamma* radiations another unit of measurement is used, the roentgen *(r)*-which is the production of the electrostatic charge in a measured volume of air at standard temperature and pressure. Unlike the *Curie*, the roentgen *(r)* does not contain any time factor ; (4) *Roentgen equivalent physical (r.e.p.)* is another unit which is defined as that dose of any ionizing radiation which produces energy absorption of 93 *ergs* per gram of tissue and (5) more recently the International Commission on Radiological Units has defined a new unit for absorbed dose :—"*rad*" which is equal to an energy absorption of 100 *ergs* per gram of irradiated material.

Fission products :—Fission products are predominantly the isotopes of elements ranging in the middle portion of the periodic table, with atomic numbers varying from 30 to 62. The '*half-life*' of these products is extremely variable ranging from a fraction of a second to decades. The chief fission products are :-the radio-active isotopes of Strontium, Iodine, Yttrium, Barium, and several rarer elements. Of these Strontium, Barium and Iodine

are absorbed easily through contaminated food material and drinking water. Their metabolism varies. Many are deposited in bones. Since Strontium (^{90}Sr) with a half-life of about 20 years is deposited in bone and is only slowly excreted; it probably represents the most toxic of all the fission products.

The biological effects of ionizing radiations are:—(1) immediate cellular injury leading to cell-death; (2) cellular injury which does not become manifest until the cell attempts to undergo *mitotic* division; (3) depression of the functional activity of a cell; (4) temporary depression of the mitotic activity of a cell; (5) production of a mutation in the case of a germ-cell (*e.g.*, the sperm or ovum) and (6) ionizing radiations may become carcinogenic, the exact mechanism of which is not yet clearly understood.

In general those tissues in which there is a relatively rapid formation of new cells are more sensitive to the acute effects of all types of ionizing radiations.

(A) *The more radio-sensitive tissues in man are:*—the lymphatic tissues; bone-marrow; epithelium of small intestine; testes (particularly spermatogonia); ovaries (especially granulosa cells); basal cells of the epidermis and the fœtal tissues.

(B) *The more resistant tissues in man are:*—the muscle tissue; nervous tissue and the mature bone tissue.

The appearance of *lymphocytes with bilobed nucleii* has recently been shown to be a more sensitive indicator of radiation exposure than the *white cell count.* Radio isotopes are widely used as diagnostic agents. Of the numerous radio-active elements, only a limited few are of diagnostic value :—

(1) Radio Iodine ^{131}I :—For the diagnosis and investigation of thyroid disorders and for labelling cells and biologic substances. (2) Radio Iron (^{59}Fe) and Radio cobalt (^{60}Co) for the study of blood disorders. (3) Radio Phosphorus (^{32}P) for investigation of bone and blood diseases and localization of brain tumours. (4) Radio Sodium (^{24}Na); Radio potassium (^{42}K) and Radio carbon (^{14}C) for metabolic studies. (5) Radio Carbon (^{14}C) for endocrine disorders and metabolism of cholesterol, steroid hormones and antibiotics. (6) Radio Copper (^{64}Cu) and Radio Arsenic (^{74}As) for the detection of brain tumours. (7) Radio Mercury (^{203}Hg) to tag mercurial diuretics for the study of fluid excretion. (8) Radio Gold (^{198}Au) (*beta* and *gamma* rays) for the lymphatic tissue and its conditions.

Finally radio isotopes may also be used as radiation sources for diagnostic radiography; for example Thulium (^{170}Tm) has been placed into a small and very portable X-ray unit for use in emergencies.

Cases and Comments

LIGNOCAINE INFILTRATION AS THE SOLE ANAESTHETIC IN GENERAL ABDOMINAL SURGERY

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LOCAL lignocaine anæsthesia has been used by me for general abdominal surgery for over a year with entire satisfaction.

One case in our series is now reported here in support of our finding:—Mr. M. A., a college lecturer, aged 46 years, who consulted us first in 1953, sought admission on 28-4-1961, complaining of a dull lumbar pain on the left side. He had been previously X-rayed; the skiagram showed three radiopaque shadows in the left kidney, measuring $1\frac{1}{2}'' \times 1\frac{1}{4}''$; $\frac{1}{2}'' \times \frac{1}{2}''$ and $2\frac{1}{2}'' \times \frac{1}{2}''$. A specimen of his urine showed numerous RBCs and many pus cells. His intravenous pyelography, showed a big hydronephrotic kidney and confirmed the position of stones in the renal pelvis and in the calyces. The left ureter could not be visualized even after 45 minutes. The right urinary tract showed normal function. He had constant pain for 2 weeks previous to admission.

He was given a preliminary course of Furadantin tablets and the urgency of a surgical operation was brought home to him. Being temperamentally over-fastidious he objected to general anæsthesia; so it was decided to operate under local anæsthesia, spinal anæsthesia being considered risky, owing to the low blood-pressure which was 100/60 mm. Hg. and to his general condition being low.

He was operated upon on 4-5-1961. The standard curved line of incision was infiltrated with 2 per cent lignocaine *plus* adrenaline. The muscles were infiltrated with 1 per cent lignocaine *plus* adrenaline. After 5 minutes, the incision was made and the muscles cut through. The perinephric tissues and fat were now infiltrated with a little more than one per cent lignocaine. The perinephric fat was then cut and the kidney separated, mobilized and exteriorized. The last rib was not dissected. The pelvic stone was localized, and after removing the fatty layer upwards, the pelvis was cut horizontally and the stone was removed. The smaller stones were then searched for, located and removed from the calyces. The calyces were washed and a ureteric catheter was passed down the ureter to ensure its patency. The pelvis was closed with 3 catgut sutures. The perinephric tissues were replaced after pushing the kidney inside. The wound was closed in layers, after putting a corrugated tube behind the pelvis. The patient was talking all the time and was co-operative throughout the operation.

Discussion.—The points of interest in this case are :—(1) *Complete relaxation* :—All operations, including exteriorization of the kidney, need complete relaxation of the muscles. In this case, the kidney could be exteriorized without resorting to the dissection of the 12th rib. In addition to local anæsthesia with lignocaine, I consider that the following points also helped very much in attaining this object *viz.* : (*a*) premedication with pethidine and largactil or the same trio with phenergan ; (*b*) good psychological preparation of the patient by reassuring him in every way and impressing upon his mind that his co-operation will reduce the time taken for surgery by about one-half and (*c*) the administration of modern tranquillizers, two or three days before the operation was very useful. (2) *Surgical shock* :—None of our patients developed visceral shock up till now. This particular patient passed flatus the same evening and had to be catheterized only twice, after which he passed urine freely. In our intestinal cases we did not see any paralytic ileus nor any dilatation of the stomach. Here again the importance of premedication is emphasized. (3) *Post-operative pain* :—The great value of modern general anæsthetics is there, but when the patient regains consciousness (this is very quick with the modern anæsthetics) he frequently suffers from intractable pain, which needs heavy sedation in some cases for 2 or even 3 days. All the advantages of the patient regaining consciousness quickly, are lost as post-operative complications develop very frequently due to the heavy sedation. Surprisingly enough, the absence of post-operative pain is a remarkable feature that we noticed in all cases which had local lignocaine anæsthesia. The patient was able to sit up on the evening of the operation, and to stand up and walk on the third day. This particular patient did the same and went back home on the 8th day, without any pain. The technique of infiltrating lignocaine in the wound and muscles to prevent post-operative pain was reported by R. E. Roder in the *Lancet* of 13-8-1960. He advocates 2% lignocaine with adrenaline in 10% Dextravan solution, to prolong the effects of lignocaine for about 10 hours, but in our experience simple lignocaine with adrenaline was found to be quite enough. Most probably it is the vicious circle, that has to be broken for which a period of 2½ to 3 hours is adequate. It is remarkable that none of the cases operated with this technique, even needed more than one or two injections of pethidine. The case under report did not require even one such injection post-operatively. With this limited experience on the use of lignocaine I consider that it constitutes a real advance in surgery. (4) *Paucity of well-equipped surgical centres* :—Surgical centres in our country are very few and quite inadequate and centres equipped with modern anæsthesia and trained staff are still fewer. Most patients are either too poor to go to far-off places or are too conservative and prefer to die

the *prasadansha* and *kittansh* (urine) and reabsorbing (प्रचूषण) the former and excreting the latter with the help of *apan vayu* to keep it first (*dharan karama*) and then to excrete it (*munchan karma*). The *pakvashya* part is the part which receives this *mala* called urine through collecting tubules, ducts etc and with the help of *apan vayu* excretes it through the *guda* or urethra.

On this basis all the varieties of *Vata*, *Pitta* and *Kapha* which play their role in the final production of *mala i.e. purish*, the same varieties of *Tridosha* must also be playing the same role in the final shaping of *mala i.e. mootra*.

This is the Ayurvedic way of dealing with various life processes of the formation of *prasad* and *kitta* part.

I shall be dealing with a number of other very important functions of kidneys, revealing some of its activities unknown to the modern science so far in my next article and shall be glad to answer any queries regarding this article.

MUSCLE WASTING COMPLICATING TREATMENT WITH DEXAMETHASONE

Muscle wasting and weakness, usually with preservation of tendon reflexes, was described in 1959 as a complication of treatment with the steroid 16-alpha-hydroxy, delta 1, 9-alpha-fluorohydrocortisone (triamcinolone). A case developed during treatment with 9-alpha-fluorohydrocortisone. More recently, Perkoff *et al* have reported five cases developing during the daily administration of at least 40 mg. of delta-1-cortisone (prednisone), and two cases developing during the daily administration of 150 mg. and 250 mg. respectively of cortisone. They have called the condition steroid myopathy. The cases reported have occurred in patients being treated for collagen diseases, asthma, rheumatoid arthritis and blood dyscrasias. Dr. Syme of Melbourne reports a case of muscle-wasting and weakness following the long-term administration of the steroid 16-alpha-methyl, delta-1, 9-alpha-fluorohydrocortisone (dexamethasone) during the treatment of temporal arteritis.

Temporal arteritis is regarded as an indication for steroids in dosage adequate to suppress symptoms and maintain a normal erythrocyte sedimentation rate, both because it relieves symptoms and because of the danger of blindness if the ophthalmic arteries become involved. Phenylbutazone was tried initially in this case because of the claim (Bjorkman, 1958) that it may lead to a rapid relief of symptoms and may subsequently be discontinued without risk of relapse. However, it proved ineffective.

Dexamethasone is said not to cause appreciable sodium retention though in this case the development of œdema and raised venous pressure, relieved by chlorthiazide, suggested that it did so when a dose equivalent in anti-inflammatory effect to about 100 to 125 mg. of hydrocortisone was given for four months.

It is believed that the quadriceps femoris weakness and wasting in this patient represent a side-effect of dexamethasone, because they developed during the administration of the drug and the weakness was gradually relieved after its withdrawal, because they resembled the weakness

and wasting of muscles sometimes seen with other steroids, and because there was no other apparent cause. At no time were serum potassium levels of an order likely to be associated with muscle weakness observed, and the onset of the weakness occurred when the patient's primary disease was in clinical remission.

In all reported cases of steroid myopathy the weakness and wasting have been reversible with cessation of the causative steroid. It is possible that the prednisolone at present being given is preventing the complete reversal of the myopathy in this patient. In most reported cases the quadriceps femoris muscles have been involved early and severely; but a more extensive distribution, involving the proximal muscles of all limbs and limb-girdle muscles, may occur also. When biopsy of affected muscles has been reported, the histological findings have been variable and sometimes relatively normal as in this case.—(*Med. J.*, Australia, 10-9-1960).

MOTOR MECHANISMS OF DYSPHAGIA

The use of combined pressure measurements and cine-radiography has given a clear picture of the normal mechanisms of swallowing. Pharynx, cricopharyngeal sphincter, œsophagus and gastro-œsophageal junction are involved in a single peristaltic action with co-ordinated relaxation of the sphincters Dysphagia may be produced by inco-ordination of the peristaltic wave or sphincters in any of these four sites.

Absence or gross weakness of pharyngeal propulsion has been seen in myopathy and certain vascular lesions of the mid-brain. This produces a picture of retention of barium in the pharynx that may be indistinguishable from that caused by a failure of the cricopharyngeal sphincter to relax. This is again produced by cerebrovascular accidents, usually a severe form of thrombosis of the postero-inferior cerebellar artery. These two physiological upsets can only be distinguished by pressure measurements.

The principal inco-ordination of the œsophagus is diffuse spasm, where the peristaltic wave is replaced or obliterated by abnormal, simultaneous contractions of the lower half which are vigorous and often repetitive. These contractions cause the radiological picture of a rippled or frankly corkscrew œsophagus where barium is trapped and not propelled. In this condition the gastro-œsophageal junction relaxes normally and offers no obstruction.

Achalasia of the cardia is characterized by a failure to relax the gastro-œsophageal junction and also by a complete loss of usual œsophageal peristalsis. Abnormal œsophageal contractions are present but these fail to obliterate the lumen, a distinguishing point from diffuse spasm, for where the œsophagus is not dilated these conditions may cause a similar radiological picture.—(*Proc. Royal. Soc. Med.*, June 1960).

DIAGNOSIS IN ASTHMA

Determination of carbon dioxide content of blood offers a guide to therapy in severe asthmatic attacks. The patient, despite exertions may be over-breathing or under-breathing. Patients who are actually under-breathing may well require cortisone or other agents to increase oxygen intake. On the other hand, breathing into a paper bag can be a simple procedure to increase carbon dioxide content of the blood relative to oxygen.—(*Bull. National Jewish Hospital*, Denver, via *Western Section, American Federation for Clinical Research*, Carmel, Calif., Jan. 28, 1960).

CANDIDIASIS*

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CANDIDIASIS may be acute, subacute or chronic; the infection is usually caused by C. albicans and may involve the skin, nails, oral or vaginal mucosa, bronchi or lungs; occasionally it may cause septicæmia, endocarditis or meningitis. There are reports of candidiasis occurring after intensive antibiotic therapy. The increased incidence may be due to 'direct enhancement of growth, elimination of competing organisms, avitaminosis or lowered resistance due to therapy, original infection or low nutrition.' About 15% of pregnant women show the presence of C. albicans in vaginal culture, whether they had had antibiotics or not. It is also frequently isolated from patients with lung trouble.

C. albicans is seldom found on the normal skin though it is a common symptomless inhabitant of the gastrointestinal tract. The source of infection is mostly endogenous though occasionally contagious infection occurs. No age, race, or sex is exempt.

It is essentially a mucocutaneous infection. Occasionally it involves the systems and the clinical picture varies with the site.

Mucous membranes.—*Oral*:—(*a*) Creamy white lustreless patches of thrush loosely attached to the bright red, moist mucosa of the cheeks, palate or other parts. 'Fiery red mucosa in hypersensitives,' (*b*) chronic glossitis–beefy-red, smooth, with atrophic papillae on sides and under surface of the tongue and stomatitis. Localized lesions, firmly adherent are slightly elevated and corrugated. Patches are discoloured in heavy smokers. It is associated with 'hairy tongue,' perleches. The lesions are macerated, eroded, moist, red cracks, or fissures with suface-pellicle in corners of the mouth and may spread to the skin. Lips become increasingly red and scaly.

Asymptomatic gastro-intestinal form.—C. albicans is present in the saliva or stools of carriers. In many cases of cutaneous moniliasis, C. albicans can be detected in the excreta.

Vulvovaginitis.—Low grade inflammation is present with vulvar pruritus and copious white thin discharge. Secondary pyogenic infection and eczematization may result. It resembles simple eczematoid dermatitis, or excoriated *vesiculopustules* or rarely ulceration. There are red, scaly lesions on the outer vulva and the inner surface of the thigh. It may not be accompanied by any skin lesions.

Cutaneous lesions.—(1) Localized; and (2) generalized candidiasis.

*Specially contributed to the ANTISEPTIC.

LOCALIZED:—Onychia and paronychia due to periungual fold infection, are common local involvements. Chiefly the finger-nails are affected, single or multiple. There is a painful, reddened swelling without pus. The nail becomes hardened, thickened, grooved, eroded, brownish with a narrow, dark-green, striping of the lateral margins of the nail. The nails are not lustreless, not brittle, not yellow, and there is no debris beneath.

Intertrigo:—This is a frequent lesion with well-marginated, irregular, red, oozing patches with papulo-squamous whitish borders, surrounded by small vesiculopustules and fissure-formation at the bottom of the fold accompanied by violent smarting or itching. The sites are axilla, inframammary area, umbilicus, intergluteal fold, groin, webs of the toes (like tinea pedis caused by filamentous dermatophytes), webs of the fingers, and labia majora. About 50% of the cases are in the 3rd digital space and never in the first. From the webs of the foot the infection may spread on to the foot as circinate erythematous and vesicular patches. Erosio-interdigitalis blastomycetica is the involvement of the webs of the hands, usually the 3rd or 4th, with a bright red base and moist surface and peeling border. Perianal-pruritus ani of the white macerative type, may be due to the direct effect of oral broad spectrum antibiotics, especially when accompanied by diarrhœa.

Water-bed dermatitis:-This occurs after continuous baths or wet bland applications over a long time, or by occlusive dressings. The skin is macerated, peeling off with a red base and satellite vesiculopustules. *Eezema*:—The occurrence of C. albicans in some cases of infantile ecezma has been noted.

GENERALIZED CUTANEOUS CANDIDIASIS:—This is fortunately uncommon.

Acrodermatitis enteropathica occurs in infants while changing from breast to bottle-feed. There are skin lesions of generalized cutaneous moniliasis, alopecia and recurrent diarrhœa due to C. albicans.

CANDIDIS OR LEVURIDS are sterile, grouped, vesicular lesions on the hands and localized or widespread erythematous, vesicular, exudative patches caused by the dissemination of the products of C. albicans through the blood stream, and like all "ids" heal by treatment of the initial focus.

In the lungs the infection is usually subacute or chronic but may be acute with no characteristic features to distinguish it from other pulmonary mycoses. *Broncho-pulmonary*:—Broncho-moniliasis first described by Castellani in 1910, is found especially in tea-tasters of Ceylon. It has a characteristic, distressing, refractory cough, the sputum is colourless, mucoid, gelatinous with small grey flakes, sometimes blood-streaked. Medium

coarse rales are heard at the lung bases. *Pulmonary*:—This is less common but more serious than the bronchial type. The cough is harassing with mucoid, gelatinous, occasionally blood-streaked sputum. It may be purulent due to secondary pyogenic infection. Pleural pain is common and occasionally also effusion. The temperature and pulse are elevated. In the bronchopneumonic type the lesion is scattered over 2 or more lobes with medium rales. Bones and joints are very rarely involved.

Investigations.—The blood does not usually show a leucocytosis. In the severe pulmonary type the neutrophils are increased. B.S.R. is normal or slightly raised in the bronchial type, but is elevated in the severe pulmonary type.

Mycology:—The genus Candida includes mycelia-producing, yeastlike fungi. C. albicans alone is pathogenic to laboratory animals.

Direct examination:—Scrapings from the nail and skin warmed gently in 10 to 20% KOH, on a glass slide show a few hyphæ or budding cells. Thrush and intertrigo show a tangled net work of fine mycelia and clusters of spores.

It grows easily on Sabouraud's 2% glucose medium from scrapings and swabs at 37°C or at room temperature. Growth occurs in 2 to 4 days with a distinct yeasty odour.

Animal inoculation:—1 cc. of 1% saline suspension of C. albicans injected intravenously into rabbits, kills the animal in 4 to 5 days, with small abscesses in the cortex of the kidneys.

Pathology.—C. albicans grows on the surface of the skin and oral and vaginal mucous membranes chiefly superficial and involving the epithelium but deeper involvement may occur.

Hypersensitivity:—Skin tests with intracutaneous injection of vaccine or extract of C. albicans is not diagnostic but should be done to guide in the course and management of the case. Complement fixation may be from patient's serum and candida.

Diagnosis.—It is easy by direct examination and from cultures made from the oral, vaginal and cutaneous lesions. Intertrigo in candidiasis is a bright red sore with satellite vesiculopustules. Paronychia of pyogenic origin is painful and discharges pus. Paronychia of pyogenic and trichophyton origin is acute and painful. Candidids are diagnosed by clinical lesions and hypersensitivity.

Bronchial and pulmonary lesions:—'C. albicans may be a secondary invader in carcinoma of the lung, pulmonary tuberculosis, pneumococcal pneumonia, asthma, lung abscess, bronchiectasis and congestive heart failure.'

In bronchopulmonary candidiasis the X-ray shows non-specific peribronchial thickening and sometimes a peculiar

fibrosis. In the pneumonic type the X-ray picture presents a variable appearance resembling broncho-pneumonia with edges less sharply defined. Apices are usually spared. The lesions are 'labile.' In severe infections there may be a massive dense, smooth shadow covering almost the entire lobe, often at the base. Some lobes may be affected with a complete consolidation and broncho-pneumonic patches in other lobes.

Course and prognosis.—Infection localized to the skin or mucosa, usually responds rapidly to treatment but relapses are common, especially if "predisposing factors are duplicated, *e.g.*, chronic glossitis and vulvovaginitis or in perleche, cure is often difficult unless the mouth is treated." Generalized mucocutaneous candidiasis or candidids with hypersensitivity are very resistant to treatment and prognosis is obscure. Fatalities may be due to secondary infection. 'Any form of candidiasis should be considered potentially diabetic.'

Pulmonary candidiasis is grave. Though many of the cases heal spontaneously and completely, incomplete recovery may result in the chronic bronchial type of infection. Occasional death occurs in cases with 2 or more infected lobes with dense pneumonic process.

The prognosis should be a guarded one in the generalized and granulomatous types. In acrodermatitis enteropathica the ultimate prognosis is poor because the general health suffers. It is difficult to eradicate the fungus from the gastrointestinal tract. The prognosis is hopeless in endocarditis and meningitis.

TREATMENT:—*General*:—(1) For debilitated cases nourishing diet with vitamins; (2) correction of predisposing factors *e.g.*, soap and water, use of cotton and rubber gloves; ill-fitting dentures, excessive sweating etc.; (3) diabetic regulation when present; (4) weight reduction in the obese; (5) stop antibiotics if candidiasis develops during therapy; (6) eradicate all foci in the skin and gastrointestinal tract; and (7) low-calorie (doubtful value), low-starch diet with dextrose in place of cane sugar.

For oral infection:—(1) Alkaline mouth washes with 10% glycerine borate; (2) gentian-violet 1: 100,000 for gargles and 1: 10,000 in 10% alcohol, as paint every 6 to 12 hours for 4 or 5 days and then stop for avoiding irritation to the mucosa; (3) gentian-violet aqueous 1 to 2% for skin and for thrush; (4) sodium caprylate; (5) application of Lugol's solution diluted 50% in water.

For vulvovaginitis:—(1) Alkaline douches with borate or bicarbonate; (2) gentian-violet 1: 10,000 aqueous, paint weekly, biweekly or on alternate days; (3) application of vaginal jelly containing sodium or calcium bentonite; (4) autogenous

r.) vaccine in resistant cases; and (5) gentian-violet suppories for vaginitis.

For pruritus ani:—Gentian-violet suppositories (2 gr.)

For cutaneous candidiasis:—Easily treated with 2% Eosin in oholic solution, or Castellani's paint or Whitfield's ointment strength): Onychia, paronychia, intertrigo-1: 4,000. Potasum permanganate or 1: 5,000 of perchloride of mercury bath or aks, thrice daily, followed by the application of gentian-violet %; also rubbing with 3 to 10% Hydrarg ammoniata ointment. or resistant-lesions-onychia, paronychia and perleche-unfilered X-rays-75; weekly for 4 to 8 weeks. For more resistant esions, desensitization with vaccine. One per cent Silver nitrate in nitrous ether for intertrigo. One per cent Tincture of iodine. Large doses of iodides, orally. Five to 10% chrysarobin in collodion for painting daily for paronychia. Boric acid ointment and sodium perborate.

For systemic candidiasis:—(1) Saturated solution of Potassium iodide. Begin with 5 drops *t.d.s.* Increase by 1 drop per dose to 20 drops *t.d.s.* or even 100 drops *t.d.s.*, with water or milk. If symptoms of iodism appear, stop and restart when symptoms have disappeared. This should be continued for months or even years. Desensitization of hypersensitive patients and elimination of tuberculosis are necessary before starting iodide treatment. (2) Potassium iodide 10 to 12 gms. a day for 3 to 6 months; (3) some cases benefit by ethyliodide inhalation; (4) 0·5% gentian-violet filtered (in Seitz or Berkefeld) intravenously for pulmonary candidiasis, doses being 5 mg./kg. of body weight repeated daily or alternate days, for 7 to 10 days; (5) specific antialbicans rabbit serum for pulmonary candidiasis with negative skin test and negative agglutination test; (6) "Griseofulvin 250 mg. tablet for a dose 1 to 2 gms./day orally is nontoxic, moderately fungicidal and markedly fungistatic "but has no action on nonmycelial fungi and so may not be effective for candidiasis." Nystatin (Mycostatin) is effective locally for cutaneous moniliasis; and orally given with other antibiotics suppresses the tendency to monilial infection. Fungicidal when directly in contact. For vaginal insertion tablets of 100,000 μ. Amphoterin B (Fungizone) is curative for systemic candidiasis, the dose being 1·0 mg./kg. day by intravenous slow drip, at daily intervals, to a total dose of 1·0 gm. Nausea, vomiting and febrile reaction are common during treatment. Watch kidney function and hæmopoietic system; (7) favourable reports have been made with the nontoxic, inexpensive brilliant-green aerosol; (8) in acrodermatitis enteropathica-Diiodohydroxyquin orally 600 mg. four times daily, for weeks or months give favourable response; and (9) for candidids treat primary focus with cortisone.

Case report.—Mrs. S. K., a Hindu female housewife, 52 years, was brought to us on 4-8-'59 for severely itchy, widespread, vesicular, oozing crusted lesions, soreness of the mouth with excessive salivation of 2½ months' duration. It started nine months

CANDIDIASIS

FIG. 1.

FIG. 2.

back with a sore-throat. According to the advice of a dentist, total extraction of teeth was done about 2½ months back, as a treatment for the sore-throat which however, continued. After extraction, small erythemato-vesicular lesions appeared over the front of her chest. The vesicles ruptured and left red, denuded, oozing areas. These lesions spread to the entire front and back of the trunk and later the condition flared up and involved both the groins, the perineum, the natal cleft under her pendulous breasts and then became generalized. Simultaneously the mouth became sore and white patches appeared on the tongue and buccal mucosa. Examination revealed that she was greatly distressed and was pale. The skin of the sternal, inframammary umbilical and pubic areas, the back and extremities were all full of vesicular lesions, excoriations, denuded raw oozing areas and crusts. The lower lip was sore and its right side was covered with crusted, granulomatous-looking lesions and there was constant dribbling of saliva. The mouth was sore and the tongue and the palate were covered with white patches. Speaking and eating food were difficult. The itching was irresistible and caused insomnia. There was no involvement of the genitalia. She was diagnosed as moniliasis and investigated and treated with [illegible] by mouth, antiseptic drying lotion with Ichthyol and Injections of Liver extract and Vitamin B complex as supportive. Since the condition did not improve she was given Mysteclin V capsules on 17-8-'59 one every six hours. New

lesions appeared, though the older ones got better, and her general conditions was worse ; she was hospitalized on 24-8-1959.

Her temperature was 98·4°F and pulse was 92 minute. The nails were normal. Lungs appeared normal, clinically. The C. V. system and abdomen showed nothing abnormal.

FIG. 3.

FIG. 4.

She was given saline intravenously ; Mysteclin V capsules, one 6 hourly ; Deltacorlin 5 mg. six hourly orally ; Injections of Liver extract and vitamin B complex 1 cc. each daily. Locally gentian-violet 1 : 1000 solution was painted and she was placed on a low starch diet.

Investigations.—*Urine* :—Reaction : – acid ; sugar : trace ; acetone : nil ; cubical and squamous epithelial cells ++ ; occasional pus cell was seen.

Stools :—No cysts or ova—found ; when repeated the urine had albumin—present ; sugar : trace, greenish reduction.

Smear and culture from bullous skin lesions :—spores of fungi, staphylococci, gram-negative bacilli detected and isolated.

Oral lesions :–Direct smear : yeast-like budding cells present also gram-negative bacilli +.

Growth on tartaric acid dextrose agar medium showed candida-like colonies with fine mycelial fringes from the periphery of the colonies.

Sugar reactions :—Glucose : acid and gas ; Maltose : acid and gas ; Sucrose : acid and gas ; and Lactose : no fermentation.

Animal inoculation :—Intracutaneous inoculation of a 24 hours' suspension grown in peptone-water produced no abscess-formation. I.V. inoculation

Blood:–Hb. 10·5g.%; R.B.C. 4 mill./cmm.; W.B.C.—6, 400/cmm.; P. 68; L. 30; M. nil; E. 2%; E.S.R. 44 m.m. fall in 1st hour.

Glucose-tolerance test:—

	F	I	II	III	IV
Blood mg%	90	120	175	180	170
Urine sugar	Nil	Nil	Nil	trace	trace.

X-ray chest:—Normal: B.P. 110/70 mm. of mercury.

A fortnight after admission, she was much improved. The skin and mucosal lesions were healing. Later she continued to progress satisfactorily; but at intervals fresh crops of skin lesions developed with severe itching. She was discharged on 24-10-'59 in a much improved general condition but with bouts of exacerbations. Now she is having gentian-violet 2% in zinc paste and Mycostatin ointment besides supportive therapy. Her urine repeatedly examined for sugar, was normal.

Summary.—A review is presented from literature of the ætiology, pathology, diagnosis, prognosis and treatment of candidiasis. A case report of generalized candidiasis due to C. tropicalis infection is presented.

Acknowledgement.—My grateful thanks are due to Dr. L.N. Mahapatra, Major Chopra; L. R. Das Gupta for the laboratory data and Dr. I.P. Bhalla and Mr. Nair, our artist for their help in preparing this report. I am thankful to the Medical Superintendent for according permission to utilize hospital records.

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ENDOCARDITIS AND AGE

The clinical picture of subacute bacterial endocarditis in elderly persons is often confusing and atypical. Clinical features prominent in younger patients with endocarditis are either lacking in elderly patients or obscured by other disease processes. Gleckler reports ten consecutive patients over 55 years of age who were admitted to a county hospital with subacute bacterial endocarditis—fever, petechiæ and splenomegaly—present. The remaining cases were thought to be senile psychosis (three patients) and atypical cases of gastrointestinal disease, renal insufficiency, simple wasting and apoplexy. The author emphasizes the importance of serious consideration of any cardiac murmur in the aged patient with an obscure clinical problem. The murmur may point to an underlying subacute bacterial endocarditis.—(*Geriatrics*, *15*: 152, 1960, via *G.P.*, August 1960).

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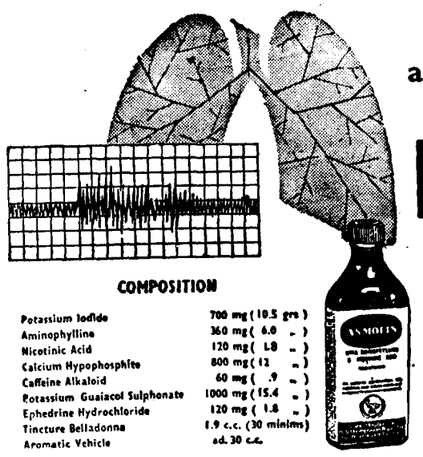

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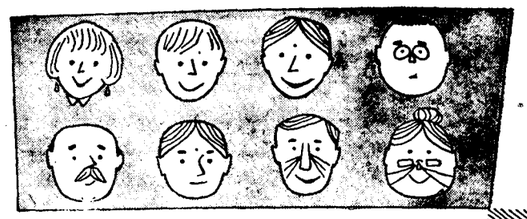

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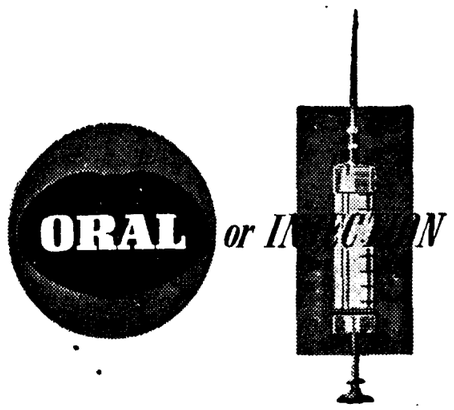

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at home, rather than go out of their homes for surgical treatment. Inspite of the fact that many of us possess the requisite knowledge and experience of major surgery, we restrict ourselves to very minor operations merely because of the lack of facilities for anæsthesia and so do not dare to attempt major surgery. This local anæsthetic lignocaine will prove a boon to those surgeons, who are prepared to undertake major surgical work but do not do so for lack of anæsthesia-facility. I plead for an extensive trial of this technique by more surgeons and request them to publish the results of their experience so as to be of benefit to still other surgeons, working in backward areas and under difficult conditions where modern general anæsthesia is not available and will probably take decades to reach.

LIGNOCAINE

The manufacturers of lignocaine state that 500 mg. should never be exceeded and for children the figure is proportionately lower. Most medical publications support this figure, and if a firm ruling must be given for everyday use it cannot be bettered. However, more can be given if it is injected into a relatively avascular area and if the rate of absorption is further slowed by vasoconstriction produced by the addition of adrenaline. The concentration of a local analgesic drug injected should never be greater than that needed to produce a given effect. Lignocaine *is about twice as powerful as procaine* and need rarely be given in a stronger concentration *than 1% (1·5% for extradural analgesia)*. The stronger the concentration the smaller the volume which can be used. Thus if 500 mg. is the maximum dose, 100 ml. of 0·5% solution, 50 ml. of 1%, and 25 ml. of 2% provide it.

Adrenaline in a local analgesic solution causes vasoconstriction, leading to a reduced rate of absorption and longer analgesia. By delaying the rate of absorption of a drug in relation to the rate at which the drug is destroyed in the body it also gives some protection. The perineum, particularly in labour, is certainly a highly vascular area, so that toxic reactions are particularly likely to follow too high doses of lignocaine, particularly when injected *without* the addition of adrenaline to delay absorption. But adrenaline is *not* without its own hazard. Too many "reactions" are due to an excess of adrenaline rather than the local analgesic drug itself, in consequence of a failure to appreciate that the *maximum safe dose of adrenaline in the adult is 0·5 mg. (0·5 ml. of the usual 1 : 1,000 solution)*. This allows a volume of 100 ml. of solution with a concentration of 1/200,000 adrenaline to be injected, and since stronger solutions may cause local damage to the tissues there is no reason why a higher concentration should ever be used. In any case, solutions as weak as 1/6000,000 cause effective vasoconstriction, though the effect may be delayed slightly. Lignocaine is a more effective local analgesic than its predecessors, and it has gone far towards restoring local analgesia to its useful place in practice. *This applies particularly to pudendal block in obstetrics.*—(*Br. Med. Jour.*, 6-1-1962).

RHINOPHYMA: SURGICAL TREATMENT

The aim of surgery is to remove the excess growth while preserving the deep epithelial elements necessary for re-epithelialization. Suggested method of treatment consists of sharp dissection for quick removal of the major portion of the mass, followed by dermabrasion, which affords a better control over the irregularities of the nasal contour and more safety in preserving the deep epithelial layer.—(*Arch. Otolaryng.*, Vol. *74*: 251, Sep. 1961, via *J.A.M.A.*, 23-9-1961).

LOWER-URINARY-TRACT

At the annual meeting of the British Association of Pædiatric Surgeons held on 12-9-1961, Dr. D. I. Williams (London) discussed the diagnosis and operative treatment of urethral valves and stricture. He pointed out that the narrowest part in the urethra in the child is at the penoscrotal junction, whereas in the adult it is in the bulb, and that strictures in the child appear quite soft and dilate easily but are often very resistant to treatment. In his opinion there is incontrovertible evidence in support of fibroelastosis in one type of posterior urethral obstruction in male children, an opinion which did not meet with general acceptance. N. O. Ericsson (Stockholm), discussing posterior urethral valves, the commonest form of obstruction in this region in the male child, emphasized that a voiding cystourethrogram was essential. Of those cases in which dilation of the urinary tract was restricted to the posterior urethra, enuresis was present in 67%, whereas infection was found in only 8%. When the dilatation affected the upper urinary tract as well, enuresis was found in only 32% but infection in 66%. Resection of the valves had reduced upper-urinary-tract dilatation in 21 of his 36 cases, and of his entire series only 2 had incontinence after operation and none had strictures. In incongenital bladder-neck obstruction endoscopy alone or with cystourethrography was not enough; the neck must be observed during voiding cystourethrography. Infection, which was found in 80% of his cases, was cured by operation in only about half.—(*The Lancet*, 7-10-1961).

ULCERATIVE COLITIS IN CHILDREN

At the annual meeting of the British Association of Pædiatric Surgeons held on 12-9-1961, Dr. Th. Ehrenpresis (Stockholm) reviewed the cases of ulcerative colitis which had been treated in the four children's hospitals in Stockholm and showed that the incidence of this disease had increased considerably. In the 9 years to 1960, 23 patients (27% of the total) were operated on, the indications being perforation of the colon, fulminating disease, total disablement for 1 year, or partial disablement for 5 years. 7 of these operations were undertaken as acute emergencies. The operation which was chosen depended partly on the degree of involvement of the rectum. In 10 colectomy and anastomosis of the ileum and the rectal stump was done when the rectum was not involved. In 8 other moderate involvement of the rectum led to ileostomy with colectomy, and in 5 in whom there was severe rectal involvement the colon and rectum had to be excised. The rapid improvement and gain in weight which was constantly observed after operation was associated with only 2 to 5 stools a day in those in whom the ileum was joined to the rectum, but with rather more frequent movements when ileostomy remained. A recent psychiatric investigation of the patients treated by operation showed remarkably good tolerance of the ileostomy and no difference between those treated surgically and those who had responded to conservative treatment.—(*The Lancet*, 7-10-1961).

TRIAMCINOLONE IN DERMATOLOGY

M. Laugier *et al* (*Sem. Hop. Paris*, Jan. 20, 1961) treated 82 patients who had skin diseases with 8 to 60 mg. of triamcinolone daily. The drug was most effective for simple eczema, toxic erythroderma, and erythroderma psoriaticum. There was a fair response in patients with parakeratosis and chronic ulcerous eczema. In patients with lichen plannus, treatment with 16 mg. daily for at least one month was necessary. In patients with psoriasis this drug was more effective than other corticoids. There are no contraindications to its use. It is well tolerated even when given for a long period.—(*J.A.M.A.*, 9-9-1961).

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Editorials

THE POLIOMYELITIS PROBLEM— PREVENTION AND CONTROL

(A review of currently available knowledge)

ANY infectious disease can be eradicated when the chain of transmission necessary for the survival of the infective agent in nature is broken. The alimentary tract of human beings has now been definitely shown to be the site for polio viruses to multiply. It was not until September 1912 that poliomyelitis became a compulsorily notifiable disease in England and it was only in 1926 that the number of cases approached minor epidemic proportions. Suddenly and for no very obvious reason, a severe epidemic broke out in 1947, a hot year, with more than 5 times as many cases as in the worst previous year. Possibly massive movement of the people during and immediately after the second world war played their role in introducing new and virulent virus strains into susceptible counties of England and Wales. During the same period there was an enormous increase in the number of polio cases in the U.S.A., much greater than in England, and in 1952, the peak year, nearly 58,000 cases were notified in U.S.A. This alarming rise stimulated intensive research and in 1955 the Salk vaccine for preventive inoculation was made widely available[1]. In 1949, Dr. JOHN ENDERS of Harward University working with Dr. THOMAS WELLER and Dr. FREDERICK ROBBINS found that polio virus could be grown in test tubes on a tissue culture of monkey kidney cells. This was the first practical attempt at growing the virus in quantities which could make a prophylactic vaccine possible. Enders' work paved the way for Dr. JONAS SALK and his co-workers at the University of Pittsburgh, who conceived the idea of growing all the three types of virus, inactivating them with formaldehyde and then combining them into a complete vaccine. The large-scale cultivation of the viruses in monkey-kidney tissue-cultures remains the keystone of production. All necessary precautions are taken during every stage of the bulk manufacture of this vaccine, against bacterial contamination. To make certain that no live virus remains in the vaccine, samples are injected into healthy monkeys and the animals observed for a month. Vaccine samples are also added to tissue cultures to see if any growth takes place, indicating the

presence of live virus. Samples from each lot are also tested in mice, guineapigs and rabbits to insure safety standards which often surpass the scrupulous requirements of the National Institutes of Health.[2]

Salk vaccine thus prepared was found on actual use to exhibit marked variations in its antigenic potency from lot to lot. Improvements desired in commercial Salk poliomyelitis vaccine were the elimination of lot-to-lot variations in potency, increase in mean vaccine potency, and elimination of foreign antigens, particularly host (monkey kidney) antigen. These objectives were achieved by the inactivation of purified, concentrated poliomyelitis virus to give a vaccine containing standard optimal quantities of poliomyelitis antigen which are essentially free from nonviral antigens. The relatively avirulent Parker type I poliovirus was substituted for the highly neurovirulent type I Mahoney strain. Removal of the monkey kidney antigen minimized the hazard of inducing allergic or auto-immune reactions[3].

"Though the incidence of the paralytic disease was appreciably reduced, field and experimental studies have now shown that the immunity provided by this vaccine does not prevent the multiplication of the polio viruses in the intestinal tract. Thus, in a community in which a large proportion of the population has been protected against paralysis by the Salk (killed-virus) vaccine, the polio-viruses readily maintain a continuous cycle of transmission and can paralyse those who have never acquired immunity or have lost it. This phenomenon, obviously accounts for the continued occurrence of thousands of paralytic cases of poliomyelitis in the United States and of epidemics of considerable magnitude during recent years in Hungary, Canada and Israel where the Salk vaccine had been administered to the major portion of the susceptible population[4].

Although the Salk Vaccine was considered in many countries to be effective and good enough for prophylaxis there were obvious difficulties in the administration of the vaccine. It is usually injected 3 or 4 times every 18 months, in spite of which it was found that about 30 per cent of the vaccinated children did not acquire immunity. Again as with all vaccinés, the parenteral administration of the Salk vaccine calls for great care and skilled personnel.

For some considerable time now, research had been going on in U.S.A. to produce a thoroughly satisfactory vaccine that can be taken orally and will still be quite efficient in preventing the disease. This research culminated in the production of the new Sabin vaccine. The essential difference between the two vaccines is that, while the former is a dead culture, the Sabin is a

live culture, in which the virulence and disease-causing potentialities of the virus have been attenuated (bred out)[1].

Dr. Sabin claims that "the immunity produced by this live attenuated orally administered poliovirus vaccine not only protects the individual against paralysis but also alters the susceptibility of the intestinal tract to multiplication of the polioviruses[1]." Shortly after it is taken by mouth a mild and symptomless illness is produced, which stimulates immunity. The virus is eliminated from the intestine of the subject and he cannot become a carrier while he remains immune himself. This new vaccine is also useful to control effectively an epidemic which has already started. The main advantages claimed for the new vaccine are: that it may give better immunity; it can be given by mouth, and it is cheaper to produce. Comparative tests made in Russia showed that the incidence of polio in children who had received 3 doses of the Salk vaccine was 6·8 per 1,00,000 while in children who had received one dose of the new Sabin oral vaccine it was 1 per 1,00,000 giving a protection rate of 48 per cent for the Salk and 92 per cent for the oral vaccine of Sabin. That this oral Sabin vaccine was found quite safe to use, was vouched by Prof. Dick and Dr. Dane of the Belfast City Hospital in a report published by them to the *British Medical Journal* in 1958, to the effect "To the best of our knowledge no illness definitely attributable to the use of attenuated polio virus vaccines has so far been reported in thousands of persons after different trials.[1]" The exhaustive researches since made by them in England, by workers in Russia and other countries and also by Dr. Sabin himself in Cincinnati, Ohio, have all been documented in leading medical journals during the last 2 years.[5,6,7,8,9] Dr. Sabin presented his research findings on his oral vaccine to the 42nd Annual Session of the American College of Physicians held at Miami Beach early in May last year. A short but concise abstract of the findings will be found at page 270 of this issue under "*Gleanings from the Medical Press.*"

The manufacture of oral poliomyelitis vaccine was started in Russia in 1956 by the eminent Soviet virologist Prof. Mikhail Chumakov,[10] who visited the U.S.A. and obtained live cultures of Sabin's attenuated vaccine and in England in 1959 also from the Sabin's poliovirus strains according to specification laid down by him[11].

A report issued in October 1961 by the British Information Service describes the success of an important trial initiated by the British Medical Research Council and conducted by the Public Health Laboratory Service[12]. Over 300 infants between six and 12 months old were divided up into three groups. The first group was given one dose of vaccine containing all three types of protective virus; the second group, three doses of the

same vaccine at four-weeks' intervals; and the third group, three separate doses of vaccine, each containing only one type of protective virus, at four-weeks' intervals. The infants were visited twice weekly until one month after the last dose was given, and no ill-effects due to the vaccine were seen. The results showed that the best protection was achieved in the second group, closely followed by the third; that immunity at least as good as with the injected vaccine was maintained for over one year; and that immunity only developed after the protective virus had established itself in the bowel. The results mean that whole population can now be protected by three doses of only one vaccine containing all three types of protective virus, and the possibility exists of wiping out the disease as it is known now.

The introduction of the oral vaccine, was naturally followed by a controversy as to the relative merits and usefulness of the Salk and Sabin vaccines. "The reliance on safety and efficacy must rest primarily on the results obtained from the immunization of man, and there is evidence from large-scale vaccination campaigns conducted in Czechoslovakia, Mexico, and the U.S.S.R. that the Sabin vaccine is safe and effective.[13] Recently the results of an extensive campaign in Cincinnati, U.S.A., have provided additional confirmatory evidence.[4] "These conclusions, however, were not based on the results of strictly controlled trials, which are difficult to conduct successfully with living poliovirus vaccine: they are based mainly on the results of clinical surveys after vaccination, on the incidence of poliomyelitis in vaccinated groups compared with that in appropriate control groups, and on the ability of the vaccine virus to colonize in the gut as well as to raise the level of poliomyelitis antibodies in the blood. Nevertheless, in view of the overwhelming evidence from the extensive campaigns in which many millions of persons were vaccinated, it would be difficult to doubt that the Sabin oral vaccine is in fact safe and effective. A great advantage of the oral vaccine is the case with which it is administered, compared with the repeated injections necessary with the Salk inactivated vaccine, and this undoubtedly leads to the readier acceptance by the public of vaccination by the oral preparation. Sabin vaccine has also been accepted by many countries as an effective prophylactic. It has been shown to produce antibodies in a high proportion of susceptible persons either by direct vaccination or by contact with those who have been vaccinated, to boost antibody production in those who have previously received the Salk vaccine, and notably to reduce the incidence of paralytic cases.[11,14,16]

"The oral vaccine as stated already has the property of producing an intestinal resistance to infection, and thus when mass vaccination of a whole community is carried out over a short

period of time there is a break in the chain of transmission of polioviruses, which quickly disappear from the population. On these grounds it is argued that oral vaccination should be conducted on a community-wide basis during a period when the incidence of interfering enteroviruses is low, that it should be given to the largest possible number of persons regardless of whether they have had Salk vaccine, and that special attention should be paid to the vaccination of pre-school children, the most active spreaders of polioviruses[11]."

Oral poliomyelitis vaccine differs from other living vaccines in that the virus is grown in monkey-kidney tissue which can harbour simian viruses that are difficult to detect and of unknown pathogenicity for man. One such virus, vacuolating agent, has undoubtedly been present in batches of oral vaccine that have been administered to man, and although Drs. D. I. MAGRATH and J. O'H. TOBIN and Mrs. KATE RUSSELL[11] report that it appears to be non-infectious when given by mouth it would be wise at this stage to require that the vaccine should be entirely free from all extraneous viruses. Oral poliomyelitis vaccine also differs from other living vaccines in its capacity to spread from vaccinated to non-vaccinated persons and in the doubtful genetic stability of the viruses used in its preparation. We would therefore like to commend the advice contained in the concluding para of the Editorial in *B.M.J.* of 29-7-1961 to the effect "It is therefore, of the utmost importance that careful community surveillance should be exercised when the vaccine is used for routine immunization. With proper safeguards in its manufacture and use, oral poliomyelitis vaccine offers the greatest possibility of completely eliminating poliovirus as a human pathogen."

As a result of specialized research at the Human State Institute for Serobacteriological Production and Research at Budapest, and the Institute of Microbiology University Medical School at Pecs, Drs. MAROCZI, RETHY, KELEMEN and PACSA[15] have reported their observations on the efficacy of a trivalent oral poliomyelitis vaccine and combined diphtheria-tetanus and pertussis immunization in a trial made by them on 3 to 9 months' old infants alongside of suitable controls. The results of their experiments justify the view that immunological inhibition does not arise in respect of any of the components if oral trivalent poliomyelitis vaccine and combined Di-te-pe are given together.[15]

In this necessarily brief and impassioned review we have attempted to bring before our readers as clearly as possible the state of our present knowledge regarding the prophylaxis and control of poliomyelitis. We hope that this review will furnish all available information to date and help our readers in their choice of the proper prophylactic to suit their requirements.

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CARDIOVASCULAR DISEASES

Two very important Conferences on heart diseases were held at Indore and Bombay on the 19th of January 1962 and 3rd February 1962 respectively.

In the course of his presidential address to the annual conference of the Cardiological Society of India held at Indore, Dr. A. K. BOSE laid special emphasis on the preventive aspects of heart disease, as the mortality in India from cardiovascular diseases is quite as high as in other countries of the world. Referring to the important advances made in the field of cardiology, he said that preventive methods in the light of present knowledge could be taken with benefit against the three very important heart diseases *namely* :—coronary heart diseases, high blood-pressure and rheumatic heart diseases. Regarding the various factors which produced coronary heart disease what the cardiologists could do was to advise people in general what they had been advising their individual patients : *namely*, reduction of obesity, avoidance of sedentary life and smoking and drastically limiting the intake of fat in diet, particularly animal fat and the hydrogenated vegetable oils.

About high blood-pressure, he said that a large number of them could be brought back to normal stage, and kept so, provided certain environmental changes could be produced. In India the largest number of deaths from heart disease, occur in people below 30, due to rheumatic heart disease; this condition is increasing in India due possibly to lowering of living conditions, particularly in big cities.

A three-day International Seminar on 'Arteriosclerosis' was inaugurated by the Chief Minister of Maharashtra at Bombay on the 3rd February 1962. Twenty-five delegates from all over the world, including Dr. PAUL D. WHITE, President of the International Society of Cardiology Foundation, U.S.A., participated in the seminar. The W.H.O. had also sent an observer.

Lt. Gen. S. P. BHATIA, Director-General, Armed Forces Medical Services, welcomed the delegates. Inaugurating the scientific session of the seminar, Dr. PAUL D. WHITE praised the work of Indian experts on the subject and said "you in the east are already setting an example to the rest of the world in your co-operative activities in the cardiovascular field." Dr. K. K. DATEY of Bombay in his short but very informative address, called attention to the wide prevalence of arteriosclerosis that is responsible for the cardiovascular diseases, accounting for over 50 per cent of the deaths in the civilized world. The tragic part of the whole affair is that these catastrophes afflict people in the prime of life and when they are at the zenith of their usefulness to society. He traced the history of heart pains from the time of Seneca, the Roman physician (65 A.D.) through those of BONET of Paris (1679), LEONARDO DA VINCI, the Italian artist (15 century), LANCISI of Rome (1706), WILLIAM HEBERDEN of London (1782), and JOHN HUNTER, the great anatomist (1790), and CORVISART, Napoleon's physician (1816) down to the present day and said that though the cause and effect are now clear, the reason for the arteriosclerosis itself was still being feverishly sought all over the world.

Our hopes of being able to prevent heart diseases naturally therefore, depend on the success of these endeavours. So far, only a glimmer of light is becoming visible in the far horizon. We certainly know now more about arteriosclerosis than we did in the last century ; thus we have noticed that the arterial wall degeneration is more common in certain families and that it is associated often with obesity, diabetes mellitus and high blood-pressure. It is more prevalent in certain parts of the world and even in certain races, but we do not know why ! The International Seminar held at Bombay, was summoned mainly for the purpose of getting together the heart specialists from all over the world, on a common platform and having a free and frank exchange of ideas so that knowledge can progress and humanity benefit. Numerous delegates from distant lands, Belgium, England, U.S.A., Australia, Japan, Switzerland etc. gave the results of their experiences and of their original researches on the subject. It is the hope of the organizers to establish firmly the Indian Heart Foundation which has been a cherished wish of the Indian medical profession. Such foundations have been doing excellent work in other countries of the world in the direction of providing improved facilities for research, and thereby evolving better methods of treatment for cardiac patients.

Dr. PAUL D. WHITE, the renowned Cardiologist of America, participated actively in the seminar. He also delivered public

lectures on heart diseases. In a very interesting paper on *'Atherosclerosis in its widespread clinical manifestations and comparative worldwide prevalence'* he referred to two of the most fascinating newer concepts in the field of medical science based on the research findings of recent years, relating to atherosclerosis. "They are, *first*, its wide distribution throughout the entire body and its manifold clinical evidence when it reaches disease proportions, and *second*, its very great variability in world-wide distribution."

"Quite naturally, it was the pathologist who first became interested in this abnormality of the arterial wall, finding it most prominently and commonly in the aorta. Then it was the clinician especially interested in cardiovascular disease who discovered its importance when it seriously invaded the coronary arteries. In its turn, involvement of the iliac and femoral arteries attracted the attention of the peripheral vascular surgeons. The neurologists discovered in their turn that many of the strokes, previously ascribed to hæmorrhage, were actually due to obstruction by this disease of the blood-flow through the carotid and other arteries supplying the brain. And, finally, atherosclerosis of the arteries to the viscera, including the kidneys, now and then challenges the diagnostic and therapeutic acumen of the internist and abdominal surgeon. Thus, this disease is bringing several specialists together in research as well as practice."

Whereas many diseases, such as the common infections of tuberculosis and rheumatic fever, cancers of various sorts, high blood-pressure, and mental disorders, appear to be common the world over, atherosclerosis of clinical importance varies tremendously, 'being quite evidently more common in the prosperous countries of the world or in that segment of any population in the world which lives the "soft life." Thus, those in the U.S.A. and the Bantus in Africa are antipodal in this connection, the Americans on the one hand being subject to important degrees of presenile atherosclerosis all over the body in about half the population, while in Africa this disease is rare.' Research is therefore, still needed to determine how much of this difference can be accounted for by race and how much by environmental factors, chiefly the ways of life. We quite appreciate his candid expression of the fact that time, money, and energy should give the answers within a decade or two and we would only impress on our readers the need for their active co-operation in this important research.

Several important papers of outstanding merit and research value were presented at this seminar and discussed by the delegates. Madras was represented by Dr. M. G. Varadarajan, Radiologist in the Government X-ray Institute, who presented a joint paper on 'Carotid Occlusion' by himself and Dr. B. Ramamurthi, Neuro-surgeon of the Madras General Hospital. We hope to be able to give our readers a review of the more important and interesting papers in our future issues.

THE ERADICATION OF SMALL-POX IN S.E. ASIA REGION

(Foreign experts to assist in Research)

More than half a century of vaccination has not been able to control the incidence of this dreadful disease in India. In fact, the disease has been on the increase during recent years, making people feel that vaccination does not help. But in other countries of the world, this disease has practically been wiped out, with the help of intensive campaigns of successful vaccination. If it has not been possible to do likewise in India, there should be valid reasons for the failure. Several factors operate to our knowledge, besides any others still to be found. Among the chief reasons we would unhesitatingly place the ignorance, apathy and deliberate evasion of the majority of the people in rural areas—even urban dwellers are not exempt from this weakness, in fear of the induced reactions often causing complications. At the mere sight of the vaccinator on the village border all children in the village disappear from view and no amount of persuasion, cajoling and threats of prosecution would appear to have brought these recalcitrants to their senses; and again, we have had authentic reports from responsible officers of the Public Health Department, that people who produce their children for vaccination, under fear of prosecution, wash or wipe off the marks and the applied lymph immediately the vaccination is over. The poor vaccinator is helpless to prevent this.

We have also heard that people resort to devious and improper methods of evasion by obtaining false certificates, to which unscrupulous doctors are privy. This was mentioned by no less a person than our esteemed Chairman of the Madras Legislative Council Dr. P. V. Cherian who inaugurated the seven-day Inter Regional Seminar on Small-pox at Madras on the 16th February 1962.

Dr. Zahra, the Regional Adviser of the WHO in his welcome address referred to the work of the organization in eradicating smallpox in other areas and urged the need for the Governments in the S.E. Asian Region actively helping in the mass-vaccination programme. This programme sponsored in India by the Indian Council of Medical Research in co-operation with other organizations and the Union Government has not made much

headway till now, though the aim was to get the entire population of India vaccinated in 3 years, through organized effort.

It is now widely accepted, conscientious objectors, and sceptics not withstanding, that vaccination offers effective protection against the virus of smallpox and this fact was again prominently stressed by Dr. N. Parthasarathy the State's Director of Public Health at the Seminar. He mentioned several reasons why inspite of vaccination, the incidence of the disease remained high :—Unprotected persons constitute a potential danger to the community; the nonreporting of smallpox cases and the ineffective supervision of vaccination work. The element of conscience in some of those entrusted with the work of protecting the people against this horrible disease, is found to be often lacking and the desire of the ignorant folk to escape vaccination, offers added incentive to such persons to abet the crime—for crime it is to deny a child the right to live free from infectious diseases.

Dr. B. V. Sundarababu, the Health Officer of the Madras Corporation recounted the difficulties he experienced in vaccinating fifteen lakhs of people in the Madras City particularly when their hearty and willing co-operation is greatly lacking, even in the presence of endemic cases in their midst.

We are told that a laboratory is to be attached to the City's Infectious Diseases Hospital, which has now been reorganized and placed on a very efficient footing. It is proposed to carry out important research work on the efficacy of the new compound No. 23 in treating cases of smallpox and on the effect of *gammaglobulin* obtained from the sera of smallpox patients in preventing smallpox among contacts. Two experts, Dr. Kempe from the Colorado University and Prof. Dowine of the Liverpool University are expected to guide this research from July of this year. We do hope results of outstanding merit and practical value will emerge from this cooperative team work.

Delegates from Australia, Malaya, Hongkong, Japan, Korea, Borneo, Newzealand, Singapore, Vietnam and the Philippines attended and participated in the deliberations of the Seminar. WHO personnel and observers were also present.

RESISTANCE OF GONOCOCCI TO PENICILLIN

The sensitivity to penicillin of 1,984 strains of fully identified gonococci isolated before treatment was determined at 9 centres in England in 1959-60. Most strains were highly sensitive, but 13·2% were inhibited only by 0·125 to 1·0 unit/ml. penicillin. The incidence of these relatively insensitive strains varied in different areas and at different times during the survey. No evidence was found that the increase in resistance was progressive. Tests on strains isolated from patients in whom treatment with penicillin had apparently failed showed that such strains were often relatively insensitive to penicillin.—(*Lancet, 2 :* 226, July 29, via *J.A.M.A.*, 30-9-1961).

weeks in parts of the world and at times of the year when interference from other enteric viruses is minimal.

4. A varying proportion of unvaccinated persons becomes immune by intimate contact with young, vaccinated children.

5. Intestinal resistance in a large proportion of the child population leads to a break in the chain of transmission of polioviruses with a consequent protection of the unvaccinated as well as of the vaccinated persons in a community.

The fact that intestinal resistance to reinfection develops after infection by the attenuated polioviruses has now been amply documented by a number of independent investigators in the U.S.A., the USSR. and Holland. The expectation that such intestinal resistance to reinfection in a large proportion of very young children, who are the most important spreaders of the polioviruses, would lead to a break in the chain of transmission can now be documented both by epidemiologic observations and by extensive virologic studies that were carried out in his laboratory under two totally different field conditions.

Virologic observations:—The virological observations were made in the course of two separate studies (1) in Toluca, Mexico, on about 26,000 children in August 1959 who were given the trivalent vaccine within a few days and (2) in Cincinnati in April 1960 on pre school children who were given at monthly intervals the three types of oral vaccine in the order of I, III, II, each type being administered to a total of about 67,000 pre-school children within one week. Tests on rectal swabs from about 2,200 vaccinated and unvaccinated children, at different times after administration of the three types of vaccine, showed that an initial extensive spread of polioviruses to unvaccinated, susceptible persons both within the family and outside was followed by a rapid disappearance of polioviruses from the community by the end of September, which is the peak period for dissemination of enteric viruses. Under the conditions obtaining in Cincinnati, 100% of pre-school children who were without antibody developed antibody to all three types after receiving each of the three types of vaccine.

Available data indicate that intestinal resistance may persist for at least two years after vaccination, the longest period tested thus far.

In oral poliovirus vaccine therefore, we now have a simple tool with which we may attempt to rid large parts of the world of both paralytic poliomyelitis and the virulent viruses which cause it.

Gallop rhythms.—(*B.M.J.*, 30-12-1961).

Recordings of the heart sounds in healthy people reveal two sounds which the ear cannot usually detect as well as the normal first and second sounds. These "sounds" become audible in certain circumstances and then the listener hears a "triple" or "gallop" cadence in the heart rhythm.

The first of the "sounds" is the third heart sound, which is thought to occur in the following manner. Blood is returned to the heart throughout systole and diastole; during systole it cannot pass into the ventricles because the mitral and tricuspid valves are closed and it becomes dammed up in the atria. In diastole the ventricle relaxes, these valves open, blood rushes in the ventricles from the atria, and this stretches the ventricular walls. This sudden stretching produces a noise, rather in the way the wind will produce a noise as it fills an empty sail. As diastole progresses the ventricles continue to fill from the atria through the atrio-ventricular valves, which are wide open. Towards the end of diastole the atria contract, thus "super-charging" the ventricles by squeezing into them some of the blood which remains in the atria. This squeeze from the atria is sudden and stretches the already partially stretched ventricular wall. Once again a small and normally inaudible "sound" is produced. These two sounds may be accentuated in various ways and

they then reach levels at which they can be heard with the stethoscope. When the third heart sound is audible, as it frequently is in normal children, it produces the third-heart-sound gallop. When the atrial sound is audible it produces the atrial gallop. If a normal person has tachycardia diastole is shortened and the atrial "sound" follows so soon after the third heart "sound" that the ear gets the impression that they are synchronous. When this occurs the addition of two previously inaudible elements to each other may bring the volume of sound up to the level which the ear can detect. This is the so-called "summation" gallop, and unlike the other two it can occur in healthy adults. These three types of gallop—the atrial, third-heart-sound, and summation—are all caused by ventricular filling and they are the only once we recognize today. The simple nomenclature based on the physiology of the heart has helped to clear up some of the previous confusion, which was caused in part by the curious nomenclature adopted by earlier authors. Gallop rhythms may be produced either in the left side of the heart or in the right, as a result of disease which increases the intensity of the atrial or third heart "sounds," and sometimes both of these may be heard together, producing a four-beat cadence. If a gallop is produced in the left ventricle it is usually heard best at the apex during expiration; if in the right ventricle, it is usually heard to the left of the sternum at its lower end during inspiration. An atrial gallop usually indicates that the related ventricle is working under stress. Thus, a left atrial gallop rhythm may be heard in essential hypertension or in cardiac infarction. A right atrial gallop may be heard in pulmonary stenosis or in pulmonary hypertension. A third-heart-sound gallop may be heard in heart failure, in mitral incompetence, or in constrictive pericarditis, and it implies that the pressure in one or other of the atria is raised and that rapid filling of the ventricle occurs through a widely open or dilated atrio-ventricular valve.

Tuberculous meningitis.—(*Practitioner*, London, January, 1962).

The treatment of tuberculous meningitis remains somewhat controversial but, whatever the routine followed, there is no doubt that the earlier in the course of the illness it is begun the better, and that the prognosis is more favourable in the younger patient.

One routine which has given excellent results in conservative hands is 1 g. of streptomycin daily by intramuscular injection, with 50 mg. intrathecally in 5 ml. of saline each day for at least the first month of treatment; and 5 to 10 mg. per kg. body weight of isoniazid daily. Some authorities advise the addition of 10 g. of *para*-aminosalicylic acid (PAS) daily to the above routine, others a larger dose of intramuscular streptomycin (2 g. daily for the first four months) in place of intrathecal injection with its discomforts and its tendency to cause adhesions, to say nothing of the risk of accidental infection. The administration of cortisone during the first months of treatment reduces the tendency to exudation and fibrosis and diminishes fever and toxicity.

Treatment must be continued for at least six months, its intensity being controlled by serial C.S.F. examinations. Isoniazid and PAS can be continued with profit for a further similar period.

Chemotherapy of non-tuberculous infections of the lungs.—(*Practitioner*, London, January, 1962).

Dr. Neville Oswald, Physician, St. Bartholomew's Hospital and Brompton Hospital, says:—The management of acute non-tuberculous infections of the lungs is chiefly the responsibility of general practitioners treating patients in their hormones, and most infections respond to chemotherapy without a firm clinical, radiological or bacteriological diagnosis being made.

In general, if the illness is sufficient to cause a fever and constitutional upset antibacterial drugs should be given; if it is not, drugs are not immediately necessary. In addition to acute infections, the possibility of modifying the course of chronic and recurrent pulmonary infections by intermittent or prolonged chemotherapy has been investigated in recent years, and the results in chronic bronchitis and bronchiectasis have been encouraging.

Bacteriological examination of the sputum reveals a pathogen in about one-half of the specimens. If it is a pneumococcus, antibacterial therapy is straightforward, usually in the form of penicillin.

Choice of chemotherapy: Sulphonamides:—Sulphonamides are cheap. A preparation such as sulphadimidine is rapidly absorbed from the gut, maintains an effective blood-level and is excreted by the kidneys in a more soluble form than most sulphonamides, thus lessening the risk of crystal formation. It is effective in pneumococcal pneumonia and is a suitable choice for patients who are sensitive to penicillin. An initial dose of 3 g. may be followed by 1 g. four- or six-hourly with gradual reduction over a week.

Penicillin:—This is the most useful antibiotic in acute pulmonary infections. The *pneumococcus* and *Strep. pyogenes* never become resistant to it and severe infections of indeterminate bacterial origin, such as aspiration pneumonias and lung abscesses, are more likely to respond to it than to any other antibiotic. The dosage is up to 4 mega units a day according to severity, but 1 mega unit a day usually suffices. In children and in less urgent circumstances, an oral preparation such as phenoxymethylpenicillin is an alternative.

Tetracyclines:—The tetracyclines inhibit the growth of many gram-positive and negative bacteria, including the pneumococcus and *H.influenzae*, but strains of *Staph. pyogenes* are becoming progressively resistant to them. They are particularly useful in warding off infections in children and chronic bronchitics. Bronchitics with an intermittent or persistent mucopurulent sputum can often be saved from much disability in the winter by the judicious taking of a tetracycline. Ideally, they should have a small supply of tablets of which they may take 0·5 g. twice or three times a day as soon as a respiratory infection threatens.

Chloramphenicol:—This drug is among the most effective against *H. influenzae*, but has the great disadvantage that it may cause aplasia of the bone marrow. It is valuable in the treatment of postoperative pulmonary complications. It must *not* be used repeatedly or continuously in the treatment of chronic bronchitis or bronchiectasis.

SURGERY

Lung abscess—A review of forty-one cases.-(*Ann. Inter. Med.*, Vol. 55: 223, Aug. 1961, via *J.A.M.A.*, 14-10-1961).

Forty-one patients with pyogenic lung abscess, admitted to the Ohio State University Hospital over a 5-year period, were studied. They were evaluated from the standpoint of age, sex, location of abscess, predisposing factors, associated pulmonary disease, bacteriology, methods and results of therapy and residual pulmonary disability. Of the patients with a primary diagnosis of lung abscess, 42% had other pre-existing pulmonary lesions including bronchiectasis, bronchogenic cysts, asthma, and emphysema. Multiple sputum cultures showed that in 91% of patients a change from a gram-positive to a gram-negative organism occurred, or a new gram-negative organism emerged. Six patients had a more serious primary disease and were treated medically; none resolved their abscess. Of the patients treated successfully by non-surgical means none had associated bronchiectasis or symptoms for more than 4 weeks. Only surgical resection effected cures in those with bronchiectasis and/or symptoms present over 4 weeks. Of the patients with a primary diagnosis of lung abscess 71% were considered cured. The mortality was 6·4% and the remaining patients have chronic disease.

Surgical treatment of essential trigeminalgia.—*(Arq. Neuropsiquiat, 19*: 143, via *J.A.M.A.*, 30-9-1961).

Twenty-six patients with cervicofacial neuralgia, who had been unsuccessfully treated with medication, underwent retrogasserian neurotomy under general anæsthesia with endotracheal intubation. Neurotomy was selective in 24 patients, cutting the lower two-thirds of the trigeminal triangular plexus and preserving the motor root within Meckel's cavity behind the gasserian ganglion. In 2 patients there was total sectioning of the nerve. Complete relief from pain was obtained in the immediate postoperative period by 25 patients. A follow-up study of 19 patients indicated that there had been no recurrence of the neuralgia 3 years after the operation, but one patient complained of mild discomfort in the ophthalmic area and another complained of paresthesia in the trigeminal area. Postoperative complications were temporary facial paresis in 2 patients, corneal ulcer in 2, and labial herpes in 2. The development of corneal ulcer was attributed to cutting of upper neurofibrils originated in the ophthalmic root, a technique that was then discarded. Neurotomy of the lower two-thirds of the triangular plexus behind the gasserian ganglion is considered effective for permanent cure of trigeminal neuralgia and possibly of other cervicocephalic neuralgias.

Control of cirrhotic ascites.—*(Arch. Surg., 83*: 364, via *J.A.M.A.*, 9-9-'61).

The high mortality in operations in the presence of uncontrolled cirrhotic ascites may be reduced if ascites is controlled; but the usual medical regimen may require weeks and operation may be urgently needed. Ultrafiltration dialysis of the ascitic fluid, with removal of water and sodium and intravenous infusion back to the patient, is a practical method of performing paracentesis without protein loss. An unexpected result of this treatment in 8 of 9 patients with refractory ascites was a diuresis of sodium and water and stabilization of ascites without reaccumulation of ascites. Though not fully clear, it holds promise in preparing cirrhotic patients with uncontrolled ascites for urgently needed operations.

Treatment of dissecting aneurysm of the aorta.—*(Circulation, 24*: 290, via *J.A.M.A.*, 9-9-1961).

Dissecting aneurysm of the aorta pursues a rapidly fatal course in a high percentage of cases. Follow-up data on 72 patients treated surgically indicate that effective surgical treatment significantly alters the course of the disease and removes the threat of death by rupture. The operative mortality in these 72 patients was 26%. For lesion distal to the left subclavian artery, resection of the descending thoracic aorta with replacement by aortic graft, using hypothermia or the bypass pump, was successful in 80% of cases. Most patients surviving operation have been able to resume previous activities with minimal risk of sudden death by rupture of the aneurysm or failure of the aortic graft. The importance of (1) recognizing characteristic clinical manifestations; (2) precise roentgenographic diagnosis, and (3) effective surgical treatment in the management of this condition has been stressed.

Treatment of chronic duodenal ulcer by vagotomy and gastric drainage operation.—*(Gut., 2*: 158, via *J.A.M.A.*, 30-9-1961).

Hundred patients upon whom a vagotomy plus a drainage operation was performed were followed up for chronic duodenal ulceration. They found that vagotomy and a gastric drainage operation is usually an easier and safer procedure than partial gastrectomy, and is associated with a lower operative mortality and morbidity. Symptoms recurred in only those patients in whom the postoperative insulin response indicated that vagotomy had been incomplete. It is therefore, essential that vagotomy should be complete. The long-term sideeffects of this procedure are less frequent and less debilitating than those of removal of part of the stomach.

PÆDIATRICS

External cardiac massage in children.—(*Practitioner*, London, October, 1961).

Attention is drawn by W. B. Mc Kelvie and P. McKelvie (*British Journal of Anaesthesia*, July 1961, *33* : 371) to the value of external cardiac massage as a means of resuscitation of young children. Details are given of three cases (aged 4¾, 3¾ and 5 years, respectively) in which the children were successfully resuscitated after cardiac arrest. In two, external cardiac massage alone was successful; in the third this had to be supplemented by trans-abdominal (open) massage. The method is as follows: 'The operator stands on the right side of the patient; the flat of both hands is placed low down on the left side of the thorax, to cover some of the area over the sternum and floating ribs; very firm pressure followed by relaxation is applied at about the normal pulse rate. Adequate pressure may be applied with the patient supine on the Sorbo-covered operating table. In the case of a very small child, it is advantageous to place one hand behind the left side of the chest and the other in front to effect compression. The procedure may be carried out by the anæsthetist during the short time in which the surgeon is preparing to open the chest for direct cardiac massage.' It is suggested that should a heart beat not be felt after twenty to thirty 'strokes', internal direct cardiac massage should be carried out at once.

Teats.—(*Br. Med. J.*, 20-5-1961).

Dr. Rosemary Graham, M.B., B.S., Medical Officer, London County Council, says:—"It is surprising how little guidance on the use of teats for artificial feeding of infants is offered to the medical student or even doctors and nurses whose special interests lie in the field of child care. Many pædiatric textbooks deal fully with artificial milks but make slight reference to the necessary equipment for giving a bottle-feed. The result is that the practical difficulties facing a young inexperienced mother whose baby is not managing to suck successfully from a bottle may present as big a problem to her medical adviser. Hunger, vomiting, colic, and excessive crying can all be caused by faulty feeding technique and the use of the wrong teat, whilst infection such as gastroenteritis or moniliasis may follow, should cleansing and sterilization of the feeding utensils be inadequate.

For effective sucking from a teat a baby must be able to compress the rubber between his tongue and hard palate, occlude the neck of the teat between his jaws, and eject the milk through a hole that is large enough. Should the teat walls be too rigid and this applied to some of those we examined—it becomes more difficult to clamp the neck, and as the infant's tongue compresses the rubber against the hard palate, milk rushes *back* into the bottle as well as forward into the child's mouth. Alternatively, a teat that is too soft will collapse too readily and make sucking difficult. The wasted effort on the baby's part can be further aggravated if the ejection hole is too small to allow milk to be expelled freely from the teat. There is a wide variation in the size of hole in different makes regardless of claims of small, medium, and large, and one teat examined had been sold without any hole. Except in the case of the teat made entirely from silicone, subsequent sterilization alters the position further, for as the rubber swells it absorbs water and tends to occlude the original hole.

With a hole diameter of approximately 20/1,000 in. (0·51 mm.) (which corresponds roughly to a small-hole teat) a column of milk 22 cm. high will drip out of a bottle at a rate of 15 ml. a minute, while a slightly larger hole, 26/1,000 in. (0·66 mm.), speeds the rate to 28 ml. a minute. The flow-rate we obtained with similar pressures in our investigations prior to sterilization of the teats varied from 0·2 to 25 ml. a minute. From this it will be seen how important it is to inspect the individual teat when a baby has difficulty in sucking. From clinical obser-

vation a flow rate of 60 drops a minute from an inverted bottle seems to be well managed in the majority of babies.

The elasticity or resilience of the rubber affects the speed at which the teat can refill, and so is one of the controlling factors in the time taken for the baby to suck his feed. It also influences the ease with which the base of the teat can be stretched over the neck of the bottle during the preparation of the feed. As the teat is usually lifted directly from the sterilizing solution it is wet and slithery, and this, combined with poor elasticity, may make for excessive handling by the mother in her attempt to attach it to the bottle. This increases the risk of infection to the child should the mother's hands not be clean, and it is not unknown for the teat to shoot completely out of her hands on to the floor and subsequently be offered to the baby without re-sterilization. Certain manufacturers have added a flange to the rim of their teat to enable the teat to be grasped more firmly, but the teat-bulb/flange junction interferes with cleansing and is in itself a possible source of infection.

The type of teat used is thus of importance in bottle-feeding. Guidance should come from the medical adviser, if necessary after observing a feed, rather than be left to sales persuasion.

A good teat should not absorb excessive amounts of water, should be resilient, should have a medium-sized hole which can be enlarged as the rubber deteriorates, and there should be no attachments in the form of anticolic valves, rims, or flanges.

Dry sterilization of teats preserves the rubber longer than wet procedures. Hypochlorite solution causes less deterioration than boiling.

Acute laryngitis and obstructive emphysema in newborn.—(*The Lancet*, October 7, 1961).

Dr. G. R. Osborn and Mr. R. L. Flett consider that obstructive atelectasis and obstructive emphysema were frequently found in the lungs of the newborn. Full microscopic examination often revealed the local valvular mechanism responsible. In an important group, however, examination from the trachea to the alveoli failed to disclose the cause. Most, and probably all, of these residual cases were due to acute laryngitis. Laryngitis might develop very soon after birth. Histologically the lesions in the larynx were similar to those associated with indwelling tubes in the œsophagus, trachea, and urethra. In the larynx the lesions were not due to mechanical factors such as intubation, nor were they primarily bacterial in origin. The cause was laryngeal spasm. During this the inferior folds (vocal folds or cords) were damaged by pressure against each other; the superior folds (ventricular bands) might be similarly affected. Spasm was explained by the evolution of the larynx. This organ was not evolved for speech: it was an inlet and outlet valve. Alveoli were not filled with fresh air during inspiration. Their filling depended largely on expiration against the resistance of the contracted bronchial musculature and partly closed larynx. Excessive resistance would produce obstructive emphysema, which might progress to interstitial emphysema and pneumothorax. Complete failure of this resistance at birth could be the cause of the formation of hyaline membrane in the alveolar ducts; whether this was so or not could only be proved by the laryngologist.

Hypersensitivity to milk and sudden death in infancy.—(*Lancet*, 10-12-1960).

The possibility that cow's milk proteins in the air passages of sensitized infants can cause anaphylactic shock leading to death (Nov. 19) is of immense interest to evaporated milk manufacturers. The interest arises from two of the major advantages claimed for this type of milk *viz.*:—

(1) The fine soft curd derived from the casein content. Tolerance of this curd has been demonstrated in normal and difficult infant feeding over the past thirty years, and opinions suggest that regurgitation of evaporated milk is extremely unlikely. Thus, if shock be due to aspiration of regurgitated food from the stomach, wider use of evaporated milk could lead to some reduction in deaths in infants from this cause.

(2) The proteins of evaporated milk which have generally been regarded as less likely to cause allergic reaction, because of:—*(a)* The triple heat treatments peculiar to evaporated-milk processing; and *(b)* the very substantial physical pressure (in excess of 1 ton per sq. in.) used to homogenise butterfat, and which also exerts influence on the proteins. There is evidence that the whey proteins of evaporated milk undergo changes during these processes and become more suitable for use in, say, the eczema/asthma syndrome.

The findings do not suggest major changes to casein, but little attention has been given to this fraction, since it was commonly held that the whey proteins were at fault and research, therefore, was mostly confined to lactalbumin and lactoglobulin.

Although results of clinical or laboratory studies are not detailed, Bray, Evans and Mac Keith, and Stanfield, and several other authorities apparently approve evaporated milk as a hypoallergenic milk.

OBSTETRICS AND GYNÆCOLOGY

Basic contributions to medicine by research in obstetric and gynæcology.—(*J.A.M.A.*, 16-9-1961).

Each pregnant woman who registers with her doctor immediately conveys to him the responsibility for 2 patients, the mother and the fœtus. Multiplying this single example appropriately, it is obvious that the medicine and surgery of human reproduction carries a dual responsibility, faces 2 distinct sets of clinical problems. The speciality has attached each of these problems in sequence and has made definite strides in each of these areas. The point which needs to be stressed and which dominates our current research situation is that the techniques and approaches which led to the conquest of the first set of problems have proven totally useless in solving the second set of problems.

Regarding the contributions which have come primarily from workers within the field of obstetrics and gynæcology, one would have a point first to our increased freedom to tap the amniotic cavity. This procedure has been used primarily to record pressure changes within the uterus and hence has become our principal weapon in studying the nature of uterine contractions, and establishing the physiology of labour and the action of oxytocin on the human myometrium. This same technique has also been used, however, to sample the amniotic fluid and sequential determinations of the composition of the fluid, as well as of the partial pressure of oxygen, both normally and after the administration of oxygen to the mother have been carried out.

Closely related and perhaps dependent on amniotic fluid-tapping has been our increased freedom to tap the intervillous space. This has again permitted both pressure-recording as well as sampling of the intervillous blood for analysis. These studies in human subjects have contributed intensely to our understanding of maternal-fœtal relationships, fœtal nutrition, and fœtal oxygenation.

The techniques of keeping the placenta alive, both for placental perfusion studies, and tissue slice cultures, have contributed greatly to our knowledge of the chemistry of placental function.

The contemporary advances in instrumentation have also contributed to our keeping track of the fœtus. Difficult and complicated clinical trials and electronic studies have made the fœtal heart rate by phonocardiography and the heart pattern by fœtal electrocardiography, available. As a society, we should consider it an obligation "to monitor the welfare of the traveller in inner space as accurately as we do the voyager in outer space."

We shall never comprehend uterine activity, either throughout the mens-

trual cycle or during pregnancy and labour, until we have completed the studies on intracellular chemistry. The investigators who are primarily interested in the reproductive hormones have also pushed their studies back to the cellular level. The delineation of the biosynthetic pathways of the steroids represents one of the signal contributions of the decade. We have also had called to our attention the hormonal control of enzymatic actions at the cellular level. The adrenogenital syndrome has been translated into its basic endocrine chemistry, and immunochemistry has indicated the species specificity of the pituitary hormones.

The situation with respect to the malignancies of the female reproductive tract is perhaps more favourable than in other areas. The contribution of cytology and the concept of the noninvasive cervical lesion belonged to a previous decade, but we have been reaping since 1950 the benefits of earlier diagnosis which remains our greatest asset. Therapeutically it would appear in a preliminary fashion that ovarian carcinoma has perhaps as good a chance as any tumour of responding to chemotherapeutic measures.

Posture in parturition.—(*Amer. J. Obst. Gynaec.*, 1961, 82, 943, via *Practitioner*, January, 1962).

The theory has been advanced that the supine position in parturition is abnormal and unphysiological, whereas the upright position is advantageous in that it reduces the duration of labour and the need for forceps, as in the upright position the direction of gravity and the direction of the expulsive force are synergized. One of the arguments advanced in favour of this thesis was that the upright position was the common one among primitive tribes. Striking confirmation of this latter suggestion is forthcoming from a study carried out by Frada Naroll and her colleagues, and based upon 104 first-hand reports on 76 non-European societies, mostly primitive tribes. In 62 of these the women normally give birth in an upright position.

Four variations of the upright position are described: (1) sitting, in which the woman rests chiefly on her buttocks although she may also lean against some support; (2) squatting when the woman's weight rests mainly on her feet but her knees are markedly bent; (3) upright kneeling, in which the weight is mainly on the knees; (4) standing, when the weight is chiefly on the feet, and the knees are bent only slightly or not at all. Of the 60 societies in which the detailed relevant information was available, 19 used a sitting position, 15 a squatting position, 21 a kneeling position, and five a standing position. In 32 of these societies some form of mechanical support was provided to allow the woman to maintain an upright position. This might take the form of stakes driven into the floor or ground for her to hold on to, a rope suspended from the roof for her to hang on to, or merely a post or wall for her to lean on. Almost always the parturient woman is attended by female relatives, one of whom 'physically supports the parturient, often holding her in the midwife's lap, or grasping her from behind.'

Gestational diabetes: unsuspected, asymptomatic diabetes in pregnancy.—(*New Eng. J. Med.*, Vol. *264*: 1082, May 25, 1961, via *J. A. M. A.*, 10-6-1961).

Gestational diabetes is defined as unsuspected, asymptomatic diabetes in pregnancy, with an oral glucose tolerance test (GTT showing elevations of 3 or more of a fasting and 3 hour combination of the following values: fasting, 110 mg. %; 1 hour, 170 mg. %; 2 hour, 120 mg. %; 3 hour, 110 mg. %; (Somogyi-Nelson determinations). Of 20,070 screened pregnancies, the incidence of gestational diabetes approximated one in 116. The subsequent course of the 146 gestational diabetics followed up showed a postpartum return to normal GTT in 92·9%; but 28·5% of them again met the diagnostic criteria within 5½ years, and statistical correction, using the life-table method, reveals a 67% incidence of diabetes at that time.

The Medical Annual, 1961—Edited by R. BODLEY SCOTT, M.A., D.M., F.R.C.P., and R. MILNES WALKER, M.S. (Lond.), F.R.C.S., Seventy-ninth year, 1961. Published by M/s. John Wright and Sons Ltd., Bristol.

This book is a collection of the writings by about 40 well-known authors on advances made in the various branches of Medicine. Notable among the contributions are a chapter on the Management of Paraplegics by Dr. L. Guttmann, Psychotropic Drugs by Dr. Linford Rees, Blood diseases by Dr. Bodley Scott and a section on cardiovascular disease by Dr. Wallace Brigden. The section on Neurology contains a description of the use of anti-coagulants in cerebro-vascular accidents which promises to be a new approach to the problem. There is an interesting section on Plastic Surgery by Dr. T. Gibson. The section on Respiratory tract contains a description of some rare lung diseases like pulmonary alveolar microlithiasis, chronic diffuse interstitial fibrosis of the lungs, pulmonary alveolar proteinosis. There is an interesting chapter on Veterinary medicine and its relation to human medicine and in which African horse sickness, which has been prevailing in our country during the past few months, is described. There is a separate chapter wherein all the recent Pharmaceutical and Dietetic preparations as well as appliances commonly used are detailed alphabetically.

There are a number of very fine photographs and valuable tables. The publishers have drawn our attention to Table 3 on page 41 where the dosage of the drugs is given in grammes whereas the figures should actually indicate milligrams.

These are only some of the many valuable and interesting features of this book painstakingly compiled and in which the authors have rightly placed their hopes to "reduce the burden felt by many a general practitioner in striving to keep up with the increasingly voluminous literature of the day." —U.V.R.

Carcinoma of the Colon—By Edward G. MUIR, M.S., F.R.C.S., Published by Edward Arnold Ltd., London, Local agents are Orient Longmans Ltd., 36, Mount Road, Madras. Price 42 sh. net.

This book on a fairly common and deadly affliction of the colon has been written mainly for the use of the post-graduate student and the house-surgeon working in the surgical wards. The author has dealt with the subject fairly exhaustively. After describing the surgical anatomy of the organ, the author goes on to the subject of the pathology of the disease and diagnosis of the condition in every day practice. He then describes in detail the surgical procedures adopted in the treatment of this condition. There is a detailed description of the Paul-Mikuliez resection. Mention has also been made of the use of radio-therapy in tackling this condition. One wishes that this had been done in greater detail since with the advances made in the field of High-Voltage therapy, a discussion of its use would have been of great benefit to the reader. The book is very well got up on art paper and is extremely useful especially to the post-graduate student of surgery.

—U.V.R.

Tropical Nutrition and Dietetics—By LUCIUS NICHOLLS. Fourth Edition, revised by H. M. SINCLAIR and D. B. JELLIFFE. 1961. Published by Bailliere Tindall and Cox. 7 and 8, Henrietta St., London. Price 50 sh.

Man, from the earliest times, has realized the importance of nutrition in health and disease and there is so much research being done to-day; yet so much more has to be discovered in this field. Most of the latest knowledge is being derived from the West, with reference to the conditions prevalent there. But this book Tropical Nutrition and Dietetics by Lucius Nicholls *et al* is a boon to the doctors in the Tropics, particularly to those in India. In addition to the brief discussion of the essential nutrients, the book has a very good account of the commonly occurring diseases in India

and other tropical countries and treatment for certain deficiency diseases. Special mention must be made of the chapter on Kwashiorkor, the dreadful disease caused by protein malnutrition in infants and young children—for it has been receiving considerable attention by nutritionists and physicians today.

The short notes on foodstuffs used in the tropics, will be particularly useful to the physicians. One of the later chapter discusses the various approaches to improve community nutrition by health education, nutritional rehabilitation, food distribution, good enrichment and organisation, and liaison. This information will be of great interest to doctors in India when such steps are being included in the Nation's Plans for development.

In short, this book gives "as shortly as possible, the general principles of nutrition and dietetics, and collected under one cover the salient points of this scattered information." —U.V.R.

Evaluation of the Carcinogenic Hazards of Food Additives—Fifth Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Tech. Rpt. 220 of 1961, pp. 36. Price 3/6d.

Chemical substances have been in use since time immemorial, to improve the appearance of flavour of foodstuffs, to enhance their keeping quality or stability; or to assist in their processing. These additives have often been used without any idea of their effect on health and in recent years some of them have been suspected of causing cancer.

A report of a Joint FAO/WHO Expert Committee which went into the potential dangers of cancer from food additives deplores the absence of correct information on the toxicity or potential carcinogenicity of many food additives; also a large number of the tests for carcinogenicity, on which the evidence for or against their harmlessness is based, are inadequately designed and executed, and the results achieved not properly interpreted. This Expert Committee accordingly examines in detail the principles to which such tests should conform, the factors that must be taken into account, and the criteria on which the interpretation of the results must be founded. The report realizes the difficulty in applying to man the results of experiments in animals, and as yet not enough is known about the possible summating or potentiating effects of the different carcinogens in the human environment. The ideal is to exclude all carcinogenic agents from food-stuffs; but this is not always possible, and the risk of the additives must be carefully balanced against their benefit to the community and to the individual consumer.

The report indicates the fields in which more research is needed. One of the two annexes contains information on the carcinogenicity of food additives and contaminants examined by the Committee, the other the data that in the Committee's view should be contained in publications reporting investigations on carcinogenicity.

—T.N.S.R.

Rehabilitation in Leprosy—W. H. O. Technical Reports—1961, No. 221, pp. 37: Available through Orient Longmans Ltd., Madras.

Price 3s. 6d.

Only a fifth of the total of 10 million people suffering from leprosy in the world are believed to receive treatment of any kind for the severe disabilities that the disease often causes. A scientific meeting on Rehabilitation in Leprosy, through an on-the-spot examination in leprosy patients with typical varieties of deformity at a research sanatorium in Vellore, South India, set out to determine the extent of the problems of disability, to advise on the best application of available knowledge in prevention, treatment, and rehabilitation of disabled leprosy patients, and to recommend further research.

This very exhaustive and informative report classifies the conditions which produce deformities under nerve involvement, trophic ulceration, bone changes and absorption, deformities of the face, and ocular damage. Each condition, and the disablement it produces, are described in detail and suitable treatment (medical, surgical, and physiotherapeutic) is recommended; and suggestions are made for research into some hitherto unsolved problems. A classification of deformity devised by the WHO Expert Committee on Leprosy is presented in an annex.

The report attaches great significance to the restoration of treated leprosy patients to normal physical and mental activity, through rehabilitation, reconstructive surgery, and re-education. It describes methods of combating some of the special difficulties inherent in their social reintegration by educational campaigns and re-employment schemes, etc.

The training of health personnel and social workers is singled out as being the greatest requirement for efficient leprosy control particularly in areas with limited health services. The importance of auxiliary workers is emphasized, and the kind of training needed to enable them to recognize and prevent deformities at a early stage is described in an appendix.

—T.N.S.R.

Bacteriology and Immunity for Nurses—By RONALD HARE, M.D., Published by Longmans Green and Co., Ltd., London, 1961; pp. 193; Available in Messrs. Orient Longmans Ltd., Mount Road, Madras-2. Price 17sh. net.

The author is the Professor of Bacteriology in the University of London and Consulting Bacteriologist to St. Thomas's Hospital, London, for over 15 years. Dr. Hare has designed this well-illustrated and instructive book, for use primarily as a Text book for nurse-students undergoing the S. R. N. diploma course and it will serve the purpose exceeding well. He has described the microorganisms found in temperate climates, but equal weight has been given to those found only in tropical countries. There is a great deal of very interesting and useful material in this book that will undoubtedly be valuable to graduate nurses, staff nurses, matrons, sister tutors, health visitors and students of domestic science and food hygiene.

In the fifteen chapters contained in the book, adequate and essential information is provided that must help the nurses in their daily routine practice. Dr. Hare has taken special care to deal with the different aspects of the subject on broad lines, and to stress the mischief that the microorganisms are capable of doing. The modes of infection and transmission are very ingeniously described by means of suitable diagrams. There are twelve plates to illustrate the activities of the organisms, and other difficult points, not otherwise easily understood. The chapters dealing with spirochætes, and viruses deserve special mention, as they are usually difficult of easy explanation; these have been lucidly described and important points prominently brought out.

This really good book, must be on the shelf of every nurse, health visitor, and health inspector for constant and ready reference. —T.N.S.R.

NEWS AND NOTES

New Cardiovascular Unit at Lucknow Medical College

Dr. Tara Chandra, F.R.C.S., after completing his studies of cardiovascular surgery in Britain will take charge of a team which will run the new cardiovascular unit at the Mahatma Gandhi Medical College, Lucknow, where he is Reader in Surgery.

He went to Britain in September 1960 on a Commonwealth Scholarship, and got attached to the cardio-thoracic unit in Southampton for a time; then he went to the Post-graduate Medical School at Hammersmith, London, in 1961 to work with one of the foremost cardiac surgery teams in Britain, including Mr. Denis Melrose, of the Melrose heart-lung machine fame.

Some of Dr. Chandra's students are already in Britain taking post-graduate courses in general medicine, with particular emphasis on the heart. They will form the nucleus of new Lucknow unit. Dr. Chandra said that there has been a marked improvement in the standard of work in British hospitals since he was last in London 10 years ago, for his F.R.C.S.

Dr. Chandra will return to India at the end of March 1962.

Britain to Build 110 New Hospitals

At a Cost of £ 600,000,000 : (National Plan)

A national plan for hospital building and development in Britain, estimated to involve a capital expenditure of nearly £ 600,000,000 spread over the next 10 years, is outlined in two White Papers submitted to Parliament and published on January 23, 1962 by the Minister of Health and the Secretary of State for Scotland. The plan will be undertaken as part of the progressive development of the country's National Health Service.

The hospital plan for England and Wales—for which the Minister of Health is responsible—is expected to require an expenditure of about £ 500,000,000 over the 10 years 1961-62 to 1970-71.

Building schemes:—The England and Wales plan provides for the commencement of the building of 90 new hospitals, and the substantial rebuilding of 134 existing hospitals. In addition, there will be about 360 other building schemes for major additions and improvements to existing hospitals which will cost over £ 100,000 each.

In future, the hospital service will be centred in district general hospitals with a wide range of facilities for in-patients and out-patients, and providing such services as maternity, geriatric, and short-stay psychiatric units.

For Scotland, the national plan provides for an expenditure of about £ 70,000,000 on modernizing the hospital service in the next 10 years. This will involve the building of 20 new hospitals and the modernization and rebuilding of several of Scotland's principal teaching hospitals.

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I, Dr. U. Vasudeva Rau, hereby declare that the particulars given above are true to the best of my knowledge and belief.

Date *28th Feb. 1962.*

(Sd.) U. VASUDEVA RAU,
Signature of Publisher.

Eradication of poliomyelitis by Sabin's oral vaccine.—(Albert B. Sabin, M.D., *Ann. Internal Med.*, *55* : 3, 353, Sept. 1961)

In this communication Dr. Sabin reviews the recently acquired knowledge which justifies the expectation that poliomyelitis can be eradicated from large areas of the world.

An infectious disease can be eradicated when the chain of transmission necessary for the survival of the infectious agent in nature is broken. Work in recent years has established :—(1) that the alimentary tract of human beings is the primary site for multiplication of the polioviruses which maintain themselves in nature by passing with contaminated fæces directly or indirectly from one susceptible human being to another, and (2) that, following natural infection, the alimentary tract develops a complete or partial resistance to reinfection, which can greatly limit the soil on which the polioviruses have to multiply in order to persist in nature. In countries with high standards of hygiene and long periods of cold weather, an extensive epidemic year may be followed by many years with only minimal dissemination of the polioviruses until enough newborn children with susceptible intestinal tracts are accumulated to provide a suitable soil for unbroken cycles of transmission. A high incidence of the paralytic disease is associated with a high incidence of viral dissemination when the spreading polioviruses are of high virulence. Recent studies have indicated that naturally occurring polioviruses can be of low, intermediate, or high virulence for the nervous system without reference to their capacity for multiplication in the intestinal tract.

Killed-virus vaccine (Salk) :—Though the incidence of the paralytic disease could be greatly reduced, field and experimental studies have now shown that the immunity provided by this vaccine does not prevent multiplication of the polioviruses in the intestinal tract. Thus, in a community in which a large proportion of the population has been protected against paralysis by the Salk vaccine, the polioviruses readily maintain a continuous cycle of transmission and can paralyze those who have never acquired immunity or have lost it. This phenomenon accounts for the continued occurrence of thousands of paralytic cases of poliomyelitis in the United States and of epidemics of considerable magnitude in recent years in Canada, Hungary and Israel, where the killed-virus vaccine had been administered to the major portion of the susceptible population.

Oral attenuated virus vaccine (Sabin) :—The immunity produced by orally administered, live attenuated poliovirus vaccine not only protects the individual against paralysis but also alters the susceptibility of the intestinal tract to multiplication of the polioviruses. The extensive work that has now been carried out with the *oral* poliovirus vaccine permits formulation of the following *five* basic principles :-

1. The selected vaccine strains can multiply extensively in the alimentary tract of human beings, but lack the capacity for significant *in vivo* multiplication in other extraneural tissues and in the central nervous system of higher primates.

2. The immune response depends on adequate multiplication of poliovirus in the intestinal tract, and manifests itself not only in development of homotypic antibody but also in varying degrees of homotypic resistance of the intestinal tract to reinfection.

3. The degree of subsequent intestinal resistance to reinfection is independent of the antibody in the blood but depends rather on the extent of the initial viral multiplication in the intestinal tract, which is optimal when each type multiplies separately as long as possible without interference from other viruses. This is why each of the three types of vaccine is separately given at intervals of not less than six

Special Feature

NEWSLETTER FROM THE UNITED STATES

MODERN knowledge of inheritance as a factor in development of disease has, often led to early detection and correction of a medical condition. Each year brings us close to curing or controlling diseases before they become full-blown. *Diabetes does not develop suddenly,* even in a person whose symptoms begin late in life (*J.W. Conn.* of *Michigan*). Although new methods of identifying diabetes in its earliest stages are needed, one clue is the "high incidence of fœtal complications of pregnancy in women who are destined to become diabetics many years later." Dr. Conn states that every victim of diabetes is born with the disorder, and "the prediabetic state is certainly not the lull before the storm. It's a dynamic period in the evolution of clinical diabetes."

Psychomotor epilepsy is considered to be a disease primarily of older children, adolescents, and young adults. However, about 10 per cent of epileptic patients under 5 years of age have this type of attack. Holowach and co-workers, reporting in the September issue of *The Journal of Paediatrics, 59:* 339, 1961, outline a mode of treatment for children with psychomotor epilepsy. Patients were given 15 to 90 mg. of phenobarbital at bed-time. This dosage was rarely exceeded, even in the absence of side-effects. If phenobarbital alone failed to control the seizures, diphenylhydantoin (Dilantin) was added. The dosage of Dilantin tolerated by most children is 4 mg. per kg. of body-weight per day in one or divided doses. The dosage may be increased as required as long as the drug is tolerated. Other drugs may be used in refractory cases. In this series, two thirds of patients were available for follow-up and of these, about half had their psychomotor epilepsy completely controlled.

A seven-year follow-up study has revealed that *children who withstand an initial acute attack of rheumatic fever with heart-damage are not likely to develop heart disease.* A. R. Feinstein points out in the summer issue of *Heart Research Newsletter, 6:* 3, 1961 that 180 patients whose hearts were not damaged during an acute attack of rheumatic fever did not at all develop heart disease subsequently. He also observed that even if subsequent attacks of rheumatic fever occurred in these patients, they still did not develop heart disease.

A new "bite-size apparatus" capable of taking small samples of living tissue from the small intestine without surgery has been developed by R. J. Bolt and A. B. French at the University of Michigan Medical Centre. The new instrument is unique in that, after the patient has swallowed the tiny stainless steel capsule, which is attached to a length of soft plastic tubing, the apparatus can be left in place for multiple samplings. Thus, physicians are able to observe the effects of drugs and other substances on the intestinal lining by taking tissue samples before and after the drugs are administered. Inside the capsule, a razor-sharp cylinder is activated by hydraulic pressure transmitted down the plastic tube. As the cylinder moves, it crosses an opening in the capsule and slices off a microscopic layer of the lining of the intestine. The sample is washed up the tubing for analysis.

PUDENDAL HERNIA

A pudendal hernia resulting from a defect in the muscle or fascia of the pelvic outlet presents as a mass in either labium. Disastrous consequences occur from mistaking this hernia for a benign labial cyst or abscess. A case report and discussion of diagnostic criteria to enable a correct diagnosis to be made are presented. The treatment is surgical, the best initial approach being the abdominal one.—*(New Engl. J. Med.,* Vol. *265*: 435, 31-8-1961, via *J.A.M.A.*, 23-9-1961).

SEED AND CAKE CRUSHERS.

456. Jean Joseph Badart, Bishopsgate-street, London, *Improvements in the preparation of cotton-seed cake.* Application dated 19th February; provisional protection, 6th March; patent sealed, 5th May, 1863.

*1093. Joseph Badart, 9, Bishopsgate-street, London, for an invention of *Improvements in the preparation of rapeseed-cake, linseed-cake, &c.* Application dated 1st May; provisional protection, 22nd May; notice, 2nd June; patent sealed, 14th July, 1863.

*2927. Francis Gregory, of Manchester, agricultural machinist, *Improvements in presses for pressing seeds, fruits, hops, and other substances.* Application dated 31st October, 1862; notice, 10th March; patent sealed, 24th April, 1863.

2857. James Harrison, of Kingston-upon-Hull, seed-crusher, *Improvements in mills for cleaning cotton-seed.* Application dated 14th November, provisional protection, 11th December, 1863.

1244. Benjamin Hebblewhite, of Kingston-upon-Hull, draper, *Improvements in machinery or mills for crushing or reducing oilcake, seeds, and other substances. (A communication from Samuel Hebblewhite, of Sydney, N. S. Wales.)* Application dated 18th May; provisional protection, 5th June, 1863.

MALT-MAKING MACHINERY.

1539. Joseph Watts, of Coventry, *Improvements in machinery or apparatus for the manufacture of malt.* Application dated 19th June; provisional protection, 17th July; patent sealed, 18th November, 1863.

STABLE FITTINGS, HARNESS, APPLIANCES FOR HORSE MANAGEMENT, &c.

2091. Henry Balt, of Kentish Town, *Improvements in the roughing of horses by the application of an iron clog, instead of taking off the shoe.* Application dated 20th August; provisional protection, 2nd October; notice, 8th December, 1863,

1685. George Bartholomew, Linlithgow, N. B., edge-tool maker, *Improvements in shoes for the feet of horses and other animals, and in the means of connecting them.* Application dated 7th July; provisional protection, 7th August; notice, 10th November, 1863.

462. Charles Billingsley, of Manchester, saddler, *Improvements in saddlery, harness, driving-straps, and similar articles.* Application dated 23rd February; provisional protection, 6th March; notice, 23rd June; patent sealed, 15th August, 1863.

1375. G. H. Cottam, of the St. Pancras Iron-Works, Old St. Pancras Road, Middlesex, *Improvements in saddle-brackets and in bricks suitable for being used for paving stables and other places.* Application dated 2nd June; provisional protection, 24th July; notice, 28th July; patent sealed, 27th November, 1863.

1852. Abraham English, of Hatfield, Herts, inspector of police, *Improvements in apparatus for securing and protecting horses and other cattle during their transit by rail and other ways, and on board ship.* Application dated 24th July; provisional protection, 7th August; notice, 1st December, 1863.

3041. John Green, of Greenwich, veterinary surgeon, *Improvements in horse-shoes.* Application dated 3rd December [illegible] 25th December, 1863.

1607. F. J. Mayor, of Park-street, Middlesex, veterinary surgeon, *Improvements in horse-shoes.* Application dated 11th July; provisional protection, 7th August; notice, 15th September; patent sealed, 16th October, 1863.

1584. S. Middleton, of Newtown Cottage, Hants, near Newbury, Berks, mechanic, *Improvements in iron or other metal shoes, and in the method of securing the same to the hoofs of horses and other animals, without nails.* Application dated 19th June; provisional protection, 10th July, 1863.

780. Frederick Norrington, of Tavistock, Devon, *Improvements in girths or bands and knee-caps for horses.* Application dated 18th March; provisional protection, 27th March; notice, 7th July; patent sealed, 1st September, 1863.

1756. Carl Opperman, of Peckham, Surrey, chronometer manufacturer, *Improvements in means or apparatus to facilitate the connecting and disconnecting horses and other animals with carriages.* Application dated 14th July; provisional protection, 24th July, 1863.

*2692. Robert Page, of Great Yarmouth, Norfolk, builder, *Improvements in stables and stabling, applicable in part to kennels and to the floors of fish-houses.* Application dated 6th October, 1862; patent sealed, 7th March, 1863.

1378. Thomas Page, of Adelphi-terrace, Middlesex, civil engineer, *Improvements in shoeing horses.* Application dated 2nd June; provisional protection, 12th June, 1863.

1600. Thomas Page, of Adelphi-terrace, Middlesex, *Improvements in horse-shoes and their fastenings.* Application dated 25th June; notice, 3rd November; patent sealed, 21st December, 1863.

*2794. H. A. Rémière, of 52, Rue de l'Arbre-sec, Paris, harness-maker, *An improved horse-collar.* Application dated 16th October, 1862; patent sealed, 3rd March, 1863.

419. Hugh Smith, of 3, Regent's Park-terrace, Gloucester Gate, Middlesex, *Improvements in apparatus for feeding horses.* Application dated 16th February; provisional protection, 27th February, 1863.

3061. F. J. Walthew, of Surbiton, Surrey, Esquire, *Improvements in apparatus for sustaining and lifting draught-horses, to prevent them falling or injuring the vehicle to which they are attached.* Application dated 5th December; provisional protection, 25th December, 1863.

621. William Wells, of Ryder's Court, Leicester-square, Middlesex, *Improvements in horse-shoes and in the method of fastening the same.* Application dated 5th March; provisional protection, 20th March, 1863.

Brick and Tile Machines.

*2973. R. A. Brooman, of No. 166, Fleet-street, London, patent agent, *Improvements in machinery for moulding and compressing artificial peat, bricks, tiles, and other substances.* (*A communication from abroad by Jean Baptiste Defrasne, of Paris.*) Application 3rd November, 1862; notice, 10th March; patent sealed, 28 1863.

3129. Henry Clayton, of the Atlas Works, Upper Park-place, Dorset-square, *Improvements in machinery for manufacturing bricks.* Application dated 18th December, 1863.

789. George Cowdery, of Llanymynech, Salop, civil engineer, *Improvements in machinery for making bricks.* Application dated 26th March; provisional protection, 1st May; notice, 16th June; patent sealed, 18th September, 1863.

647. James Cowley, of Oxford, engineer, *Improvements in machinery or apparatus for manufacturing bricks, tiles, pipes, and mouldings.* Application dated 9th March; provisional protection, 3rd April; notice, 7th July; patent sealed, 29th August, 1863.

49. Julius G. Dahlke, of Battersea, Surrey, *Improvements in machinery for cutting clay in the manufacture of bricks, tiles, &c.* (*A communication from Germany.*) Application dated 6th January; provisional protection, 23rd January; notice, 19th May; patent sealed, 3rd July, 1863.

*3303. Peter Effertz, of Manchester, engineer, *Improvements in machinery or apparatus for making bricks, tiles, drain-pipes, and other similar articles.* Application dated 9th December, 1862; notice, 21st April; patent sealed, 2nd June, 1863.

2335. Peter Effertz, of Manchester, engineer, *Improvements in machinery or apparatus for making bricks, tiles, pipes, and other similar articles.* Application dated 22nd September; provisional protection, 2nd October, 1863.

1692. George Haseltine, 12, Southampton-buildings, Chancery-lane, *Improvements in brick-machines.* (*A communication from J. Gregg, of Philadelphia, U. S.*) Application dated 8th July; provisional protection, 24th July; notice, 13th October; patent sealed, 20th November, 1863.

*2696. Samuel Holland, of Oldbury, Worcestershire, machinist, *Improvements in machinery for the manufacture of bricks, drain, sanitary, and other pipes, tiles, quarries, and other articles of like manufacture made from clay, marl, and other plastic substances.* Application dated 6th October; provisional protection, 17th October, 1862; notice, 10th February; patent sealed, 27th March, 1863.

2166. Joseph Lewis, of Manchester, engineer, *Certain improvements in machinery or apparatus for preparing and drying clay, and also in machinery to be employed in the manufacture of bricks and tiles.* Application dated 2nd September; provisional protection, 11th September, 1863.

*3166. William Longley, of Leeds, builder, *Improvements in machinery for making bricks.* Application dated 25th November, 1862; notice, 24th February; patent sealed, 7th April, 1863.

450. John Platt, of Oldham, and William Richardson, of the same place, engineers, *Improvements in the preparation of clay for the manufacture of bricks, tiles, &c.* Application dated 4th September; provisional protection, 26th December, 1862; notice, 13th January; patent sealed, 27th February, 1863.

18[illegible] John Platt and William Richardson, of Oldham, Lancashire, mechanical engineers, *Improvements applicable to the burning of bricks, tiles, and other articles of earthenware.* Application dated 4th September, 1862; provisional protection, 26th December [illegible] 24th January, 1863.

3041. Jo[illegible] sha[illegible] 25th

46. E. Platt and W. Richardson, of Oldham, Lancashire, mechanical engineers, *Improvements in the preparation of clay for the manufacture of bricks, tiles, and other articles which may be made of such material.* Application dated 12th December, 1863.

***3116.** Charles Stevens (Stevens and Henderson), of 31, Charing-Cross, patent agent, *An improved brick-making machine.* (*A communication by Alois Milch, of Paris.*) Application dated 20th November; provisional protection, 28th November, 1862; notice, 31st March; patent sealed, 15th May, 1863.

MANUFACTURE OF PEAT.

597. Theodor Erich, of 77, Newgate-street, London, *Improvements in machinery for pressing peat.* (*A communication from Christian Augustus Erich, of Munich.*) Application dated 3rd March; provisional protection, 20th March, 1863.

2163. Theodor Erich, of Newgate-street, London, *Improvements in machinery for pressing peat.* (*A communication from C. E. Erich, of Munich.*) Application dated 1st September; provisional protection, 18th September, 1863.

528. Thomas Vincent Lee, of 6, Bank-chambers, Lothbury, civil engineer, *Improvements in machinery for digging, compressing, and moulding peat or turf, and for retorts and kilns for drying peat or turf, and making peat or turf charcoal through the agency of hydro-caloric or super-heated steam, and for collecting the products of distillation whilst charring the peat or turf.* Application dated 25th February; provisional protection, 13th March; patent sealed, 10th August, 1863.

WIRE-FENCING, &c.

1311. George Hunt, of Glasgow, patent agent, *Improvements in posts and pillars for fences and gates.* (*A communication from D. Middleton, New Zealand.*) Application dated 25th May; patent sealed, 20th November, 1863.

1720. A. R. Johnston, of Yoxford, Suffolk, gentleman, *Improved portable fence for sheep and cattle pens and other enclosures.* Application dated 10th July; provisional protection, 24th July; notice, 27th October patent sealed, 29th December, 1863.

1651. John King, of Chadshunt Farm, Kineton, Warwickshire, *Improvement in fencing land and in hanging gates.* Application dated 2nd July provisional protection, 7th August; notice, 3rd November; paten sealed, 8th December, 1863.

2978. J. A. R. Main, of No. 5, Renfield-street, Glasgow, gentleman, *Improvements in the mode of connecting and sustaining the intersecting bars of iron fences, hurdles, gates, and other analogous structures* Application dated 27th November, 1863.

1626. Joseph Simpson, of Darlaston, Staffordshire, manufacturer, *Improvements in iron hurdles and fencing.* Application dated 30th June provisional protection, 10th July, 1863.

3205. F. W. Collins, of Morris, county of Otsego, State of New York, U. S., *A certain improvement in apparatus for training hops.* Application dated 19th December, 1863.

624. John Miller, of Upwey, near Dorchester, Dorset, gentleman, *Improvements in horticultural buildings and other glazed structures, part of which improvements is also applicable to ventilating other buildings.* Application dated 5th March; provisional protection, 20th March; patent sealed, 29th August, 1863.

METHOD OF WARPING LAND, &c.

1762. William Wood, of Monkhill, near Pontefract, Yorkshire, *Improvements in warping or covering land, bog, or peat, with earth or soil.* Application dated 14th July; provisional protection, 24th July; notice, 6th October; patent sealed, 18th November, 1863.

ARTIFICIAL MANURES, TREATMENT OF SEWAGE, &c.

2208. T. H. Baker, of Tunbridge, Kent, engineer, and G. Friend, of the same place, engineer, *Improvements in treating excrementitious and sewage matters, and in the means or apparatus employed therein.* Application dated 8th September; provisional protection, 25th September, 1863.

2849. George Barker, of Pendleton, Lancashire, merchant, *Improvements in the construction of syphons for taking off liquid sewage, overflow of rivers, and other like purposes.* Application dated 14th November; provisional protection, 27th November, 1863.

2731. J. A. Barral, chemist, and L. A. Cochéry, of Paris, *Certain improvements in the manufacture of manure.* Application dated 4th November; provisional protection, 13th November; notice, 8th December, 1863.—French patent dated 29th October; Belgian patent dated 6th November, 1863, *for fixing fertilising elements in phosphate of lime.*

***2712.** John and Mary Anne Beale, of Maidstone, *Improvements in the preparation or manufacture of manure.* Application dated 7th October, 1862; notice, 17th February; patent sealed, 6th April, 1863.

1118. Edwin Chesshire, of Birmingham, surgeon, *Improvements in apparatus for intercepting the solid portions of the soil of water-closets.* Application dated, 5th May; provisional protection, 15th May; notice, 25th August; patent sealed, 25th September, 1863.

221. W. Clark, of 53, Chancery-lane, engineer and patent agent, *Improvements in syphons applied to draining, irrigation, and other purposes, whereby they self-suspend and resume action according to requirements.* (*A communication from François Triballat, of 29, Boulevart St. Martin, Paris, merchant.*) Application dated 24th January; provisional protection, 13th February, 1863.

761. W. Clark, of 53, Chancery-lane, engineer and patent agent, *Improvements in the separation or obtaining of ammonia from azoted matters in the preparation of manure.* (*A communication to him from abroad, by L. H. Blanchard and Theodore Chateau, of Paris.*) Application dated 21st March; patent sealed, 2nd September, 1863.

1362. W. Clark, 53, Chancery-lane, patent agent, *Improvements in the manufacture of manure.* (*A communication from A. F. Mosselman, of 29, Boulevart St. Martin, Paris.*) Application d[illegible]th May; provisional protection, 12th June; notice, 22nd [illegible] sealed, 10th November, 1863.

162. Joseph Daniels, of Leigh, Lancashire, *Improvements in artificial manure.* Application dated 22nd July; provisional protection, 1st August; notice, 25th November, 1862; patent sealed, 13th January, 1863.

253. T. Bell Fletcher, M.D., of Birmingham, *Improvements in apparatus for collecting the solid portions of sewage.* Application dated 15th April; notice, 18th August; patent sealed, 2nd October, 1863.

432. John Harrop, of Manchester, analytical chemist, *Improvements in the treatment of organic fecal and urinous matters for the purpose of deodorising the same, and in the preparation of a portable manure therefrom, and in the treatment of ashes or other refuse of combustion to be combined therewith, also for improvements in machinery to be employed in the manufacture of the said manure.* Application dated 15th January; provisional protection, 6th February; notice, 17th March; patent sealed, 10th July, 1863.

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606. Thomas Henry Morrell, of Leyland, Lancashire, gentleman, and Joseph Williamson, of Willicross, Gisburn, Yorkshire, gentleman, *Improvements in the purifying of the noxious vapours or gases given off from night-soil or other similar substances during the heating, drying, or evaporating of such substances.* Application dated 4th March; provisional protection, 20th March; notice, 24th March; patent sealed, 29th August, 1863.

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all other domestic animals, poultry, and game. Application dated 18th August; notice, 10th November; patent sealed, 29th December, 1863.

1279. John Fawcett, of Huddersfield, Yorkshire, cattle-food manufacturer, *Improvements in the preparation of food for cattle, horses, and other animals.* Application dated 21st May; provisional protection, 5th June; notice, 6th October; patent sealed, 18th November, 1863.

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MISCELLANEOUS.

363. Robert Burley, of Glasgow, *Improvements in handles for hammers, mallets, picks, mattocks, and similar tools.* Application dated 10th February; provisional protection, 20th February; patent sealed, 4th August, 1863.

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476. R. V. Dodwell, of Manchester, district engineer to the Magnetic Telegraph Company, *An improved method of preventing the destruction of plants by insects and certain descriptions of animals, and in the means for effecting the same.* Application dated 21st February; provisional protection, 6th March, 1863.

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CONTENTS

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revent fibrogenesis, along with standard anti-tuberculous drugs.)ne such drug, which has recently come to play an important ole in the therapy of tuberculosis, is the corticosteroid, natural)r synthetic. Natural corticosteroids *e.g.*, cortisone and hydro-)rtisone, often produce many side-effects; these have been liminated by new synthetic hormones, like Prednisolone, Prednisone, Triamcinolone and Dexamethasone. They prevent he laying down of collagen tissue, thereby interfering with the process of fibrosis. However, they will have no effect, once the ibrous tissue has formed.

Scheme:—The prevention of excessive fibrosis will be desirable in the following cases:—(1) Tuberculosis of tubes: ureters, intestines, fallopian tubes and bronchi; (2) tuberculous meningitis and (3) tuberculosis of serous membranes like the pleura, the pericardium and the peritoneum.

In such situations the physician should initiate treatment with streptomycin and isoniazid. Streptomycin, according to British practice, which also accords with blood-level studies, should be given in dosages of 1 g. intramuscularly once a day for a period of atleast 4 to 6 months, except when toxic manifestations appear. Isoniazid, should be given in a dosage of 10 to 15 mg/kg. body-weight per day in 3 to 4 divided doses. It is customary to give a larger dosage of this drug for the reasons stated *supra*. For prophylaxis, it is advisable to combine Pyridoxine hydrochlor with Isoniazid in the ratio of 1 mg. for every 10 mg. of the Isoniazid. Prednisone or prednisolone, are the synthetic corticosteroids usually preferred these days. They should be given orally in a dosage of 20 to 40 mg. a day in four divided doses. The precautions to be observed and the duration of such therapy have been summarized elsewhere (Khanna and Mathur, 1961). After 4 to 6 months of continued streptomycin and isoniazid therapy, PAS in a dosage of 8 to 10 g./day given orally, should replace streptomycin for the next 18 months. Isoniazid should continue to form a part of the therapy from beginning to end.

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TREATMENT OF RENAL SUPPRESSION ASSOCIATED WITH ACUTE SALICYLATE POISONING

The authors report on 1 boy and 2 girls, between the ages of 15 months and 3 years, with acute salicylate poisoning resulting in renal failure for which they were treated successfully by peritoneal dialysis. The lack of need for trained teams of physicians and expensive equipment, the ease of implementation, and the availability of commercially prepared solutions used for dialysis make this procedure an important tool for the treatment of acute renal failure or for the removal of any water-soluble dialyzable toxin in infants and small children.—(*J. Urol.*, *86*: 205, Aug. 1961, via *J.A.M.A.*, 30-9-1961).

THE SURGICAL TREATMENT OF PARKINSONISM

This paper is devoted to the study, over a period of the past five years, of the effect of thermal electrocoagulation lesions in the globus pallidus, internal capsule, and thalamus, separately or in combination, in 60 patients with Parkinsonism. The largest group were between the ages of 50 and 60. The first two patients were treated by open operative procedure. Although the results were satisfactory, the procedure is exacting under local anæsthesia and has obvious hazards. Therefore, a simple stereotaxic method based on that described by Guiot (1958) has been followed since April, 1957. The remaining 58 patients were treated by this method. The operative procedure described in detail is carried out in two stages. The 60 patients were divided into broad preoperative groups, since it is impossible to assess the results of any method of surgical treatment for Parkinsonism unless the preoperative severity and extent of the condition are known exactly in the sample of cases under discussion.

Of these patients, 53 (88%) have had tremor and/or rigidity abolished or significantly reduced without complications in the treated limbs, and have been followed up for five years. Six patients, despite successful treatment of limb tremor and/or rigidity, have persisting complications of the operations. In only one case have limb tremor and rigidity been unimproved. These results have been achieved by accurate siting of the lesion and by making it as small as would be compatible with maintained improvement. The method used has evolved progressively, and is unique in allowing the creation of lesions in the globus pallidus, internal capsule, or thalamus with one electrode track at different depths. Such combined lesions are usually necessary to eliminate contralateral limb rigidity and tremor. The best type of lesion for the effective and prolonged relief of tremor and rigidity in this series appeared to be the double one, made at the same time in the ventrolateral nucleus of the thalamus and in the globus pallidus 16 mm. from the midline, both lesions bordering on the internal capsule. The results indicate the need for selection of patients for surgical treatment and help to define the pertinent features in the clinical picture which guide selection. The one absolute contraindication to operation is the definite evidence of increasing mental confusion of a moderately severe degree, not dependent on toxic reaction to drugs. It is felt that the selection of patients for operations should be governed by the degree of widespread manifestations of Parkinsonism pre-operatively. Where widespread manifestations are present, surgical lesions to treat limb tremor and rigidity cannot be large or inexactly placed, otherwise mental deterioration characterized particularly by akinesis will be accentuated.—(*Brit. M. J.*, *2 :* 1395-1402, November 12, 1960, via *Digest of Neurology and Psychiatry*, February, 1961).

DETERMINATION OF ARSENIC IN URINE

This procedure was developed as a means of quantitating urinary arsenic faster than, and as sensitive as, the Gutzeit method. The new reagent used is a *fresh* Pyridine solution of silver diethyldithiocarbamate. It changes from yellow to various shades of red, depending on the amount of arsenic present. The urine is wet-ashed with sulphuric and nitric acids, decolourized with hydrogen peroxide, and finally placed in an arsine generator. The gas is collected in the pyridine solution of silver diethyldithiocarbamate and the colour change is measured against an arsenic calibration curve. The amount of recovery of known quantities of arsenic from the urine varied from approximately 0·2 to 2·2 mcg./100 ml.—(*Amer. J. Clin. Path., 36 :* 373, October 1961, via *J.A.M.A.*, 21-10-1961).

HYPOTENSIVE THERAPY TODAY*

(A review of the indications and methods of treatment of hypertension and of the drugs of choice)

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(The term hypertension as defined by Grollman[19] is loosely used here as a synonym for an elevation in arterial blood-pressure, and also in a more specific sense to designate a widespread chronic disorder characterized by a sustained elevation in both systolic and diastolic pressures).

BEFORE undertaking hypotensive therapy, it is important to undertake thorough investigations of every case to rule out the possibility of a curable type of hypertension[22] such as may be due to unilateral renal disease, obstructive lesions of the ureters, total vascular obstruction with renal infarction, unilateral hydronephrosis and pyelonephritis; disease of the suprarenal gland *e.g.*, phæochromocytoma or the hypertensive variant of adreno-genital syndrome due to congenital adrenal hyperplasia; coarctation of the aorta and primary aldosteronism. This is specially the case if the disease is of recent origin and is severe or when malignant hypertension arises in childhood or in patients over the age of 50 years, for in such cases renal origin of the disease is very likely and it is essential to carry out aortographic studies. Once the diagnosis of primary or essential hypertension has been established, a hypotensive regimen should be planned and individualized, according to the severity of the hypertension.

Hypotensive drugs.—An ideal hypotensive drug should be one which is completely absorbed from the gastro-intestinal tract, which reduces the blood-pressure effectively and uniformly throughout the 24 hours without causing any undesirable side-effects, which is non-toxic and which is without cumulative effect.

None of the hypotensive drugs currently available is ideal. However, with a large number available at present having different modes of action, it is possible to arrive at a combination to control hypertension effectively without causing any significant side-effects in nearly all cases.

Classification of hypotensive drugs:—Many of the drugs used in the past to control hypertension, such as thiocyanates, nitrites and adrenergic blocking drugs are no longer used because of many undesirable side-effects and toxicity. Hexamethonium compounds given parenterally, were the first group of hypotensive drugs, which effectively reduced high blood-pressure

*Specially contributed to the ANTISEPTIC.

levels. Drugs and methods used to reduce blood-pressure are listed below :—

1. Hypnotics, sedatives and simple re-assurance. 2. Tranquillizing drugs *e.g.*, Rauwolfia alkaloids, Chlorpromazine, Meprobamate. 3. Gravity augmented hypotensive drugs :—(*a*) Quarternary ammonium compounds *e.g.*, pentolinium ; (*b*) secondary amines *e.g.*, mecamylamine and (*c*) tertiary amines *e.g.*, pempidine, M & B 4500, M & B 5409 A. 4. Hypotensive diuretics *e.g.*, mercurial diuretics, chlorothiazide and its congeners. 5. Hydralazine. 6. Veratrum and its alkaloids. 7. Sympatholytic drugs *e.g.*, Bretylium tosylate and guanethidine. 8. Corticosteroids *e.g.*, cortisone, hydrocortisone, prednisolone triamcinolone and dexamethasone etc. for treatment of hypertensive variant of adrenogenital syndrome due to congenital adrenal hyperplasia. 9. Miscellaneous group including (*a*) physical agents and physiological means to reduce B.P. ; (*b*) sodium restriction and (*c*) dorso-lumbar sympathectomy.

Smirk[44], has broadly classified hypotensive drugs into :—(1) Those suitable for background therapy *e.g.*, rauwolfia alkaloids ; (2) hypotensive diuretics *e.g.*, chlorothiazide and its congeners and (3) gravity-augmented hypotensive drugs.

This classification is very useful in planning a hypotensive regimen. I will now discuss some of the more important hypotensive drugs and their modes of action, as at present understood.

Tranquillizing drugs.—(*a*) *Rauwolfia* drugs by dulling the impulses from bulbar centres decrease blood-pressure levels. The sedative effect of reserpine is due to a lowering of the serotonin content of the brain rather than to the reserpine content of blood which is not detectable 12 hours after an intravenous dose. Reserpine stimulates the trophotrophic system of the brain, releases serotonin and *nor*-adrenaline and in large doses mimics the effects of sympathectomy. Reserpine lowers the blood-pressure by direct action on the hypothalamus and reticular formation[19] and slows the pulse moderately during the fall of blood-pressure. For lowering the blood-pressure, rauwolfia alkaloids may be used alone or in combination with gravity-augmented hypotensive drugs.

The commonly used preparations of rauwolfia are :—*Reserpine* :—Dose : oral 0·75–1·5 mg./day. Intravenous dose 2·5 to 5·0 mg. given at 4 hourly intervals to a maximum of 10 mg. per day when used to lower the blood-pressure in cases of malignant hypertension and hypertensive encephalopathy. The rapid action of the drug obtained by intravenous injection is not due to central action as obtained when the drug has been administered for long periods, but is probably due to a peripheral sympathomimetic action.

Rauwolfia serpentina (Raudixin) : is the powdered whole root of rauwolfia serpentina. Dose 200 to 400 mg. per day in divided doses.

Other commonly used preparations of Rauwolfia are : *Serpasil*, *Rauwoloid* and *Desperidine*.

SIDE-EFFECTS OF RAUWOLFIA ALKALOIDS :—In short-term therapy the side-effects are few and toxicity low but when given for prolonged periods, the drug may induce serious side-effects. In therapeutic doses, the nasal congestion and obstruction may be such as to require discontinuation of therapy in some cases. More serious side-effects, which may occur with prolonged administration of even small doses are :—mental inertia, lack of ambition, depression, apathy, crying spells, introspection, nightmares, suicidal tendencies and loss of *libido* in the male. Rarely skin eruptions, epistaxis, peptic ulcer, or a Parkinson-like syndrome may develop. Serpasil is stated to retain the hypotensive effects of rauwolfia alkaloids without their more serious side-effects when given in doses of 1–2 mg. daily. In view of the above mentioned side-effects, rauwolfia alkaloids are contraindicated in cases with a history of a recent nervous breakdown or emotional crises.

(*b*) *Chlorpromazine* (Largactil, Thorazine 25 and 50 mg. tablets ; 50 mg. ampoules). This drug depresses the CNS, through its autonomic centres in midbrain and this coupled with its blocking effect on the sympathetic is responsible for its efficacy in lowering blood-pressure.

(*c*) *Meprobamate* (Miltown, Equanil etc.) available as 400 mg. tablets the dose being 1 to 2 tablets three times a day.

Meprobamate reduces the increased muscle-tension produced as a result of nervous tension by blocking long internuncial neuronal circuits between the cortex and thalamus, thereby inducing relaxation and sleep. Some cases, however, show paradoxical excitement. Skin eruptions following the use of the drug have been reported.

Gravity-augmented hypotensive drugs[44] :—By interfering with sympathetic nervous system these prevent the homeostatic adjustments of circulation which in hypertensive patients is responsible for keeping the blood-pressure at abnormally high levels. This explains also the mechanism of postural hypotension which occurs because of interference with homeostasis and which should not therefore be regarded as a side-effect. Thus it is easy to understand why the effect of gravity-augmented hypotensive drugs is greatest when the patient is standing, less while sitting and least when he is lying flat on his bed. Venesection enhances the response to hexamethonium[32] by causing a compensatory increase of activity of the sympathetic nervous system

and hence more impulses to be removed by hypotensive drugs which act upon the homeostatic mechanism[32, 37]. A low sodium diet further augments the action of this group of drugs and the same happens after exercise and meals. The former acts by dilating vessels in the voluntary muscles and the latter by causing dilatation in the splanchnic system. Purgatives and diuretics by decreasing either the extracellular volume of fluid or the plasma volume increase the response to gravity-augmented hypotensive drugs. Procedures such as infusion of fluids intravenously[32], or immersion of the body in water or the administration of pressor drugs, like adrenaline or *nor*-adrenaline[11] diminish the response to this group of drugs.

Thus it will be seen that in order to get the maximum benefit from this group of drugs, with the minimum effective dose, the patient should be standing or sitting during the day and propped up in bed with a back rest maintained at an angle of 45° at nights. In cases with severe hypertension, the reduction of blood-pressure during sleep is not sufficient and the use of an extra pillow is quite ineffective and a simple cardiac bed as designed by Smirk[43] on which the patient can sleep with sitting position must be provided.

The ganglion-blocking agents interrupt sympathetic vasoconstrictor impulses, thereby inducing a medical sympathectomy. This group of drugs decreases the cardiac output and venous return to the heart by pooling blood in the splanchnic bed and therefore this group of drugs is most effective when the patient is standing. The medical sympathectomy induced by its effect on venous tone is responsible for its beneficial effects in congestive heart-failure.

Hexamethonium compounds orally are not very much in use at present, and will therefore, not be discussed. Intravenously, they are used in dealing with hypertensive emergencies.

Pentolinium (Ansolysen M & B) when given orally is better absorbed from the gastrointestinal tract than hexamethonium. In seriously ill-patients, or when a better control of hypertension is desirable, parenteral administration of the drug is advisable because of the erratic absorption, unpredictable effects and sudden decline in the level of blood-pressure when it is administered orally. When it is given orally, this drug should be given initially in divided doses at 8 hourly intervals starting with an initial dose of 20 mg. per day and increasing it gradually until stabilization of blood-pressure is attained. As much as 1400 mg. of the drug had to be given per day in some cases, but when such high doses are necessary or tolerance to the drug has developed and made the control ineffective, a combination with other hypotensive groups of drugs should be tried.

Side-effects :—The drugs may cause constipation, paralytic ileus, postural hypotension, retention of urine, dilatation of the pupils, loss of accommodation with consequent interference with near vision, dryness of the mouth and skin and development of tolerance to a variable extent. During the last several years that it has been in use no blood dyscrasias have been reported and when used with care, the drug is comparatively safe.

Chlorisondamine hydrochloride :—Ecolid (Ciba) available in 25 and 50 mg. tablets, is more potent than pentolinium, but less powerful than mecamylamine. Its action lasts for 8 to 12 hours after a single therapeutic dose. Its absorption from the gastrointestinal tract is rapid though a bit erratic and so a more precise control of blood-pressure is obtained by parenteral therapy. *Ecolid* should be used only for the more severe cases of hypertension and given under close supervision. Its side-effects are similar to those of pentolinium. Initially 12·5 mg. of the drug is given in the evening, the same dose is repeated next morning and evening, and repeated every 8 hours on the 3rd day ; or 12·5 mg. is given in the morning and 25 mg. in the evening on the third day, depending upon the duration of effect of Ecolid in the particular case. The dose is thus gradually increased by increments of 12·5 to 25 mg., until the desired effect is obtained. The drug should not be used for cases of mild hypertension, renal or coronary insufficiency, pyloric stenosis, obstruction to the bladder-neck or after cerebrovascular accidents.

Mecamylamine hydrochloride :—(Inversine, Mevasine) is a secondary amine which is completely absorbed from the gastrointestinal tract and to which no appreciable degree of tolerance develops. Its absorption is more predictable when given on an empty stomach, and is given initially in doses of 2·5 mg. *b.d.*, and gradually increased at intervals of not less than 2 days[19] until the desired effect is obtained. The individual susceptibility to the drug is great and a difference of 1 mg. may be enough to cause very severe side-effects from a dose which till then was well tolerated. Again some cases may require very little of the drug to induce hypotension and a dose of 2·5 mg. *b.d.*, may prove excessive.

Side-effects :—Occasionally when the drug is given for prolonged periods it causes severe mental disturbances, gross tremors and even death in a few cases. If toxic symptoms appear, the drug should be promptly withdrawn when spontaneous improvement will occur.

Tertiary amines :—Pempidine tartrate is a pentamethyl derivative of piperidine, is completely absorbed from the gastro-intestinal tract and its action is more predictable than

quarternary ammonium compounds. Pempidine,[44] M & B 4500 and M & B 5409A are at present the most potent ganglion blocking agents and do not lead to drug tolerance. Pempidine tartrate should be given initially in doses of 2·5 mg. at 8 hourly intervals, preferably at 6 A.M., 2 P.M., and 10 P.M. and the dose gradually increased. The following procedure has been recommended in order to bring down the blood-pressure rapidly when the patient is under observation and the blood-pressure readings are being taken at half to one hourly intervals. The drug is initially given in a dose of 2·5 mg. and repeated after every 90 minutes' interval until the blood-pressure has fallen perceptibly, when the interval of administration of the drug is decreased until an effective dose has been found which may vary from 2·5 to 18·0 mg. per day. When given along with background therapy, it is possible to maintain an effective control of blood-pressure even when very small doses are used.

The dose of M & B 4500 is approximately half that of pempidine and that of M & B 5409A is 10% higher than that of pempidine tartrate. A number of other gravity-augmented hypotensive drugs such as Azamethonium (*Pendiomide*) and trimethidinium methosulphate (*Ostensin*) have also been used for their hypotensive effects.

Hypotensive diuretics.—These act by causing natriuresis, thereby diminishing the sodium content of the body, and so, they are a substitute for salt-restriction. Chlorothiazide and its congeners have extensively been used as hypotensive drugs for background therapy because of their relative lack of toxicity in therapeutic doses. These drugs inhibit the absorption of sodium by the renal tubules. Given alone, these drugs induce a fall of blood-pressure in hypertensive patients and when given in combination with other hypotensive drugs enhance their action. Both salt-restriction and this group of drugs act by decreasing the volume of plasma and extracellular fluids, decreasing the cardiac output and right auricular pressure and lower the high levels of blood-pressure, whether an associated heart failure is present or not. The extent to which the blood-pressure falls by severe sodium restriction (daily sodium intake not exceeding 0·5 g. daily) or by giving this group of drugs is very variable in different patients and depends upon the dosage used and individual sensitivity to sodium restriction. The hypotensive effect is due to its cumulative effect on electrolyte-excretion, for it is well known that this effect does not occur for some days after the commencement of the therapy although the diuresis starts within 2 hours[44] after the administration of the drug. This also clearly demonstrates how a regimen which combines salt-restriction along with hypotensive diuretics and gravity-augmented hypotensive drugs can be very successful in establishing an

efficient control of blood-pressure without causing any undesirable side-effects and when only small doses of the individual drugs are used. The hypotensive effect can be further augmented by making the patient sit or stand during the day and making him sleep in a sitting position at night. The danger of excessive potassium loss should always be kept in mind when hypotensive diuretics are prescribed for prolonged periods especially when chlorothiazide or flumethiazide are used. The danger of hypokalæmia is much less with bendrofluazide and methyclothiazide [13,14,15]. Supplemental citrus fruit juices or potassium chloride g. 1·0 two to three times a day in gelatin capsules should be given when the hypotensive diuretics have got to be prescribed for prolonged periods or in large doses fall in blood-pressure with the aid of hypotensive diuretics has also been observed in those cases who failed to respond to dorsolumbar sympathectomy.

The following preparations of hypotensive diuretics are in common use:—Chlorothiazide (Chlotride) available as 50 mg. tablets; Hydrochlorothiazide (Di-chlotride and Esidrex) available as 25 and 50 mg. tablets; Hydroflumethiazide (Naclex) available in 25 and 50 mg. tablets; Bendrofluazide (Neo-naclex, Aprinox, Centyl, Plurylc) available in 2·5 and 5·0 mg. tablets and Methyclothiazide (Enduron-Abbott) available as 2·5 and 5 mg. tablets.

Most patients who are receiving methyclothiazide (Enduron) or bendrofluazide (Neo-naclex) and are having a potassium rich diet, do not require supplements of potassium chloride. Methyclothiazide a member of the benzothiadiazine family of diuretics, is a new oral hypotensive diuretic of high potency, long acting and of low toxicity. The average daily dose ranges between 2·5 and 10·0 mg. given once a day in the morning. As an adjunct in the management of hypertension, 2·5 to 5 mg. of the drug once daily will usually suffice. When Enduron was used alone or as an adjunct to other agents in hypertensive patients, Ford noticed a significant decrease in blood-pressure at the end of 3 weeks[13]. Calloway administered Enduron to 50 patients, and studied in detail 16 moderately severe hypertensives in detail out of this series. With a daily dose of 12 mg. of Enduron, per day in divided doses, over a period of 3 months he observed that the average reduction of systolic blood-pressure was 50 mm. Hg., and the average reduction of diastolic blood-pressure of 20 mm. Hg. "Some reduction of blood-pressure was noted in all cases, although there was a considerable variation in response." Blood-pressure gradually returned to pre-treatment levels, about a week after discontinuing the drug.

Side-effects of Enduron are:—Vertigo, nausea (both however, disappear with reduction of dosage), malaise, dermatitis,

arthritis, symptoms of gout, skin rashes and weakness. Weakness, lassitude, nausea and cramps indicate excessive potassium loss.

The remote possibility of developing hypochloræmic alkalosis should be considered when chlorothiazide congeners are being administered and if necessary ammonium chloride should be administered to counter this.

Hydralazine (Apresoline) has a peripheral sympatholytic action and is readily absorbed from the alimentary tract. When administered in adequate therapeutic doses, it may induce headache, nausea, vomiting and postural hypotension. Serious complications such as periarteritis, rheumatism-like affections of the joints and a DLE-like syndrome may develop in some cases. These toxic effects, however, are rarely observed if the total daily dose does not exceed 200 mg. per day. Hydralazine may be given orally in doses of 25 to 50 mg., one to four times daily. It has also been extensively used in combination with other hypotensive drugs.

The Veratrum alkaloids.—Crude extract of veratrum and its alkaloids (Unitensin, Protalba) were extensively used in the past, to reduce high blood-pressure. The parenteral administration of the drug is especially recommended for the treatment of eclampsia and hypertensive crises. Side-effects, like flushing, bradycardia, vomiting and cardiac arrhythmias are often very disturbing and require discontinuation of the drug. The drug may be used by the parenteral route in treating hypertensive crises.

Sympatholytic drugs.—These resembles quarternary nitrogen compounds in structure and act by blocking the peripheral sympathetic-vasomotor function without antagonizing the direct action of circulating adrenaline and *nor*-adrenaline. Thus their action is neither adrenolytic nor do they inhibit parasympathetic nervous system.

1. *Bretylium tosylate* (Darenthin) is available as 200 mg. tablets. Darenthin controls the blood-pressure effectively like the ganglion-blocking agents but is free from the incapacitating side-effects associated with parasympathetic block. Darenthin selectively blocks the peripheral sympathetic nervous system by acting on the adrenergic nerves in which it accumulates. The drug is absorbed irregularly from the alimentary tract[44]; it is not a very powerful hypotensive drug and when given alone in large doses may cause unexpectedly great variations in blood-pressure. Darenthin has little effect on supine blood-pressure, and when given orally its action lasts from 3 to 12 hours producing a postural fall in blood-pressure. The drug has no cumulative effect even when given for prolonged periods. To start with 100 mg. of Darenthin is given at 8 hourly intervals, preferably after meals to secure uniformity of absorption. The dose may be increased to 200 mg. eight hourly on the 2nd day, and if necessary, to 300 mg. eight hourly on the 3rd day. A ganglion-blocking agent may be added if this dose does not produce an adequate response. The maintenance dose varies from less than 100 mg. to 6 g. a day, the average dose being about 1·8 g. daily.

SIDE-EFFECTS :—Usually these are trivial and include stuffiness in the nose, faintness, parotid pain, postural hypotension, diarrhœa, nausea, lassitude, disturbances in micturition and in some cases failure to ejaculate. Darenthin does not however, cause impotence. It is contraindicated in cases of recent cardiac infarction and phæochromocytoma ; it should be used cautiously in cases of hypertension associated with cerebral or coronary insufficiency or severe renal damage.

2. *Guanethidine* has a much more prolonged effect as compared to Darenthin. Because of its cumulative effect, once the hypotensive effect has been established, a period of 2 days may elapse before the blood-pressure returns to the normal level. Further, a dose which previously was ineffective in controlling the hypertension may if continued, cause sustained hypotension after 2 days. The drug should therefore, be used only in conjunction with other hypotensive drugs, so that reversal of hypotension produced by the drug may not become difficult to achieve, as when the patient develops coronary thrombosis. The drug should never be used to initiate hypotensive therapy. The effective daily dose orally varies from 30 to 150 g.

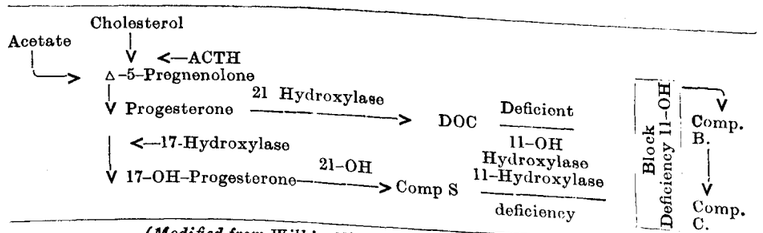
SIDE-EFFECTS :—Nausea, vomiting, malaise, nasal obstruction, nervous tension, muscle pains, failure of ejaculation without producing impotence. The side-effects are considerably reduced when the drug is combined with ganglion-blocking agents.

Cortisone and its congeners :—Cortisone and its congeners such as hydrocortisone, prednisolone, triamcinolone and dexamethasone have all been found very effective in controlling the hypertension associated with the hypertensive variant of adrenogenital syndrome due to congenital adrenal hyperplasia[25] *(See* Fig. I, p. 218). In this condition, the synthesis of hydrocortisone by the suprarenal cortex is defective, due to a deficiency of "11 Hydroxylases." This leads to increased production of 11-desoxycorticosterone and compound S and a deficiency of compound F[55]. The administration of cortisone in physiological amounts leads to the disappearence of DOC, compound S and other abnormal steroids and the hypertension of adrenocortical origin subsides.

Establishing a hypotensive regimen.—The currently available hypotensive drugs depress the blood-pressure only without correcting the fundamental disturbance which produces the

hypertension and so there is no unanimous opinion about the optimal drug requirements. By combining drugs with different modes of action and trying various combinations, one can arrive at the optimal requirement for any particular patient. Treatment must therefore, be highly individualized and the physician should try to bring the blood-pressure down to within the normal range, whenever practicable to do so. When administering a more powerful hypotensive drug, the patient should either be hospitalized or kept in the hospital for several hours during the day, so that half to one-hourly blood-pressure readings may be taken while the blood-pressure is being stabilized.

FIGURE I



(Modified from Wilkins[55])

Note:—The defect in "11 hydroxylase" results in excessive production of compound-S and DOC and a deficiency of hydrocortisone. Excess of DOC is said to be responsible for hypertension in adrenogenital syndrome due to congenital virilizing adrenal hyperplasia. When cortisone is administered in physiological amounts, the intermediate abnormal steroids (and DOC) disappear and thus the hypertension of adreno-cortical origin subsides[55].

Sedatives and tranquillizers are not substitutes for a regular and well-planned way of life; further they are not quite free from side-effects. Neither phenobarbitone nor the more modern tranquillizers have any significant effect in controlling blood-pressure in patients with severe hypertension. A period of rest during the day and good sleep at night should be ensured for every patient.

Weight-reduction should be achieved in all overweight patients. Dexedrine given in small doses for its appetite-reducing effect, commencing with a dose of 2·5 mg. per dose and increased if necessary, has not aggravated the hypertension. Preludin and Duramine also serve to reduce appetite. Dexedrine (one spansule a day) along with breakfast is particularly useful in controlling hunger.

Although sodium restriction (200 to 500 mg. of sodium-intake per day) is not essential in moderately severe to severe hypertensives when chlorothiazide and its congeners are being administered, it is still recommended, for this measure augments the

hypotensive action of the drugs, and makes it possible to reduce their dosage considerably.

Smoking should be prohibited, because nicotine stimulates the sympathetic ganglia as well as the neurogenic synapses in the central nervous system, thereby aggravating hypertension.

It is important to note that with the reduction of blood-pressure, the cerebral vessels dilate and thereby maintain the cerebral blood flow and metabolism. Excessive blood-pressure-reduction, however, decreases the cerebral blood flow resulting in disturbances to the cerebral function, such as dizziness and syncope especially when in the upright posture. This shows the importance of checking the blood-pressure both in the supine and in the erect positions when evaluating the results of therapy. Conn[8] recommends a reduction of the blood-pressure to 150/100 mm. Hg. in adults as safe, because this level also allows for some fluctuations in the blood-pressure to occur.

Initiation of therapy with mecamylamine or guanethidine is not recommended; the former, because of its dangerous side-effects and the latter because of its cumulative action. Ganglion-blocking agents should not be used to start with, in cases of malignant hypertension, because of the probable need for large doses and consequently the risk of developing paralytic ileus.

In cases of peptic ulcer and severe hypertension, sympatholytic drugs alone should not be administered unless ganglion-blocking agents are also given simultaneously to inhibit gastric secretion.

It is universally agreed that all cases with malignant hypertension or congestive heart-failure due to hypertension should be given a hypotensive regimen. Treatment should *not* be withheld in moderate cases of hypertension, or in the asymptomatic cases, *because* a tolerable regimen can nowadays easily be evolved and the hypotensive regime should not involve a patient in much distress. The avoidance of side-effects is a matter of technical knowledge and persistence. Smirk found that the outlook for the untreated cases was closely related to the basal blood-pressure and hardly related to the labile fraction, the supplemental blood-pressure. He recommends as a general indication to treat a female patient whose basal blood-pressure is 155/90 mm. Hg. and a male whose basal blood-pressure is over 145/85 mm. Hg., for in his follow-up studies he found that the mortality began to rise more steeply after these levels. His follow-up during the first 8 years' experience in treating grade II hypertensives showed that the mortality in the untreated cases was nearly twice as much as that in the treated cases. The question whether preventive treatment should be given or not is much disputed. Smirk found that among cases under treatment, very few if at all

developed malignant hypertension and except in the very advanced cases of renal disease congestive heart-failure did not develop. It is possible that with treatment the incidence of heart failure, stroke and malignant hypertension can be reduced in cases with symptomless hypertension. Smirk feels that even in mild cases of hypertension with blood-pressure of say 160/90 mm. Hg. hypotensive therapy is indicated, and the blood-pressure should be kept in the fully normal range, provided that the treatment does not produce any side-effects.

The choice of the hypotensive drugs depends on the severity of the hypertension and the individual susceptibility to different drugs. Smirk divides the procedure to be adopted into two stages *viz* :—

STAGE 1 :—Preliminary measures for reducing the blood-pressure ; and STAGE 2 : adjustments to improve the *regime* by minimizing the side-effects and to effect further improvements over the control of the blood-pressure. Drugs suitable for background therapy are the Rauwolfia group of alkaloids and the hypotensive diuretics. In mild cases, background therapy alone may reduce the blood-pressure to normal levels, for as much of the 24-hour day as is practicable. The chlorothiazide group of drugs are at present the best when only one drug is being used for background therapy. Methyclothiazide and bendrofluazide are the drugs of choice from this group because they cause diuresis, natruresis and chloruresis without significantly affecting serum potassium levels and in most cases, dietary supplements of potassium in the form of citrus fruit-juices are enough to provide for the excessive secretion of potassium. When other drugs of this group are used, potassium chloride 1 to 3 g. per day should be given simultaneously, depending on the dosage of the hypotensive diuretics. Alternatively Smirk recommends the use of Chlormethiazide (Fluitran) in doses of 4 to 8 mg. per day.

In cases where the response to chlorothiazide group of drugs is not adequate, 0·25 mg. of reserpine may be given in addition once a day. A large number of cases were well controlled on this regime.

Patients with more severe grades of hypertension and malignant hypertension will require a combination of physiologic means to reduce the blood pressure, salt restriction, background therapy with Chlorothiazide congeners and Rauwolfia alkaloids, ganglion-blocking agents or sympatholytic agents or, even a combination of the latter two types of gravity-augmented hypotensives. It is advisable not to combine hydralazine with ganglion-blocking agents. When using ganglion-blocking agents, it is very important to start with small doses initially and gradually build up the dosage until the standing blood-pressure is 150/100 mm. Hg., or symptoms of postural hypotension appear

at certain times of the day. The breakfast dose is usually the largest dose of the day, and the midday dose the smallest. The physician should be very watchful about constipation while using ganglion-blocking agents such as Ansolysen or Ecolid ; free use of purgatives may be necessary. The purgatives belonging to the Cascara sagrada group are very useful for this purpose and Elixir cascara 15 to 30 cc. may be administered at bed-time regularly or alternatively 15 to 30 mg. of prostigmine should be given an hour after breakfast. In cases where constipation is troublesome inspite of the regular administration of the cascara-group of purgatives and where prostigmine causes a colicky pain in the abdomen, the ganglion-blocking drugs should be replaced by or given in combination with Bretylium tosylate.

In hypertensive patients with renal disease and normal blood-urea there is no risk in reducing the blood-pressure to normotensive levels. In cases with raised blood-urea, no attempt to reduce the blood-pressure to normotensive levels should be made, for, because of the vascular spasticity the kidneys are unable to adjust to the lower levels of blood-pressure. Moyer and Brest recommend that after a month's treatment in which the blood-pressure has only been moderately reduced, it can further be safely reduced to normotensive levels without causing any depression in the renal function. When the blood-urea is over 100 mg. and the renal function grossly impaired, blood-pressure reduction is of not much help in reducing the mortality.

Treatment of hypertensive emergencies.—Before starting any form of therapy renal function and the state of renal compensation must be fully assessed, especially when cerebration is abnormal. Disturbances of sensorium are unlikely to be due to renal failure when the blood urea is normal. The fundus should be examined for retinal hæmorrhages which indicate the extent to which the arterioles have been damaged. Papillœdema signifies the presence of cerebral œdema and often leads to disturbances of sensorium in patients without renal failure. Hypertensive emergency may be said to exist in cases with essential hypertension when the very high levels of blood-pressure threaten life or where the severe hypertension co-exists with a specific condition like primary renal disease or eclampsia.

In those cases where 2 to 3 hours' delay in controlling the hypertension would do no harm, the administration of parenteral reserpine therapy is the treatment of choice, because of its potency, safety and ease of administration. Reserpine is administered intravenously in doses of 2·5 to 5 mg. and repeated at 4 hour-intervals if necessary, until a total of 10 mg. of the drug has been administered during a 24 hour period. With larger doses given intravenously, (as much as 30 mg. per day as recommended by Moyer and Brest) side-effects, like mental

sluggishness and a Parkinson-like syndrome are very likely to occur and several days may elapse before such effects are reversed. An excessive fall in blood-pressure induced by reserpine can easily be reversed by a *nor*-adrenalin drip.

When reserpine has proved inadequate, hexamethonium (100 to 150 mg. in 1000 cc. of 5% glucose) or pentolinium (50 to 75 mg. in 1000 cc. of 5% glucose) may be given intravenously at a suitable rate to give the desired response. Ansolysen may also be used by intramuscular injections in doses of 5 mg. and repeated in 2 hourly doses of 5 to 25 mg. until the desired response is obtained. *Nor*-adrenalin drip provides an effective antidote to overdosage against all ganglion blocking agents. Both the hypotensive agents and *nor*-adrenalin drip if recommended for hypertensive cases with fulminating heart-failure, should be given intravenously in concentrated solution in order to avoid extra-fluid overload.

Arfonad (Trimethapan camphorsulphonate) is more useful in reducing hypertension than other ganglion-blocking agents and is particularly useful in cases with acute pulmonary œdema. Because of its short-lived effect, minute to minute regulation of blood-pressure is possible, when the drug is administered by intravenous drip.

Veratrum alkaloids (Veriloid, Veralba) when given intravenously are very potent hypotensive agents and may be used in an intravenous drip to reduce the blood-pressure in those cases where the other methods mentioned already have proved ineffective. Veratrum drugs are effective both in the erect and supine positions and should be used only when other methods to bring down the blood-pressure have failed. Veriloid is initially administered in a dose of 0·5 mcg. per kg. of body weight over a period of 20 minutes[8] the blood-pressure readings being checked every minute during this period. A change is then made to a maintenance drip (4 mg. Veriloid in 1000 cc. of 5% glucose). Excessive hypotension induced by this drug is reversed by a *nor*-adrenalin drip. Once the emergency phase of hypertension has been controlled, oral treatment as detailed above should be started. In severe hypertension associated with toxæmia of pregnancy, intravenous Reserpine is the drug of choice, and if necessary may be combined with oral Hydralazine therapy. When acute nephritis is complicated by severe hypertension, intravenous reserpine and along with oral hydralazine if necessary should be given.

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RETINAL HÆMORRHAGES ASSOCIATED WITH THE ADMINISTRATION OF "BUTAZOLIDIN"

Dr. A. L. Tostevin of 163, North Terrace Adelaide, writes in the *Med. Jour. of Australia of* 14-1-1961.

I have cellected five cases of retinal hæmorrhages in cases which have been on "Butazolidin" therapy for rheumatoid arthritis over a long period. They all follow the same pattern, but I shall report Mrs. I. H., aged 66, who was seen by me on May 30, 1960. She had suffered from rheumatoid arthritis for 16 years. In August, 1958, she was given 200 mg. of "Butazolidin" twice daily and occasionally three times a day up to the day I saw her. Eight weeks prior to my seeing her, the sight in her left eye had been failing. Examination of the fundi showed flame-shaped hæmorrhages around both discs and the macula of the left eye. The vision in her right eye came up to 6/9 with correction, but in the left it was 6/36 and it would not improve. I rang her general practitioner, who said that her blood pressure and urine were normal, and I suggested that he take her off "Butazolidin" and put her on some other treatment for the rheumatoid arthritis. I last saw her on December 8, 1960, when the vision in her right eye corrected to 6/6 and in the left to 6/9, and the retinal hæmorrhages had disappeared.

I wrote to Geigy Pharmaceuticals, and asked them if any cases of retinal hæmorrhages in conjunction with the use of "Butazolidin" had been reported in the medical literature, and they said they were not aware of any such cases having been reported. For this reason, I am reporting my finding.

In all my cases, the hæmorrhages disappeared after discontinuing the "Butazolidin". I have not included cases which have been complicated by hypertension, arteriosclerosis or renal abnormalities.

X-RAY THERAPY OF SHOULDER AND ELBOW

H. Reinhold and R. Sauerbrey (*Deutsch Med. Wschr., 85:* 163, 1960) stated that before making a diagnosis of epicondylitis in patients with pain in the shoulder, it is necessary to exclude some severe diseases. Various drugs such as vitamin B_1 and circulation-improving agents have been recommended. Phenothiazine derivatives are used to influence psychic and autonomic factors. Resting the arm has proved a useful immediate measure, but active exercises should take its place as soon as possible. Stellate block may give a rapid cure in periarthritis humeroscapularis, but it fails in cubital epicondylitis. *In recent years, ultrasonic vibrations* have been preferred. None of the treatment is effective in all cases, and they may have to be used in combination. *X-ray therapy is the treatment of choice.* It should be begun as early as possible. Pain and inflammatory changes soon subside; good functional results are obtained even in cases of long standing if the patient is co-operative.

A series of 917 patients with periarthritis humeroscapularis was treated with X-rays. Cures were usually obtained in 1 to 4 weeks. *After the first irradiation, symptoms may become worse, a fact which should be pointed out to patients to prevent their becoming discouraged. The results were excellent.* Of the patients with periarthritis, 75·9% were cured, 20·8% improved, and only 3·3% were refractory to treatment. The results were not quite so good in 212 patients with epicondylitis. The results were quite so good in 212 patients with epicondylitis. Of these 58% were cured, 31·6% improved, and 10·4% showed no improvement.—(*J.A.M.A., 177*: 11, 1961).

INCIDENCE AND EPIDEMIOLOGY OF RHEUMATIC HEART DISEASE IN CHILDREN*

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THE knowledge of epidemiology of rheumatic fever has been in the past largely a series of apparently unrelated observations concerning such factors as age, seasonal, and geographical distribution. The growing belief that streptococcal infections play a role in the ætiology of rheumatic fever makes it desirable to consider the epidemiology of streptococcal infections along with the rheumatic fever. Since rheumatic fever is a notifiable disease in very few communities, definite figures about its general incidence are not available in India and even in many other Western countries of the world, where the nutritional and general health standards are very good.

Climate by itself even though variable, cannot account for the incidence of rheumatic conditions amongst the people.

In 1956, Robinson reported that through the utilization of an active 'Rheumatic Fever Registry' which maintains a current report of all cases of active rheumatic fever reported in the city and county of San Francisco among youths up to the age of 21 years, it has been noted that there has been an appreciable decrease in the number of active rheumatic fever cases from 1946 through 1955, a period of ten years. This has been accompanied by a decrease in the number of children who were hospitalized or were placed in Convalescent Homes with the condition during these years, and particularly from 1949 onwards. At the same time it was noted that the number of cases of recurrent rheumatic fever remained relatively high until 1954 when, after an educational compaign for physicians and lay persons and with the availability of prophylactic drugs through the Crippled Children Services Programme, there was an appreciable drop which was maintained through 1955. It is observed that there has been an apparent decrease in the mortality rate from rheumatic fever throughout the United States and Canada during the past few years.

A survey of children in all economic strata, reveals a high incidence of nutritional and physical disturbances and of psychological difficulties which are remediable, and what is more important, preventable. The pre-school age is important because the health of the child at this period is definitely reflected in the school-going period. The total mortality for the ten-year age-period from 5 to 14, is less than during the 1 to 4 year period. Rheumatic fever is the most important disease of this age-period, not only as a cause of death, but also as a cause of

*Specially contributed to the ANTISEPTIC.

crippling. It is significant that heart disease is the most frequent cause of death at all ages, over 25 years.

For obvious reasons, the rheumatic problem is singled out for special attention, and it may be hoped that its influence as a cause of crippling and of death will be materially reduced. The Metropolitan Life Insurance Company in 1943 reported a 70% decrease in deaths due to rheumatic fever among its policy-holders between the ages of 5 and 24, in the interval between World War I and World War II. In 1947, Keith and *Pequeguat reported* a marked decline in the mortality rate from rheumatic fever in Canada, particularly in the 5 to 20 age-group. In 1948, the Children's Bureau reported a change in the 25-year period from 1919 to 1944 showing a marked decrease in the mortality rate from rheumatic fever and rheumatic heart disease among white children. This disease was so high as 70% in the 5 to 9 age group, 64% in the 10 to 14 age group, and 57% in the 15 to 19 age group. In 1951, Wolff reported the comparative mortality due to rheumatic fever and rheumatic heart disease in the United States between 1919 and 1921 as compared with that between 1944 and 1945. There was again a 70% decrease in mortality from this disease in 5 to 9 age group and in the 10 to 14 group, with a 60% decrease in the 15 to 19 age group. In 1951, Quinn and Quinn reported similar data from New Haven in the years 1920 to 1948. In 1952, the Metropolitan Life Insurance Company reported again that among its policy-holders of 5 to 24 years of age, the mortality rate from organic heart disease of all types declined from about 28 to 4 per 1,00,000 during the period 1911 to 1950, with the mortality rate due to rheumatic fever declining from about 7 to about 1 per 1,00,000 during this period. In 1955, Wallace and Rich reported on the changing status of rheumatic fever and rheumatic heart disease in children and youth in New York City, showing that there had been a significant reduction in deaths due to rheumatic fever and rheumatic heart disease in children and youths during the past decade. While there have been many reports regarding the decreased mortality from rheumatic fever and rheumatic heart disease, there have been few reports regarding the decreased incidence of this disease during the past decade.

There is a definite seasonal incidence of rheumatic fever which varies in different localities. It has been observed that on the West coast of the United States, the peak is usually reached in January and February, and along the Eastern coast in March and April; and our own observations have been similar. The peak incidence of rheumatic fever and rheumatic heart disease in India is during the winter season, which lasts from November to mid-February. Of fifty children admitted to the Patna Medical College Hospital for Children, 32 gave a history

of attack during the winter and only 18 during summer. This observation is in conformity with those of various other workers throughout the world. The seasonal month-wise incidence, shows the highest number in December and January, which are our coldest months of the year; and in England, the largest number of cases tend to occur in November. The seasonal variation in rheumatic fever generally follows the curve of streptococcal disease such as tonsillitis and scarlet fever. A 'bad' year for scarlet fever is usually a 'bad' year also for rheumatic fever and rheumatic heart disease.

The incidence of rheumatic heart disease amongst children admitted to the Patna Medical College Hospital between 1950 and 1954 was found to be on the increase; from 51 in the year 1950 to 197 in the year 1954.

Table I

Showing the total number of patients and the number of rheumatic cases admitted during the 7 year period (1950 to 1956)

Year	Total number of patients admitted	Number of rheumatic cases admitted	Percentage
1950	3117	51	1·64%
1951	3488	49	1·40%
1952	3676	65	1·80%
1953	2990	163	5·40%
1954	2801	197	7·03%
1955	3631	64	1·70%
1956	3946	53	1·34%

It will be seen from Table I alongside that although there was a gradual decline in the total number of cases admitted in this hospital, the number of cases suffering from rheumatic fever and rheumatic heart disease has been steadily increasing. Thus there were 51 out of a total number of 3117 cases in 1950 (1·64%), 49 out of 3488 (1·4% approx.), in 1951, 65 out of 3676 (1·8%), in 1952, 163 out of 2990 (5·4%), in 1953 and 197 out of 2801 (7·03%) in 1954. With the apparent decrease in the total number of cases, both rheumatic and non-rheumatic, there was a substantial increase in the percentage of rheumatic cases, (from 1·64% in 1950 to 7·03% in 1954) while the total number of admissions declined from 3117 to 2801 in the same period.

Ditkowsky, Stevenson and Campbell (1943) have observed that during the later part of 1940 and early part of 1941 an unusually large number of cases of acute tonsillitis occurred in McLean county in the vicinity of Normal, where the Illinois Soldiers' and Sailors' Children's School is located. It was noted that an abnormally high incidence of acute rheumatic fever developed coincidently or after a latent period of several weeks. The incidence of the two diseases assumed epidemic proportions in the school where 88 children, constituting 15% of the total population of 561 contracted acute rheumatic fever; 241 children contracted hæmolytic streptococcal infection, 88 or 15% of them

contracted acute rheumatic fever. In 51 (57%) of the 88 children, the rheumatic manifestations developed following follicular tonsillitis. In 21 or 23% of the 88 cases of rheumatism, the onset followed an infection of the upper respiratory tract (not tonsillitis). In 16 (18%) of the 88 rheumatic children, no history of a preceding infection of the upper respiratory tract could be obtained. The onset of the epidemic of rheumatic fever occurred six weeks after the onset of the attacks of tonsillitis, and the peak incidence of rheumatic fever admissions lagged 8 weeks behind the peak incidence of throat infection.

The epidemiology of streptococcal infections and rheumatic fever are closely related. In England, Schlesinger (1930) described the occurrence of cases of acute rheumatic fever developing in a Convalescent Cardiac Home following an epidemic of tonsillitis. Sheldon (1931) recorded a similar observation. Bradley (1932) and Glover and Griffith (1931) reported the occurrence of cases of rheumatic fever in schools in which there were epidemics of tonsillitis. Madsen (1940) in Denmark reported a summer epidemic of rheumatic fever following a series of milk-borne hæmolytic streptococcal infection of the throat. In the United States of America, similar studies have been made by Coburn and Pauli (1932), Zuger (1933), and Hiller and Graef (1928).

Atwater (1927) and Rosenan (1928) have called attention to the fact that rheumatic fever was more likely to occur in the year when streptococcal infections were prevalent. Gray, Quinn, and Quinn (1952) found that the incidence of rheumatic fever or rheumatic heart disease, or of both, was found to be higher in the rheumatic families than in the controls. In most instances familial spread was according to the order of birth, from the eldest to the youngest—even though all the members were not affected—and there was a tendeney for successive cases in a family to occur at progressively higher ages. They found that there were many instances in which streptococcal disease preceded the onset of rheumatic fever, and some evidence that "the occurrence of rheumatic fever in the children approximated the pattern of a single autosomal recessive gene except in the mating of the two parents with the disease." It has been observed by McCulloch (1944) that congested living conditions, over-crowded schools, and shortage of essential foods etc., all of which contribute to an increased rate in this disease, have been brought about by the War with its changes in population centres and the migration of people from one part of the country to another and from rural to urban centres in search of industrial employment. Greater emphasis is being laid on the public health aspects of prevention of rheumatic fever, and communities are urged to provide better socio-economic conditions through improved housing, opportunity for outdoor activities awareness of good

nutrition and good public health control of communicable diseases, especially, streptococcal respiratory colds and sorethroats. The relation of the incidence of rheumatic fever to diseased tonsils is of public health interest. Attacks occur whether the tonsils are in or out, and good tonsils do not guarantee freedom from the disease, but it is certainly true that patients improve when diseased tonsils are removed.

Quinn, Watkins and Quinn (1948) have reported that the rate of rheumatic heart disease was 1·6% in rural children, 1·4 per cent in semi-rural children and 2·5 per cent in urban children. The higher urban incidence is however, not statistically significant. There was no significant difference between the rheumatic heart-disease rate for low-rental area urban children and the similar rate for rural children. Among the 147 children with a family history of rheumatic fever 12·9 per cent gave a personal history of rheumatic fever or showed evidence of rheumatic heart disease, compared with 3·8 per cent of children with no family history of rheumatic fever or evidence of heart disease. Crowding at home was an important factor influencing the prevalence of rheumatic heart disease. Crowding in urban homes was defined as less than one room per person and in rural homes as a number of rooms, two less than the number of occupants. The rate in crowded homes was almost twice than in non-crowded homes. These data go to support the idea that rheumatic fever is more prevalent in crowded than in non-crowded homes and that environmental influences are important in determining its presence.

Wilson and Lubschez (1948) reported that the incidence of various rheumatic manifestations during the course of the disease was :—active carditis alone in 7%; chorea in 27%; polyarthritis with or without chorea in 58%; recurrent joint pains in 10 %. Active carditis occurred in association with other manifestations in 45 per cent of patients. However, cardiac involvement was demonstrable in every patient at the last observation. Multiple valvular lesions and moderate or definite enlargement of the heart were observed in about half of the total number of patients. About 90 per cent of them aged 20 to 42 years, were able to carry on their normal activity without circulatory symptoms. The mortality rate indicated that there was an increased risk at puberty, irrespective of the age at the onset of the disease. The highest mortality occurred within the first year after the onset, and this was about three times as great as in most subsequent years. There is a higher first year mortality in children 1 to 5 years of age, during the onset of the disease than among those in whom the onset was between 6 and 11 years.

Quinn and Quinn (1951) have recorded their observations on the decline in the mortality in acute rheumatic fever in New

Haven, Connecticut. There were 1144 deaths due to rheumatic heart disease and its complications between 1926 and 1948; there was a steady decline in the death-rate for rheumatic heart disease in the 2 to 24 years age-group. In contrast, there was no significant change in the death-rates due to rheumatic heart disease *plus* heart-failure in persons over 25 years, or in those for any of the complications of rheumatic heart disease. This decline may also reflect a lowering in the prevalence of respiratory infections due to the hæmolytic streptococcal infection, since acute rheumatic fever appears to be preceded often by such an infection. As regards the epidemiological relationship between scarlet fever and acute rheumatism, Hassler (1954) states that this subject was studied in the German town of Chemnitz between 1950 and 1953, during which an increase in the incidence of scarlet fever was accompanied by a parallel increase in that of acute rheumatism. Whereas 10 cases of acute rheumatism were reported in each of the years 1946 and 1947 when there was no scarletina epidemic, the figures for 1950 and 1951 were 117 and 100 respectively. Although a few of the patients developing rheumatic fever showed any signs of a prodromal scarlatiniform eruptions, 22 children with scarlet fever of a slight degree showed evidence of cardiac damage without joint involvement, and in a few others chorea minor was noted.

Collins in his survey of 825,000 families in various states of U.S.A. found that 31·5 per 100,000 persons of all ages developed an attack of rheumatic fever during a single year. In a parallel study he found the number of children of all ages up to 25 years who had a history of rheumatic fever at any time since birth, was 4·56 per 1,000. In a survey of school children, the incidence of rheumatic fever was found to be 2 to 7 per 1,000. In Baltimore, a very careful long-term survey by Collins (1950) revealed that 7·1 per 1,000 of the population had an attack of rheumatic fever during a single year, and that an additional 1·5 per 1,000 had evidence of old rheumatic heart-disease. The incidence of rheumatic fever varied from about 0·1 per cent to 6 per cent. Rheumatic fever is primarily a disease of childhood and young adult life. The peak-incidence was noted in the age-group 5 to 10 years; over 50 per cent of the first attacks occur under the age of 15 years, and 75 per cent of all cases occur in persons under the age of 30 years. On the other hand, the disease is rare in children under five, and this has been confirmed by Hedley (1940) in his series, to be less than one per cent in the first year of life. Inspite of the fact that there is great limitation in the age-barrier for this disease, it has baffled medical science and public health authorities all over the world.

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VACUUM EXTRACTION IN OBSTETRICS

Despite the clear teaching of William Smellie much harm was done to mother and child by forceps delivery in the 18th and 19th centuries. It is not surprising that Yonge, Simpson, and McCahey turned their attention to traction by suction cups, but the methods they described attracted little attention and were not widely practised. In the present century difficult forceps delivery has gradually been replaced by lower-segment cæsarean section, and instrumental delivery is now confined to low cavity or outlet forceps, often under local anæsthesia. The forceps operation, restricted in scope, is safer for mother and baby than it has ever been; but despite this improvement many obstetricians believe that the vacuum extractor is a safer and simpler means of assisted delivery. Torpin, Koller, Couzigou, and Finderle reported small series of deliveries by means of various types of suction cup; but the main stimulus has come from Malmstrom, who has described his own instrument and technique. He first used the extractor in cases of uterine inertia in order to increase labour pains by keeping the fœtal head closely applied to the partly dilated cervix. Continuous traction before full cervical dilatation can result in necrosis of the fœtal scalp, it is safer to synchronize traction with spontaneous uterine contractions. More recently the instrument has been used mostly in the second stage of labour for direct extraction of the infant.

Rosa and Snoeck calculate that the intracranial tension created by vacuum extractor is a twentieth of that produced by forceps. Theoretically there should be less risk of intracranial damage, and this led Chalmers to use the extractor for the delivery of premature babies. De Watterville and Voegeli have reservations, about this use of the extractor, and believe that forceps' blades protect the premature baby's head from damage during delivery.

In some continental clinics the vacuum extractor has largely replaced forceps. Snoeck, after five years' experience, concludes that the instrument is effective, and that in use it has a wide margin of safety, requires no general anæsthetic, and permits the active cooperation of the mother; forceps have not been used in his clinic since 1959. Few centres in England appear to be using the extractor extensively; but Chalmers and Fothergill, from experience of 200 cases, agree substantially with Malmstrom and Snoeck, although not to the extent of advocating complete replacement of forceps. Fœtal distress, the after-coming head, and face presentation are named by Chalmers and Fothergill as contraindications for vacuum extraction. But they stress the simplicity and safety of the extractor, and find it more useful than forceps for rotation of occipitoposterior and

transverse positions of the fœtal head. The extractor has the added advantage that it does not encroach on the pelvic space available for the passage of the fœtus. Fothergill and Chalmers and Saunders monitored the fœtal heart during delivery with the extractor and noted no alteration in the rate; they concluded that vacuum extraction does not distress the fœtus. Fothergill and Chalmers suggest that the instrument is particularly suitable for use by general practitioners in the patient's home and in general-practitioner maternity units.

Some workers have compared the results of forceps delivery and vacuum extraction, but hitherto none has undertaken a controlled clinical trial. In Copenhagen, Lange has compared 480 cases of vacuum extraction with 376 cases of forceps delivery. The two groups were not strictly comparable, but the evidence suggested that the *extractor was safer for mother and child*. With forceps there was a slightly greater risk of trauma, infection, and postpartum hæmorrhage; babies delivered with the extractor were less likely to suffer from asphyxia, and the prenatal mortality was lower than with forceps. The differences may have been partly due to the use of general anæsthesia for the forceps cases.

The vacuum extractor is likely to be increasingly used in England. Meanwhile there is need for further collaborative studies by obstetricians and pædiatricians. By means of carefully planned trials it should be possible in time to confirm or refute the claims that have been made for this method of assisted delivery.—(Leader, *Lancet*, 22-7-1961).

THE ROENTGENOLOGIC FEATURES OF CARCINOMA IN CHRONIC ULCERATIVE COLITIS

The authors report on 29 patients between the ages of 28 and 62 years with chronic ulcerative colitis of an average duration of 17 years, in whom associated carcinoma developed. The patients complained of a recent change in intestinal symptoms, of progressive loss of weight, abdominal pains or cramps differing from the distress usually associated with colitis, an increase in the number of the stools, and an increase in the appearance of blood in the stools. Hypochromic anæmia of rather severe degree was a fairly constant finding in association with the malignant change. Roentgenologically the lesions consisted of constricting, sessile, polypoid, annular, and scirrhous defects. The most common form was the long constricting lesion with coned ends, ragged edges, small polyp-like defects in the lumen, and an adequate but ragged channel. The occurrence of carcinoma superimposed on ulcerative colitis is a well established fact. Carcinoma tends to occur in younger persons with quiescent ulcerative colitis who have a history of the disease of about 17 years' duration. Differential diagnosis is difficult, particularly in the scirrhous variety, in which the lesions may often resemble strictures roentgenologically. Occasionally, resection of the colon will reveal a carcinoma which was not suspected clinically or roentgenologically.—(*Amer. J. Roentgenol., 86:* 91, July 1961, via *J.A.M.A.*, 16-9-1961).

THE 'NEW LOOK' IN TEXTBOOKS

Much interest has been aroused by the publication of a textbook of cardiology, complete with records of heart sounds and murmurs. Known as a 'phonotexte', the idea is that, having read all about 'heart sounds and murmurs', the reader can then play the records and hear the sounds and murmurs for himself. Some of the records are 'slow action ones', so that the reader-listener has every opportunity to analyse the components of the sounds and murmurs and their time-relationships.—(*Minerva Medica*, via *Practitioner*, October, 1961).

THE PHYSIOLOGICO-BIO-CHEMICAL BASIS FOR THE ÆTIOLOGY, SYMPTOMATOLOGY AND TREATMENT OF ALLERGY AND ITS DISORDERS*

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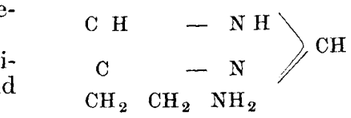
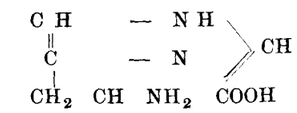
ALLERGY is a phenomenon occurring in various tissues and organs of the body due to certain changes occurring in them as a result of the liberation of histamine ; histamines are formed as a result of removal of carbondioxide (CO_2) from Histidine (Iminazol-a-amino-propionic acid) one of the amino-acids present in proteins and liberated whenever tissues are injured or subject to extraneous influences, like any trauma to the skin, or sudden variations in atmospheric conditions. Thus a sudden severe cold will cause an asthmatic type of spasms in persons already subject to such frequent attacks. Even after a long period of quiescence they may recur. The pharmacological composition and action of histamine will therefore, be of interest.

Histamine is pharmacologically B-iminazol Ethylamine and its structural formula is :—



Histidine, one of the amino-acids present in proteins is Iminazol an amino-propionic acid, with the following structural formula. Histamine has been chemically demonstrated in extracts of the mucous membrane of the small intestine, liver, lungs and the posterior lobe of the pituitary body. It has been identified in the blood leaving the muscles, in amounts, which are increased as the result of activity.



1. Histamine has a powerful *secretagogue action*, causing in animals, an increased flow of saliva, tears, gastric and pancreatic juice ; but in humans, its action is limited mainly to the gastric glands.

2. It is a *stimulant to the smooth muscles* of the intestinal wall, uterus and bronchioles, and in some animals like the guinea-pig, causes death from bronchial spasm, effectively preventing pulmonary ventilation.

3. *Circulatory action* :—In most animals, intravenous injection of histamine even in minute doses, produces a marked fall in blood-pressure. There is a sharp initial fall due to a temporary constriction of the pulmonary arterioles, resulting in interference with the output of the right ventricle ; there is a diminished inflow into the left ventricle and a smaller output into

*Specially contributed to the ANTISEPTIC.

the systemic circulation. The right ventricle soon recovers and resumes its unembarrassed activity, and blood-pressure may rise slightly even above the normal level. But a further steady and prolonged fall of B.P occurs, owing to a state of circulatory failure, inadequate blood-flow to the brain and cessation of respiration.

Histamine produces arteriolar dilatation and capillary paralysis. A subcutaneous injection of 0·3 mg. of histamine causes a general flushing of the skin, a rise in temperature of 1 or 2°C, a small decline of the systolic with a great fall of the diastolic pressure, and an appreciable rise in the pulse-rate; the flush is most conspicuous in those parts, which are previously red. Even a dose of ·06 mg. causes flushing of the face, and a rise of 0·5°C in temperature. Histamine increases the permeability of the capillaries, so that protein and fluid escape from the vessels into the tissue spaces, further reducing the volume of the circulating fluid and aggravating the circulatory collapse. The red-blood count and hæmoglobin percentage consequently rise. The resulting increased viscosity of the blood, throws a further load on the circulation, because there is a greater frictional resistance in the narrow arterioles and so œdema of the tissues is not very evident in histamine-poisoning.

The action of histamine on the human skin and its relation to the triple response, and traumatic shock, will now be considered. Histamine is liberated in the skin, when the peripheral ends of the posterior nerve roots are stimulated (Lewis).

Capillary tone and nerve supply to the capillaries.—When the capillaries all over the body relax as after the injection of a histamine, they can retain so much blood within them, that when they are filled, very little blood will reach the veins. The venous return falls, the cardiac output diminishes, and the brain and tissues generally suffer severely from a lack of oxygen, owing to the impaired blood supply. The same capillaries in any area are not contracted continuously, alternating contractions and relaxations of groups of capillaries occur one after another and thus the blood comes in contact with different parts of the tissue, and an even state of nutrition is maintained. Under normal conditions, the majority of the capillaries in the skin are open, and their tone is relatively stable. Sympathetic fibres pass to the Rouget Cells of the capillary wall. Tonic constrictor impulses normally pass from the vaso-motor centre to the capillaries.

PHYSICO-CHEMICAL AGENCIES THAT CONTROL THE CAPILLARY TONE:—*(i) Metabolites*: during activity, as while exercising, marked dilatation occurs in the capillaries and arterioles of the skeletal muscle; this is probably due to some product of tissue activity—metabolites, the factor at work may perhaps be the

rise of CO_2 tension, or *p*H or the appearance of some non-acid substances. *(ii)* Whenever a tissue is injured, a histamine-like substance, probably histamine itself, is liberated causing capillary dilatation, increased capillary permeability and by means of an axon reflex, also local arteriolar dilatation. *(iii)* Adrenaline and pituitrin produce local capillary constriction.

The triple response of the skin.—If the skin on the front of the abdomen is very lightly stroked, a white line appears which is strictly limited to the area of the skin stimulated and is quite sharply outlined. The line appears after a definite latent period, persists for one or two minutes and then gradually fades away. This white line is due to local capillary constriction. In subjects with more sensitive skins or when a heavier stroking is employed, a triple response may be obtained. The triple response will be seen in three stages, one after the other:—*(a)* After a short latency, a sharply defined *red line* develops at first bright-red in colour but gradually assuming a bluish tinge, indicating that the blood is stagnant, and its hæmoglobin is therefore, undergoing excessive reduction. This red line can on the basis of the above criteria be shown to be due to capillary dilatation; this can also happen when the local nerve supply has degenerated. (*b*) After a further interval of 15 to 30 seconds, a widespread flush or *flare* appears in sensitive subjects. This is primarily the result of arteriolar dilatation. The flare spreads for a variable distance from the area stimulated, is mottled in colour from alternative islets of hyperæmia and normal skin, and the edge is crenated, as would be expected from the manner in which arterioles are distributed to the skin. The colour is red throughout and does not tend to become purple from oxygen deficiency, proving that blood flow is rapid. The temperature of the skin over the flare, rises by 0·5°C to 2°C, as a result of the increased blood-flow. As this flare depends on an intact nerve supply to the skin it is abolished when the local nerve fibres have degenerated. It is still obtained if conduction in the sensory nerves leading from the part is blocked by the injection of novocaine into the nerve trunk; the reaction is therefore, *not* a reflex through the central nervous system, but probably results from a local *axon reflex i.e.*, a reflex depending on the branching of the local nerve fibres in the skin. (*c*) In susceptible subjects, a *wheal* develops at the site of the red line, and reaches its maximum height in about five minutes, projecting one to two millimetres, above the general surface of the skin. It is due to increased permeability of the minute vessels, which permits the escape of fluid, closely resembling plasma into the tissue-spaces. The fluid contains 4 or 5% of protein, and traces of fibrinogen and clots on standing. The wheal gradually becomes paler, as it increases in size, owing to

a compression of the minute vessels. A marked arteriolar flush must be present for the wheal to occur, because a rich blood supply is needed to provide the fluid. The wheal is not due primarily to increased intracapillary pressure; for if the arm is compressed so as to produce venous congestion, the wheals formed are smaller, owing to a diminished blood flow, in spite of the fact that the capillary pressure is raised. If *trypan blue* is injected intravenously into a person, it does not escape into the tissue spaces, but passes into a wheal while it is forming due to increased capillary permeability.

Triple response from histamine.—Lewis has shown that histamine, even in dilutions of 1 in 3000, when injected into the skin, produces a typical triple response:—(*i*) local dilatation of the capillaries and venules, by direct action; (*ii*) widespread dilatation of the surrounding arterioles, from a local axon reflex and (*iii*) local increased permeability of the walls of the minute vessels, increased exudation of fluid and wheal formation.

If the skin is firmly stroked and a histamine solution is inoculated simultaneously, similar triple responses develop in both cases, and they have exactly the same time relations, as regards onset and disappearance.

Evidence for "H"-substance:—The above observations suggest that the triple response, elicited by heavy stroking, must be due to a local liberation in the skin of histamine or a closely related substance. ("H"-substance). Much evidence has been brought forward, in support of the above contention:- (*a*) A large number of agents can produce the triple response:— pricking, scratching, freezing, or burning the skin, the passage of strong electric currents, the inoculation of irritants such as 5% HCl, 5% NaOH, 1% morphine, 2% atropine, cantharides, peptone, fish extracts, flea and gnat bites in susceptible subjects, alcoholic extracts of the skin, liver and lungs. Many dissimilar agents, all of which act alike, in injuring the tissues, thus produce the same complex vascular response. The explanation for this uniformity of action, is that they all liberate the same chemical substance in the skin, which alone sets up the triple response. (*b*) If histamine is punctured into the skin, a vivid flare develops, as stated above, and fades away after 10 minutes. The blood-supply to one arm is obstructed, a histamine solution is inoculated, the occlusion is kept up for about 10 minutes, and is then released. The control arm is similarly treated, except that the histamine is inoculated, a minute before the vessels are released. Both arms now become red—"*reactive hyperaemia*"— but this redness rapidly fades away, except in the regions where histamine was injected. As soon as the histamine flares are visible, their outlines are marked out in ink, and again at suitable intervals, as fading takes place. It is found that fading in

the two arms occurs simultaneously. This leads to the conclusion that when histamine is injected into the skin, in which circulation is arrested, it is retained in the skin, and produces its full effects as soon as the circulation is released. (*c*) On the basis of the above findings, a crucial experiment is performed. The observations described, are repeated, but instead of inoculating histamine, the skin of a sensitive subject is firmly stroked; exactly the same results are obtained, as with histamine injections: the flare develops and fades in the same way in both arms, when the circulation is released. This experiment proves that the mechanical stimulus itself does not reflexly produce the flare; if it were so, during the ten minutes of vascular occlusion, which followed the application of one of the stimuli, these effects should have passed away. This would naturally lead to the conclusion that the mechanical stimulus causes the liberation of some chemical substance, which behaves exactly like histamine; it is retained in tact in the skin during the period of circulatory arrest, and produces its effects as soon as the circulation is released.

The evidence so far presented may now be summarized:—

(1) A large number of agents, which injure the tissues, elicit the triple response. (2) The flare-response to heavy stroking, develops in a normal manner, after 10 minutes of circulatory arrest, suggesting that a chemical body acts as an intermediary. (3) Identical responses in all aspects, can be obtained by inoculating histamine in high dilution into the skin. There is little doubt that some substance with a histamine-like action, ("H"-substance) is liberated, when the skin is injured. That this "H"-substance, is certainly histamine is suggested by the following observations:- (*a*) Histamine has been definitely demonstrated in extracts of many organs, and of the skin. (*b*) The back of a susceptible subject, is extensively and severely stroked till a large wheal develops. Under these circumstances the "H"-substance might be expected to be formed in such amounts that some might escape into the circulation, and produce effects at a distance. It is found that flushing and a rise of temperature of the skin of the face occur like those which follow a subcutaneous injection of 0·06 mg. of histamine.

THE EFFECTS OF PHYSICAL AGENCIES ON THE SKIN, ORGANS AND TISSUES WILL NOW BE CONSIDERED:—

The effect of heat:—If the arm is plunged into a bath of water at 45°C, a marked reddening of the skin occurs, mainly due to a dilatation of the minute vessels of the skin, partly as a result of the liberation of "H"-substance, and also of the direct action of the higher temperature on the capillaries, as well as a reflex dilatation of the larger arteries and veins, leading to an increased blood-flow through the skin. At higher temperatures, a typical

flare, wheal, and a blister are produced, owing to the formation of large amounts of the "H"-substance. If the vessels of an organ are irrigated with saline at 40°C, the dilatation affects first the capillaries and the arterioles. This change is likely to occur, during tissue activity, when the temperature of the active organ rises. Heat produces a marked rise of capillary pressure in the skin.

The effect of cold : Cold produces complex effects :—(1) There is slight pallor of the skin due to arteriolar and capillary constriction, which is best noted, when the skin, reddened by warmth, is plunged into colder water. (2) If the hand is immersed into very cold water, (5°C to 10°C), for 5 to 10 minutes, the skin becomes bright red in colour, which is indistinguishable from that produced at a temperature of 45°C. The arterioles are contracted and the minute vessels are dilated. At temperatures of 110°C, however, oxyhæmoglobin undergoes very little dissociation, and the oxidative activities of the tissues are also much depressed, so that in spite of the slow and inadequate blood flow through the path, the hæmoglobin is not reduced, sufficiently, enough to give a dark colour to the blood. (3) At skin temperatures of 20 to 25°C, cyanosis is likely to develop. The vascular changes are similar to those described in (2) above. It is presumed that at this critical temperature, the blood flow is reduced more than the oxygen utilization by the tissues. Consequently, the oxyhæmoglobin is much reduced, and a dusky colour appears. (4) Freezing the skin results in extensive cellular damage, and a liberation of the "H"-substance with the usual triple response.

The action of light :—Exposure of the skin to strong light produces an *erythema*. When the skin is exposed for 20 minutes to rays from a 40,000 candle power lamp, the whole area becomes uniformly red. The erythema is due to the effect of heat, and gets less in about 2 hours. Erythema due to light appears in about 3 hours ; and it reaches its maximum in about 12 hours, and decreases after two days. The redness is associated with capillary dilatation and stasis. If the skin is previously covered with a glass plate, which keeps back the ultra-violet rays, the delayed erythema is not obtained. On the other hand rock crystal, which allows the rays to pass through, affords no protection. Clearly light erythema is due to the action of the ultra-violet rays. These rays act by causing a slow liberation of "H"-substance in the skin. The visible spectrum can also however act on the capillaries, if used long enough and in sufficient concentration. The erythema in Finsen's experiment, disappeared in 10 days, and was followed by pigmentation and desquamation. The effect on the capillaries is of a long-standing nature, as seen in the areas which had been exposed in the

experiment becoming redder than the other parts of the skin, when the skin of the area is rubbed nearly 6 months later.

Tissue fluid and lymph.—The capillaries are a closed system of vessels and the blood only comes into actual contact with the cells of the tissues in the liver and spleen, where the endothelial lining of blood-spaces is defective. The cells in all other places are bathed by the tissue fluid, which acts as an intermediary, bringing nutritive material and removing the products of metabolic activity.

The lymphatic system includes tissue-spaces, delicate lymphatic capillaries, and larger vessels, which unite to form the right lymphatic duct and the thoracic duct. The larger serous cavities like the peritoneum and pericardium, behave in many respects like tissue-spaces. Lymphatics are also a closed system of vessels, like the vascular system. A distinction should be made between tissue fluid and lymph. The tissue fluid is similar in composition to the blood-plasma, except that its protein content is a very low or negligible.

The lymph in the thoracic duct is viscid, opalescent, and faintly alkaline, contains the same constituents as plasma, but is poorer in proteins (about 4%), and richer in salts and water. It varies in composition with the degree of activity of the tissues, and may contain much fat. The lymph coming from the liver contains three times as much protein, as the lymph from the limbs, while the lymph from the intestine is intermediate in its protein content. A few white corpuscles, chiefly lymphocytes may be present.

Tissue fluid is derived from the blood. It is removed partly into the lymphatics, and partly back into the blood stream.

"Traumatic Shock" is a very definite clinical condition, which may follow direct injury to the tissues. Its important features are a profound depression of the nervous system, and marked circulatory collapse. The patient is quiet and pays no attention to what is going on around him. The skin and mucous membranes are cold and clammy grey or cyanotic in colour and there is sweating. The pulse is almost imperceptible, and very rapid. The arteries are narrowed and the blood-pressure is low. The blood volume is found to be decreased, often markedly and its viscosity is increased, owing to its greater concentration, and the hæmoglobin percentage goes up. Breathing is characterized by long deep sighing respirations alternating with very very frequent superficial ones. The reaction of the patient to stimuli is very slight and that too only to those of a painful nature. The limbs are toneless; spontaneous movements are not made, but in response to urgent orders, very brief limited movements may be executed at times. Complaints may be made of cold, faintness, and deadness of the

whole body, the temperature being subnormal. Cases of shock are usually divided into two groups :—(1) *Early or primary shock* which sets in immediately after an injury. Its causation is not definitely known, but it may be due to afferent impulses, which reflexly set up vaso-dilatation, and a profound fall in blood-pressure. The diminished blood-flow to the brain may result in loss of consciousness. Recovery may take place or the condition may merge into the succeeding one. (2) *Delayed or secondary shock* may set in after a latent period, during which nothing obviously abnormal may be noted or it may follow continuously on primary shock. This variety of shock is due to a complex set of factors and it is still uncertain as to what extent afferent nervous impulses are responsible, and what importance should be attached to the liberation from injured tissues of vaso-dilator substances. Important experiments in this connection, were made by Cannon and Bayliss. They tried to produce a similar state of shock in anæsthetised animals by seriously damaging the tissues in the hind limb. If the muscles and bones are badly smashed by repeated blows, the blood pressure falls to the shock level, and finally death occurs. They claimed that shock can be prevented if the local blood-supply is occluded, to prevent the venous return from the damaged area. Removal of the clamps allows the characteristic symptoms to appear. Division of the nerve supply to the limb does not prevent the development of shock. This naturally leads to the conclusion that shock is due to some poisonous substances, liberated from the damaged tissues. It is known that tissue extracts contain a number of depressor bodies, *e.g.*, histamine, choline derivatives and adenylic acid. Histamine would appear to be the possible causative factor for several reasons :—(*a*) Histamine can be liberated at any rate in the skin, by even the most trivial injuries ; (*b*) many of the circulatory features of traumatic shock, resemble those produced by poisonous doses of histamine. Recent investigations have led to increasing dissatisfaction with this purely chemical or toxæmic theory of the causation of traumatic shock, and there is doubt especially on the intervention of histamine. It has not been possible to demonstrate either histamine or any other depressor substance, in the blood leaving the traumatized limb. The appearances of the viscera in histamine shock, are different from those in experimental traumatic shock. In the former, they are intensely congested ; in the latter pale and anæmic. Compared to other tissues, muscle yields on extraction rather small amounts of histamine. Loss of fluid from the circulation is an important factor in the production of experimental shock. It is due partly to the escape of blood from damaged vessels in the traumatized area, and partly to the escape of fluid from vessels, that have become permeable, but

are not ruptured. Some workers claim that if the afferent nerves of a limb are severed, very little shock may follow the trauma. Further, if the spinal cord is anæsthetized, subsequent trauma is much less harmful, and it is argued that the afferent impulses set up by the injury reflex depress the circulation, but the mechanism of such depression is not sufficiently known. The non-occurrence of traumatic shock, when the limb circulation is occluded, may be due to :—(*a*) A reduction of local bleeding or exudation, in the injured limb, produced by occlusion, of the blood-supply ; (*b*) the afferent limb nerves, when deprived of blood-supply, may be unable to transmit the nocuous impulses. Re :—traumatic shock in man, the following additional factors have to be considered :—(*i*) The subject is often conscious, when the injury is inflicted and not deeply anæsthetized, as in animal experiments ; (*ii*) other factors also present which tend to reduce the blood-pressure are : (*a*) exposure to cold, (*b*) lack of food and water, (*c*) considerable sweating, causing further loss of fluid, and some lowering of the body temperature ; (*d*) obvious hæmorrhages of even 25% of the blood-volume, which may give rise to a fall in B-P., when combined with injury, (*e*) in some instances, infection may greatly aggravate the condition, (*f*) a prolonged and deep anæsthetic if administered, may give rise to a considerable fall of B-P., (*g*) in the case of abdominal operations, there may be local vaso-dilatation, which increases the capacity of this important vascular bed, and leads to a lowering of the B-P. Injury may reflexly stimulate breathing, and over-ventilation eliminates excessive amounts of CO_2 from the blood. The condition of acapnia interferes with the relaxation of the heart, so that venous filling is defective resulting in depression of the cardiac output and circulatory failure. Over-ventilation is not a constant initial symptom of shock, and only a contributory factor in some cases. The low circulation rate and low B-P. present in shock, result in a malnutrition of all the tissues. The higher centres of the brain suffer most from this anoxia, and anxiety, dullness or apathy result. If the B-P. is kept at about 60 mm. Hg. for several hours, the medullary centres, particularly the vasomotor, also fail, perpetuating the state of shock. The basal metabolism is diminished, and because of decreased heat production, the body temperature tends to fall further. Plasma bicarbonate is lowered. This is due partly due to hyperpnœa referred to above, and partly to the passage into the blood of acid products of incomplete combustion of carbohydrate or fat.

In **"Oedema"** there is an abnormal accumulation of fluid in the inter-cellular spaces and it may occur physiologically as during and after muscular activity, or pathologically as in venous obstruction, cardiac diseases, renal œdema and in conditions of *allergy* ; it has been shown that in allergy a variety of

factors, which injure the tissues, liberate in the skin a histamine-like substance, which increases the permeability of the minute vessels, and increased exudation of a fluid, rich in protein, occurs into the tissue spaces, forming the *wheals* mentioned in the *"Triple Response"* of the skin. In susceptible subjects, a light stroking of the skin may give rise to the flare and wheal—urticaria factitia; the injection of a histamine into the skin produces a normal local response and there is no state of unusual reactivity in local vessels. It would appear that the precursor of histamine, present in the skin cells, is excessively unstable so that very trivial injuries are sufficient to cause the liberation of sufficient histamine to give the full "triple response." Various poisons taken along with food or elaborated in the body, or resulting from an anaphylactic reaction, may also give rise to urticaria, possibly by liberating histamine in the skin. Calcium salts diminish capillary permeability and reduce œdema and so they are of value in conditions like chilblains in which the capillary permeability is increased, and in *albuminuria of adolescents*, by preventing the escape of albumin, through the glomeruli of the kidneys.

Anaphylaxis and its relationship to immunity and allergy:—Histamine is found wherever protein is broken down into amino-acids in the presence of putrefactive organisms. It occurs in some quantity in the intestinal contents and in the putrefaction of meat, and has been isolated from preparations of ergot, though it is doubtful if it occurs in the fungus itself; the quantity present is too small to modify the action, except when ergot is injected intravenously. The action of histamine is similar to that of a number of protein-derivatives of unknown structure, such as peptones, the split protein produced by the action of alkalies and the extracts of various organs and muscles. A very slight modification of the protein molecule is sometimes enough to change it into a poison, characteristic of this group. Histamine is also known as ergamine. The symptoms of secondary shock from severe injury in man may also be included in this group, for they resemble those produced in animals by histamine so closely that it has been suggested that they are due to the liberation of histamine or similar poisons in injured tissues.

Another form of poisoning, which very closely resembles that of histamine is *anaphylaxis*. The injection of any harmless foreign protein, produces no symptoms whatever; but, if the same protein is injected 15 days later, severe or fatal poisoning may result. This anaphylactic reaction is very specific for each protein; *e.g.*, if the first or sensitizing injection consists of horse serum, then the second injection *must* contain horse serum, that of any other animal causing little or no reaction. The sensitiveness to the second injection remains for many months

in man, perhaps throughout life, and this has come to be of great import in later years of life, since the injection of any of the anti-toxic sera in childhood, suffices to induce fatal poisoning in adult life, if a second treatment is necessary with serum from the same species of animal. When an animal recovers from even a slight anaphylactic shock, no reaction occurs from a further injection; the animal is desensitized. Many unusual reactions to certain foods or to exposure to dusts and pollen, which are harmless to most people, are now believed to have been due to their having been previously exposed to and become sensitized to them. Anaphylaxis is induced only by proteins. The various explanations given for anaphylactic shock are:—(1) The first or sensitizing injection leads to the development of a ferment-like substance, which modifies the protein injected (Antigen); on the second injection, this ferment decomposes it rapidly into a poisonous "anaphylotoxin," which produces symptoms, just as *histamine* does. (2) The sensitizing injection leads to the formation of a new antagonistic body, *Precipitin*, which penetrates into the cells of unstriated muscle, and other tissues; when the second injection is made, the antigen penetrating into the cells, reacts with the precipitin by a process akin to precipitation, which induces contraction of the muscle and other symptoms. This view accords with other known facts about the behaviour of antigens, and is supported by experiments in which the involuntary muscle reacted to the second injection, after all trace of protein had been washed out of the vessels, and in which the anaphylotoxin in the blood, must have also been removed. So, in *anaphylaxis*, there is no new poison formed in the blood, but the cells are peculiarly sensitive to the presence of the antigen, due to the formation of a precipitin in the blood and tissues, following the first injection, which is not toxic by itself, but only reacts with the antigen. This precipitin may be transferred to the second animal by transfusion, which then becomes sensitive to the antigen, though it has never come in direct contact with it. After recovery from the shock a second attack is not caused by a second injection of the antigen, since all the precipitin has been combined already. The similarity of symptoms, induced by all these, suggests that they arise from a single substance, either histamine or some other drug, different chemically, but having a similar action.

Allergic and immunological considerations also play an important part in the success or otherwise of tissue transplantation, which has a very wide field in the various surgical procedures. From the clinical point of view, the purpose of tissue transplantation is to replace by functionally normal tissue, of accidentally lost destroyed or impaired tissues. But skin, grafted from the body of one person to another, does not survive for long, and this is true of most other tissues.

Ordinarily, the only type of graft, that takes is an autograft, in which the donor is also the recipient. Skin homografts soon become inflamed and infiltrated by leucocytes mainly monocytes, and their blood vessels become congested. The grafts become necrotic scabs, which slough and are rejected within two weeks. This failure of homograft occurs also in animals. Homograft destruction is an immunological phenomenon. Like pathogenic organisms, proteins, and certain other bio-chemically complex foreign substances, grafts of some one else's tissue cells confront their hosts with substances, immunologically foreign to them, and so provoke an immunological response or sensitization, which is responsible for their rejection. Once it occurs, this state of sensitization is systemic, and is generalized throughout all parts of the body, supplied by blood vessels and may also be of long standing. Subsequent skin homografts from the original donor, transplanted to a host, that has already been exposed to and sensitized by homologous tissue cells from that donor, undergo an accelerated rejection, usually referred to as the *Second-set* reaction. In fact this constitutes an important biological test for homograft sensitization.

Graft rejection and hypersensitivity :—The pattern of cellular response provoked by homografts, along with certain other features of homograft reaction is closely related to the more familiar allergic and delayed-type of hypersensitivity responses. For example, each of these types of immunological response is susceptible to the action of cortisone, but not that of antihistaminic drugs.

TREATMENT OF ALLERGIC DISORDERS :—A number of drugs of the phenothiazine group for treatment are on the market ; the essential principle in treatment is to start with low doses, once or twice daily and gradually increase the dose to thrice daily and watch for any side-reactions, such as drowsiness, gastro-intestinal disturbances, nausea, vomiting, dryness of the mouth, urine-retention and palpitation of the heart etc. when the drug should be withdrawn. A good anti-allergic or anti-histaminic drug must be effective even in low dosage with few or no side-reactions at all. Certain points mentioned in the medical and clinical trial literature on the action of certain of these drugs, claim to have a very strong musculotropic and anti-histaminic action, but only weak anti-cholinergic properties ; these are however open to question, as the action of histamine, (the primary product responsible for the changes in tissues and the consequent signs and symptoms in allergic disorders), are akin to those of acetylcholine, the primary chemical mediator substance, responsible for para-sympathetic nervous stimulation in these disorders. Therefore a good anti-histamine must also be anti-cholinergic or cholinolytic, and not the reverse. Great

care and circumspection, are therefore needed in the manufacfacture of these drugs.

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TUBERCULOSIS—
EVALUATION OF THE HEAF TUBERCULIN TEST

"The Heaf test is a multiple-puncture tuberculin test developed by Professor Frederick Heaf of Wales, after whom it is named. It employs an ingenious spring-activated lancet which causes *six needles to be driven to a pre-determined depth through a drop of tuberculin on the skin.*"

As a mass-test the tuberculin-test should be specific, reliable and sensitive. It should be acceptable both to the subjects and the staff—it should be painless, unaccompanied by severe local reactions and safe. It should also be non-expensive. The Heaf-test fulfils all these requirements to a great extent.

The technique of the Heaf test was as follows : The skin of the forearm was cleansed with acetone ; a drop of special P.P.D. tuberculin with a concentration of 2 mg. per ml. was applied to the cleansed part with a flamed inoculating loop, a sterile tooth-pick, or a syringe with a 25 gauge needle ; the end plate of the apparatus was sterilized by covering it with alcohol and flaming it ; the end plate was then applied to the drop of tuberculin, and the needles released. The area was then allowed to dry. The reading was taken at 72 hours or after a longer period. Four types of positive reactions ranging from 4 or more discrete papules to an area of induration over 10 mm. in diameter were observed. 100 or more subjects could be tested in an hour.

"The Heaf multiple puncture tuberculin test was applied to 61,000 pupils entering 186 New York City high schools during 1958. In this concentrated eighteen-week experience it was found to be an acceptable test both to students and staff, and considerably more dependable than the Vollmer patch test. *Comparative studies with the Mantoux test in a variety of groups showed the Heaf test to be highly specific, with a sensitivity level between that of intermediate strength and full-strength tuberculin intradermal tests.*

"*Heaf reactions* can be interpreted with a *high degree of consistency,* and in certain circumstances may be susceptible to reading by the subjects themselves. *The Heaf test is a satisfactory substitute for Mantoux test in mass tuberculin* screening programmes to-day, and may prove to be equally valuable in epidemiologic investigations in the future."—(Arthur B. Robins and Joan N. Daly, *New Eng. Med. J., 262* : 1008, 1960).

THYROID CARCINOMA IN CHILDHOOD

At a meeting of the Vienna Physicians in April '61 Dr. H. W. Swoboda reported 4 cases of carcinoma of the thyroid and of an adenoma suspected to be malignant, in children between the ages of 7 and 14 years. None of the children had undergone roentgen therapy. The diagnostic value of scintillation thyreograms was emphasized. All solitary nodes in the thyroid gland of children should be excised. In one patient who could not be subjected to a radical operation, a regression of the pulmonary metastases was achieved by combined therapy with roentgen rays and thyroid preparations.—(via *J.A.M.A.*, 2-9-1961).

DOES FINGER SURGERY IMPROVE HEARING LEVEL?

Whether finger surgery can restore hearing acuity has long been debated. Medical specialists discount the procedure's validity, but certain osteopaths contend that, through finger surgery, they can restore substantial acuity both in conductive and some sensorineural impairments. To resolve this controversy, the author obtained audiograms of several deaf children prior to, and after finger surgery by one of the osteopaths in question. No change in hearing levels was observed despite the fact that the osteopath's audiograms showed substantial improvements in hearing level. Parents still maintain that each of the children actually heard better following surgery and that friends of the family would confirm this contention. The suggestion is offered that the osteopath's audiograms were either inaccurate or falsified, and auditory training following finger surgery may have accounted for apparent improvement in the children's behaviour. —(*Arch. Otolaryng.*, Vol. 74: 256, Sep. 1961, via *J.A.M.A.*, 23-9-1961).

FUNGUS AND BACTERIAL INFECTIONS OF THE EAR

Infection of the skin lining the external auditory meatus or a post-operative mastoid cavity is common. A recent study by A. E. W. Gregson and C.J. La Touche made over a four-year period in the North of England would suggest that active fungal infection, predominantly by species of *Aspergillus* or *Candida*, may be commoner than is recognized and may explain the resistance to treatment of many cases of otorrhœa.

During their investigation the authors suspected otomycosis in 180 patients out of the many they must have seen with otitis externa, and the fact that fungal infection was found in 80 of them would suggest that clinical features are informative. Irritation in the ear, often intense, with a scanty and usually odourless discharge is common.

Broad-spectrum antibiotics such as neomycin, bacitracin, polymyxin, and soframycin are effective in bringing bacterial infection under control, but have slight or no action against fungi, which can then grow unchecked if the meatus remains moist.

Treatment should therefore be initiated with a thorough but gentle removal of pus and debris, leaving a dry canal, and this is repeated when necessary. The choice of medicament which is applied after cleansing is wide, but it would seem that none should be persisted in for more than a week or two. Thus, if the first choice is a broad-spectrum antibiotic with a hydrocortisone derivative, a change should be made to one of the aniline dyes such as a 2% solution of crystal violet in 50% alcohol-water solution. This has an effective antifungal as well as antibacterial action. If fungal growth is proved, a choice of fungicides is now available which may be used locally or systemically.—(*B.M.J.*, Editorial, 20-5-1961).

ANTIBIOTIC THERAPY IN TROPICAL SPRUE

Twelve patients with tropical sprue were treated with broad-spectrum antibiotics for 2 weeks. Clinical improvement with elimination of megaloblastic anæmia occurred in one-third of the patients and partial improvement was observed in another one-third. Steatorrhœa decreased significantly in one-half of the patients. Improved intestinal absorption of vitamin A and xylose occurred in the patients showing clinical improvement, but improved absorption of Co^{60} and vitamin B_{12} was not observed in any of the patients studied. This is the *first report in which antibiotic successfully cured the megaloblastic anaemia of sprue.*—(*Gastroenterology, 41: 208*, Sept. 1961, via *J.A.M.A.*, 30-9-1961).

described quite accurately and clearly giving a precise conception of urine formation.

Genito-urinary system.—Sushruta has mentioned the genito-urinary system having various organs connected with each other in the following lines :—

नाभिपृष्ठकटीमुष्कगुदवंक्षणशेदणम् ।
एकद्वारस्तनुवृक्कदो मध्येबस्तिरधोमुखः ॥
अलाब्वा इवश्पेण सिरास्नायुपरिग्रहः ।
बस्तिर्बीस्तशिरश्चै व वौठलं वसणौ गुदम् ॥
एकसम्बन्धितो होटे गुदास्थिविवराक्षितः ॥

that the system is related to नाभि, पृष्ठ, और, मुष्क, गुद, वंक्षण, शेकस. The (kidney वृक्कदो not त्वक्दो which is the writer's slip) has been described here like *alabu* (reniform) has only one opening and faces downward and is a small organ. In the middle of वृक्क facing downward lie *basti* or *Bastishershe** called *mutra-vah-srotas* or ureters. The kidney is full of सिरायरिग्रहः (vessels) and स्नादुयरिग्रह nervous and fibrous connection. *Basti*, बस्तिशिर *Paurash* (prostate) वृषणौ (*Testis*) and *gudam* are all connected with each other and lie in गुदास्थिविव or pelvis. Here the word *guda* means the organ which excretes *mala*. Urine is also a *mala* hence *guda* here means the urethral part. गुदकीडायाम् itself denotes *guda* to be the penis or urethra here. And so the genito-urinary system has also been fully described.

Some observations.—The use of the words *amashayas* and *pakwashaya* in connection with the formation of urine give us an idea that Sushruta treats the formation of urine in the same way as the formation of faeces. Thus from mouth to the anus we have a tube like structure called *Mahasvota* in which there are *amashaya*, *agnyashayas* and *pakvashaya* and *guda* ; similarly here also in urinary systems an *amashaya* and a *pakvashaya* have been mentioned. From this we may infer that just as in the process of digestion *pranavayu kledak*, *kapha*, *pachakagni*, *saman-vayu* and *apanvayu* do their work, and bring about *madhur-amla-* and *katuvipak* to divide *anna* into *prasad* part and *kitta* part producing *rasa* and *purish*, similarly here *jala* is treated with its various useful or harmful crystalloids. *Amashaya* is the part where *Kledan* is done in Bowman's capsule and *madhur bhav* is formed. Here we know for certain that glucose is also filtered. Then the *grahani* part is that part of tubules which has a neck, proximal convoluted part, Henle's loop and distal convoluted tubule. Here a special *Agni* must be working like (*Jatalagni*) (not known to the modern scientists) and also a nervous activity like that of *saman vayu* must also be playing its part of dividing (विभजन)

*In मध्येबस्तिरधोमुखः Basti means Bastishir.

the above line is that "there are superficial and inner glomeruli; some of them are active (जाग्रतः) and some are not (स्वपतः) and they filter blood or fluid brought in afferent vessels :—

नाडीभिरुपनीतस्य मूत्रस्यामाशयान्तरात् ।

from the region of cortex or *Amashaya* of the kidney. It is done by Bowman's capsule. Hence an indirect but precise reference to this part has been given by Sushruta which has stood the test of time and is accepted today as correct.

Tubules and renal medulla.—The filtered fluid flows through the tubules called *Nadyah* (नाड्यः). This fluid after undergoing various changes of separation (विभजन) and absorption (प्रचूषण) is collected in larger collecting tubules which lie in the part called *pakwashaya* (पक्वाशय) or renal medulla. These tubules number hundreds of thousands, which give the exact idea of millions of nephrons with their malpighian corpuscles and tubules :—

पक्वाशयगतास्तत्र नाड्यः मूत्रवहास्तु याः ।
तर्पयन्ति सदा मूत्रं सरितः सागरं यथा ॥
सूक्ष्मत्वान्नोपलभ्यन्ते मुखान्यासां सहस्रशः ॥ सु. नि. ३

These tubules residing in *pakwashaya* part of the kidney are called (मूत्रवहा नाड्यः) (tubules through which urine flows; the correct translation of it being uriniferous tubules). They are microscopic (सूक्ष्मत्वात्) therefore their lumen (मुखानि) cannot be seen with the naked eye (नोपलभ्यन्ते) but these मुखानि are far too numerous (सहस्रशः).

Pyramids of the kidneys.—*Mutrashayas* having thousands of uriniferous tubules (मूत्रवहा नाड्य :) mean also the renal pyramids. They have been termed by Sushruta as *ghatas* (घटाः - pots). If a new earthen pot is filled with water, the water oozes out through several small microscopic pores in its walls. The same happens here :—

आभुत्वात् सलिलेन्यस्तः पार्श्वेभ्यः पूर्यते नवः ।
घटाः यथा तथा विद्धि बस्तिर्मूत्रेण पूर्यते ॥

These various घटाः or pyramids in the kidney through their duct of ballini etc., send forth the *salil* or fluid *i.e.*, urine. The act of sending is that of oozing. This oozing surface of the *ghatas* or pyramids is called area cribrosa an exact word for the oozing ghatas.

Calyces.—From the pyramid start calyces, minor and major which have been depicted as सरितः (rivulets) proceeding towards the सागरम् (ureteral pelvis). In the calyces the flow begins just as it begins in a rivulet. Thus the acts of निस्यन्दन (filtration), प्रचूषण (absorption), पूरण (oozing) and तर्पण (flowing) all have been

him in the plural as (वृक्कौ) signifying that they are two in number. Charaka has also made mention of वृक्कौ in connection with the counting of the various viscera in abdomen or *Koshtha*. *Vrikka* therefore must refer to the kidneys, there is no other viscus in the abdomen which is dual in number. All other viscera are mentioned and named quite correctly and only the kidneys remain, which is denoted by the term *vrikka*. The conception and the description of kidneys by Sushruta are further dealt with later.

Nephron.—This is called by Sushruta as *Mutrashaya* (मूत्राशय).

मूत्राशयो मलाधारः प्राणायतनमुत्तमम् । सु नि. ३१२४

This *mutrashaya* is the seat of the formation of a *mala* or excretion called *moothra* or urine. It is also the seat of *Prana* or life. If this unit stops working altogether as in anuria when the function of the nephrons is stopped, life will become extinct. Although the term *Mutrashaya* is mentioned in the singular number, its relation to the thousands of tubules, gives us an idea of several nephrons (*vide infra*).

Renal cortex.—Just as a nephron has a Malpighian corpuscle consisting of a Bowman's capsule and the glomerulus and lie in the cortex of the kidney and receive blood from renal vessels, so is the case with *Mutrashaya* also.

नाडीभिरुपनीतस्य मूत्रस्यामाशयान्तरात् ।

This quotation from Sushruta in *Nidansthan* Chap. 3 gives us the clue. Here the word *Amashaya* (अमाशय) means the cortex of the kidney. This *Amashaya* receives blood which contains the material from which urine is formed. In this *Amashaya* there are several afferent vessels called नाडी (it is plural depicting numerous vessels) these नाडीs bring urine-forming fluid (उपनीतस्य).

Glomeruli.—Two varieties of nephrons or glomeruli are described : one is जाग्रत : or active and the other स्वप्त : or passive. They are the superficial nephrons (superficial glomeruli) occupying the outer two-thirds of the renal cortex and the other juxtamedullary nephrons (juxtamedullary glomeruli) which occupy the inner one third of the cortex. The latter alone work in stress otherwise they remain inactive. The whole working has been described by Sushruta as :—

जाग्रतः स्वपतश्चैव स निःस्यन्देन पूर्यते ।

Filtration.—The underlined half of the above Sanskrit verse is very important as giving an indication of how the *mutrashaya* (here called by the word स) or nephron or glomerulus part of the nephron produces urine. It is done by (निःस्यन्दन) *Nihsyandan* meaning filtration. So the meaning of

the above line is that "there are superficial and inner glomeruli; some of them are active (जाग्रतः) and some are not (स्वपतः) and they filter blood or fluid brought in afferent vessels :—

नाडीभिरुपनीतस्य मूत्रस्यामाशयान्तरात् ।

from the region of cortex or *Amashaya* of the kidney. It is done by Bowman's capsule. Hence an indirect but precise reference to this part has been given by Sushruta which has stood the test of time and is accepted today as correct.

Tubules and renal medulla.—The filtered fluid flows through the tubules called *Nadyah* (नाड्यः). This fluid after undergoing various changes of separation (विभजन) and absorption (प्रचूषण) is collected in larger collecting tubules which lie in the part called *pakwashaya* (पक्वाशय) or renal medulla. These tubules number hundreds of thousands, which give the exact idea of millions of nephrons with their malpighian corpuscles and tubules :—

पक्वाशयगतास्तत्र नाड्यः मूत्रवहास्तु याः ।
तर्पयन्ति सदा मूत्रं सरितः सागरं यथा ॥
सूक्ष्मत्वान्नोपलभ्यन्ते मुखान्यासां सहस्रशः ॥ सु. नि. ३

These tubules residing in *pakwashaya* part of the kidney are called (मूत्रवहा नाड्यः) (tubules through which urine flows; the correct translation of it being uriniferous tubules). They are microscopic (सूक्ष्मत्वात्) therefore their lumen (मुखानि) cannot be seen with the naked eye (नोपलभ्यन्ते) but these मुखानि are far too numerous (सहस्रशः).

Pyramids of the kidneys.—*Mutrashayas* having thousands of uriniferous tubules (मूत्रवहा नाड्य :) mean also the renal pyramids. They have been termed by Sushruta as *ghatas* (घटाः - pots). If a new earthen pot is filled with water, the water oozes out through several small microscopic pores in its walls. The same happens here :—

आप्लुत्वात् सलिलेन्यस्तः पार्श्वेभ्यः पूर्यते नवः ।
घटाः यथा तथा विद्धि बस्तिर्मूत्रेण पूर्यते ॥

These various घटाः or pyramids in the kidney through their duct of ballini etc., send forth the *salil* or fluid *i.e.*, urine. The act of sending is that of oozing. This oozing surface of the *ghatas* or pyramids is called area cribrosa an exact word for the oozing ghatas.

Calyces.—From the pyramid start calyces, minor and major which have been depicted as सरितः (rivulets) proceeding towards the सागरम् (ureteral pelvis). In the calyces the flow begins just as it begins in a rivulet. Thus the acts of निस्यन्दन (filtration), प्रचूषण (absorption), पूरण (oozing) and तर्पण (flowing) all have been

the blood fluid in circulation and makes it clot when exposed to the air.

Little can be done to help the victims of liver disease. Treatment for the most part is based on the idea that if you give it a chance, this sturdy organ will cure itself. It often does. It is not at all uncommon for cases with a degenerative condition of the liver to be restored to health without anything more than suitable diet and ample rest.

Infectious jaundice is known as a catching liver complaint. Its victims do not turn ghastly yellow. The fact is that jaundice is an inflammation of the liver, which may look like flu, dysentery or typhoid. Many jaundice cases are not readily or properly recognized. Fortunately, it is not a killer. The patient makes good recovery from the usual treatments prescribed.

Another type of jaundice caused by injections, inoculations and transfusions, is known as "transfusion jaundice" to distinguish it from the infectious type. Doctors are nonplussed by this condition which can lead them into misdiagnosing it as a diseased gall bladder, stomach, intestine or pancreas.

Cirrhosis destroys the liver, it is not an inflammation nor the result of poisoning although poisoning or inflammation may sometimes result in cirrhosis. A liver with cirrhosis first enlarges and then shrivels as its cells are crushed by scars and strangled.

It is believed, that cirrhosis is often closely associated with over-indulgence. Doctors also declare that a connection does exist between too much of good life and liver decay. In Russia where the common man has little to spend on luxuries, the disease is rare. But in America where the adult population drinks heavily, the incidence is high.

THE INEFFECTIVE TOOTH BRUSH

The design of the tooth brush has changed little in the past hundred and thirty years. A plate in Maury's treatise on dentistry, published in 1833, shows that almost every shape of brush had already been thought of—including one pattern that was reinvented in time for a recent dental congress. The figures for the number of toothbrushes sold in Great Britain are depressing—less than 25 million toothbrushes for 35 million potential users in 1956. Most people think of the toothbrush as a semipermanent article that remains useful until it is reduced to a splayed-out collection of disheartened bristles. The public are loath to pay more than about two shillings for a brush, thus restricting enterprise by the manufacturers. Advertising has little effect on sales; but branded makes by well-known firms sell more readily than those comparatively unknown, even if of equal merit. A few years ago, there was a move to rechristen the toothbrush a "mouth brush" as a title more truly indicating its function. Proper brushing helps to keep the epithelium of the gingivae well keratinized, and will remove the bacterial plaque on the surface of the tooth (the "yellow

film" beloved of the advertisers). This is, of course, an aesthetic and hygienic improvement; but *if there is to be any real hope of preventing caries, thorough brushing must be carried out at least four times a day—for which few have either the time or the inclination.* The various toothbrush-drills by dental surgeons are difficult to carry out correctly. The awkward up-and-down movements easily degenerate into narrow, elliptical loops, not far removed from the to-and-fro scrubbing action which leaves even the most accessible interdental spaces packed with food debris. *Too much reliance is probably placed on medicated toothpastes: no dentifrice can ever be more than a detergent, in the true sense.* The inclusion of hexachlorophene, sodium ricinoleate, or sodium fluoride is of negligible value.

Obviously some new approach to tooth-cleaning is needed, and this has been made by Archer *et al.*, who have produced some interesting variants on the conventional brush. One design is for a portable brush in a cylindrical case which carries a supply of toothpaste; another is for a disposable brush, the semiflexible handle of which contains paste that can be forced through a small nozzle among the bristles. An even more unorthodox design has no bristles, the cleansing being done by a series of small-diameter nozzles supplied with water from the bathroom tap. Archer *et al.* suggest that a small block of detergent could be incorporated in the handle to make the instrument more pleasant and effective. Rubber or bristle gum stimulators could be fitted easily, and a mouth-spray based on these designs (which the authors admit are purely tentative) might prove acceptable and effective.—(Editorial *Lancet*, 16-7-'60).

VACCINATION AGAINST RABIES IN MAN AND DOG

Question:—Is the vaccination of animals against hydrophobia forbidden in Germany? What is the status of vaccination for humans? Is a vaccinated animal a danger to man and other animals as a carrier? What does one do for somebody bitten by a rabid animal? Surely it is a fairy-tale that an injection into the pancreas is desirable? Replying to the above, Prof. R. Haas, Institute of Hygiene, University of Freiburg, says:

Answer:—According to a directive from the Ministry of the Interior of Baden-Wurttemberg, the vaccination of dogs, particularly hunting dogs, is forbidden. An exception is permitted only when dogs are taken out of the country. These exceptions are authorized by the Office for Public Safety. The type of vaccine is not prescribed by regulation. In contrast to Germany, dogs are vaccinated against rabies in various countries including Japan, U.S.A., Algeria, Hungary and some Balkan countries. These countries have been satisfied with their experience with vaccines. But in Germany the vaccination of dogs is prohibited in the meanwhile, because one cannot predict the possible sequelæ and not because we consider it without value. Not only is the duration of immunity not yet established, but it is also uncertain whether vaccinated animals which do not appear to be sick, might not act as carriers or excreters of the virus. If someone is bitten or licked by a rabid or suspectedly rabid animal, a wound toilette with disinfectants and administration of vaccine are indicated: 4 ml. of vaccine should be injected subcutaneously (infraclavicular or hypogastric region) 5 to 6 times, with intervals of 24 hours between each injection. Four weeks after the last inoculation, another injection of 4 ml. is given. Passive-active treatment, *i.e.* the combined administration of rabies hyperimmune serum and rabies vaccine may be used in certain cases. According to a statement of the Minister of Health on 24-3-1958, no pre-infection immunization for rabies is practised by the Robert-Koch Institute, Berlin. It is quite right that the pancreatic injection is a fairy-tale.—(*German Medical Monthly*, July, 1960).

SAMPLING METHODS FOR MEDICAL EXPERIMENTS *

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AN inherent human tendency is to minimize the work and get maximum benefit. It is so in population studies also. A study of the entire population of any place or country is unnecessarily very expensive, time-consuming and also physically impossible to carry out efficiently; so certain methods of sampling are widely used in obtaining estimates of the characteristics of the population under study. A portion (sample) of the population is studied instead of the entire population, in such a way that the sample selected is representative of the whole population.

In any estimation of the total bacterial population in a big water reservoir, it will not be possible to examine all the water in the reservoir. So representative samples of water are taken from the reservoir, and their bacterial content estimated.

It is commonly believed that the study of the entire population will yield correct answers to the problem under study. But it is usually not so, as nonsampling errors come into the picture and vitiate the results. Nonsampling errors may be classified as follows:

(1) *Errors due to faulty definition*:—If the characteristics of the population are not properly defined it may lead to different estimates. In hospitals, the birth-order of the newly born baby is usually registered. It may happen that if the same definition of birth-order is not followed in hospitals, estimates of the characteristics which are studied against the birth-order may give misleading results, as the birth-order can be entered either as the order among live children or as the order among the ever-born children (alive or dead) to the mother.

(2) *Response errors*:—Response errors may occur in the study by accident, or may be introduced purposely by the respondents or they may be due to lack of information. Many physicians do not tell their patients that they have cancer, even though they are aware of the correct diagnosis. In such a case the patient cannot give the correct answer, being in ignorance of the fact. But sometimes, even if the patient *is* aware of it, he may fail or refuse to report the fact for various reasons.

(3) *Errors in coverage*:—When the population under study is large, it may sometimes happen that the investigator may miss some cases or even small area. He may enumerate the same cases or area twice or he may manipulate the cases intelligently whenever he experiences pressure or and urgency.

Specially contributed to the ANTISEPTIC

(4) *Errors in classification* :—Wrong classification is sometimes possible *e.g.*, in the analysis of deaths by causes, it may be that deaths have been wrongly classified.

Other types of nonsampling errors are also possible. It must be understood that nonsampling errors may enter into sampling investigations also. But since the sample is usually only a relatively very small portion of the entire population, effective controls can be introduced and nonsampling errors minimized. Also the study by means of sample saves time and money and also enables results to be obtained quicker. Further it would then be feasible to tabulate and analyse a wide variety of topics, ecnomically and well.

No effective methods are yet available to identify and quantify nonsampling errors; the sampling errors however, can be properly measured and then the sampling methods provide estimates of the characteristics with known precision at a minimum cost, or with maximum precision for a given cost.

In addition to precision in the estimates, one must have a clear picture of the tolerance limit and also the confidence with which to make a statement. The term '*tolerance*' devotes the amount of difference one will tolerate between the sample-result and the result obtained from a complete count or from the expected value. When the decision is taken to tolerate a certain amount of difference in the sample result, a sampling method provides a statement which ensures in how many per cent of cases such a thing will happen. In other words, if hundred samples are drawn from the population, the statement ensures that in so many samples one will find the sample result not differing from the population value by more than what one is going to tolerate. This is known as '*confidence statement*.' A 90% confidence will mean that in 90 out of the 100 samples drawn, one will find the results within one's tolerance limit. The smaller the difference one can tolerate, the lesser will be the 'confidence statements' attached to it for a given sample-size. The precision of the method is inversely proportional to the variance of the sample. The larger the variance of the sample the lesser is the precision and the precision increases as the variance becomes less and less. Thus tolerance, confidenee and precision are dependent on the sample-size.

The procedure to be adopted in planning a survey should be carefully outlined because of the varying practical problems. The object of the study must be clearly stated. If similar studies had been made previously one will stand to benefit thereby. If the topic is new, a pilot enquiry must be started to ascertain if a conprehensive detailed one can be launched. If so, how efficiently can it be obtained? Hence the methods of survey that

yield the maximum information per unit cost should be considered. The principal items to be considered in a survey are as under:—

1. *Planning of the survey*:—It is always desirable to study the purpose of the survey before planning to secure results of value. Similar studies made previously will enable one to get a complete picture of the exact position of the problem under study.

2. *Choice of questions*:—In preparing a questionnaire, only those questions should be included which can be readily answered and which will throw light on the particular problem under study. Extra or side-questions should be avoided as far as possible. It is always more advantageous to collect information on a few characteristics of the population and concentrate on them than to collect information on several characteristics, only to study a few of them.

3. *Definition of the characteristics of the population*:—A clear definition of the characteristics of the population is always helpful, and will prevent the committing of mistakes.

4. *Collection of data*:—All relevant information about the characteristics of the population under study should be collected without omitting or neglecting any part of it. Needless information if collected, will lead only to confusion.

5. *Methods of collecting data*:—When the decision is taken about the sort of information to be collected, a suitable method should be selected for obtaining the same most economically. The available methods are:-sending the questionnaires by post; personal interviews; registered and published data, like census reports, etc.

6. *Choice of sampling unit*:—As a preliminary to the selection of a sample, the population must be subdivided into sampling units; these will together constitute the whole population. Sometimes the appropriate unit is obvious but at others there is considerable scope for choice of a suitable unit *e.g.*, in sampling the people in a village, the unit might be an individual person, the members of a household etc. The construction of a complete list of sampling units—called a '*frame*'—may be one of the major practical problems in many cases.

7. *Selection of sample*:—The selection of sample can be made in various ways but at the planning stage one must decide about the size of the sample. The size of the sample depends upon the cost of the survey and the precision of the sample-results.

8. *Organization of the survey*:—When the method of selection of the sample has been decided, the problem of convenient

organization, will arise. For this purpose, the investigators should be trained properly and given printed instructions to guide them when in difficulty. In medical experiments, the investigator selected must have adequate knowledge of the characteristics of the study and should preferably be a medical graduate with some training in statistics.

9. *Analysis of the data*:—The type of analysis to be made with the data obtained should be determined at an early stage of the survey. The planning of the analysis should not be made to suit the data collected but made beforehand, and a decision taken about the type of information needed for the study.

The main object of the sampling method is to obtain information which will permit an estimate to be made of the properties of the entire population. In order to attain this object it is required to select a sample that will be representative of the population of which inferences are to be drawn, and that will furnish reliable data. Both are important, and neither can be neglected or minimized in importance.

The selection of a fraction of a population, *i.e.* the selection of a sample, can be made in many ways and there are no means of testing whether or not the sample so selected is representative of the population. It is now well known that a random sampling is considered sufficiently representative of a whole. In the simple random sampling method, any one combination of elements has an equal chance of being selected as any other combination This method of selection eliminates personal bias and also gives a valid basis for estimating sampling errors.

In the estimation of the percentage of hæmoglobin in the blood of children, a drop of blood will have to be taken from the body of the children. Some parents may object to this, though the child may not suffer any pain or damage in doing so. Yet other parents may allow it. In such a case, the sample may not be representative of the population, if proper care is not taken.

A method of selecting a random sample is to number the population units from 1 to N and then either these numbers are written on cards and thoroughly mixed or slips containing these numbers are folded and mixed thoroughly in a bowl. Then the procedure of selecting a random sample is to draw cards or folded slips, one by one without replacing them and enter the numbers on these cards or slips as samples.

Another and simpler way of drawing a simple random sample is by the use of the random number tables (*vide infra*). One has just to consult the tables and draw the sample by taking down the numbers from any page and column serially. Care should be

ten to omit the duplicate numbers and the numbers which are ater than the total number of people. A page from "Random mber tabless" is given in Table 1 and the hints given on 34 show how to use this statement.

TABLE 1

A Table of Random Numbers

22 17 68 65 84	68 95 23 92 35	87 02 22 57 51	61 09 43 95 06	58 24 82 03 47
19 36 27 59 46	13 79 93 37 55	39 77 32 77 09	85 52 05 30 62	47 83 51 62 74
16 77 23 02 77	09 61 87 25 21	28 06 24 25 93	16 71 13 59 78	23 05 47 47 25
78 43 76 71 61	20 44 90 32 64	97 67 63 99 61	46 38 03 93 22	69 81 21 99 21
03 28 28 26 08	73 37 32 04 05	69 30 16 09 05	88 69 58 28 99	35 07 44 75 47
93 22 53 64 39	07 10 63 76 35	87 03 04 79 88	08 13 13 85 51	55 34 57 72 69
78 76 58 54 74	92 38 70 96 92	52 06 79 79 45	82 63 18 27 44	69 66 92 19 09
23 68 35 26 00	99 53 93 61 28	52 70 05 48 34	56 65 05 61 86	90 92 10 70 80
15 39 25 70 99	93 86 52 77 65	15 33 59 05 28	22 87 26 07 47	86 96 98 29 06
58 71 96 30 24	18 46 23 34 27	85 13 99 24 44	49 18 09 79 49	74 16 32 23 02
57 35 27 33 72	24 53 63 94 09	41 10 76 47 91	44 04 95 49 66	39 60 04 59 81
48 50 86 54 48	22 06 34 72 52	82 21 15 65 20	33 29 94 71 11	15 91 29 12 02
61 96 48 95 03	07 16 39 33 66	98 56 10 56 79	77 21 30 27 12	90 49 22 23 62
36 93 89 41 26	29 70 83 63 51	99 74 20 52 36	87 09 41 15 09	98 60 16 03 03
18 87 00 42 31	57 90 12 02 07	23 47 37 17 31	54 08 01 88 63	39 41 88 92 10
88 56 53 27 59	33 35 72 67 47	77 34 55 45 70	08 18 27 38 90	16 95 86 70 75
09 72 95 84 29	49 41 31 06 70	42 38 06 45 18	64 84 73 31 65	52 53 37 67 15
12 96 88 17 31	65 19 69 02 83	60 75 86 90 68	24 64 19 35 51	56 61 87 39 12
85 94 57 24 16	92 09 84 38 76	22 00 27 69 85	29 81 94 78 70	21 94 47 90 12
38 64 43 59 98	98 77 87 68 07	91 51 67 62 44	40 98 05 93 78	23 32 65 41 18
53 44 09 42 72	00 41 86 79 79	68 47 22 00 20	35 55 31 51 51	00 83 63 22 55
40 76 66 26 84	57 99 99 90 37	36 63 32 08 58	37 40 13 68 97	87 64 81 07 83
02 17 79 18 05	12 59 52 57 02	22 07 90 47 03	28 14 11 30 79	20 69 22 40 98
95 17 82 06 53	31 51 10 96 46	92 06 88 07 77	56 11 50 81 69	40 23 72 51 39
35 76 22 42 92	96 11 83 44 80	34 68 35 48 77	33 42 40 90 60	73 96 53 97 86
26 29 13 56 41	85 47 04 66 08	34 72 57 59 13	82 43 80 46 15	38 26 61 70 04
77 80 20 75 82	72 82 32 99 90	63 95 73 76 63	89 73 44 99 05	48 67 26 43 18
46 40 66 44 52	91 36 74 43 53	30 82 13 54 00	78 45 63 98 35	55 03 36 67 68
37 56 08 18 09	77 53 84 46 47	31 91 18 95 58	24 16 74 11 53	44 10 13 85 57
61 65 61 68 66	37 27 47 39 19	84 83 70 07 48	53 21 40 06 71	95 06 79 88 54
93 43 69 64 07	34 18 04 52 35	56 27 09 24 86	61 85 53 83 45	19 90 70 99 00
21 96 60 12 99	11 20 99 45 18	48 13 93 55 34	18 37 79 49 90	65 97 38 20 46
95 20 47 97 97	27 37 83 28 71	00 06 41 41 74	45 89 09 39 84	51 67 11 52 49
97 86 21 78 73	10 65 81 92 59	58 76 17 14 97	04 76 62 16 17	17 95 70 45 80
69 92 06 34 13	59 71 74 17 32	27 55 10 24 19	23 71 82 13 74	63 52 52 01 41
04 31 17 21 56	33 73 99 19 87	26 72 39 27 67	53 77 57 68 93	60 61 97 22 61
61 06 98 03 91	87 14 77 43 96	43 00 65 98 50	45 60 33 01 07	98 99 46 50 47
85 93 85 86 88	72 87 08 62 40	16 06 10 89 20	23 21 34 74 97	76 38 03 29 63
21 74 32 47 45	73 96 07 94 52	09 65 90 77 47	25 76 16 19 33	53 05 70 53 30
15 69 53 82 80	79 96 23 53 10	65 39 07 16 29	45 33 02 43 70	02 87 40 41 45
02 89 08 04 49	20 21 14 68 86	87 63 93 95 17	11 29 01 95 80	35 14 97 35 33
87 18 15 89 79	85 43 01 72 73	08 61 74 51 69	89 74 39 82 15	94 51 33 41 67
98 83 71 94 22	59 97 50 99 52	08 52 85 08 40	87 80 61 65 31	91 51 80 32 44
10 08 58 21 66	72 68 49 29 31	89 85 84 46 06	59 73 19 85 23	65 09 29 75 63
47 90 56 10 08	88 02 84 27 83	42 29 72 23 19	66 56 45 65 79	20 71 53 20 25
22 85 61 68 90	49 64 92 85 44	16 40 12 89 88	50 14 49 81 06	01 82 77 45 12
67 80 43 79 33	12 83 11 41 16	25 58 19 68 70	77 02 54 00 52	53 43 37 15 26
27 62 60 96 72	79 44 61 40 15	14 53 40 65 39	27 31 58 50 28	11 39 03 34 25
33 78 80 87 15	38 30 06 38 21	14 47 47 07 26	54 96 87 53 32	40 36 40 96 76
13 13 92 66 99	47 24 49 57 74	32 25 43 62 17	10 97 11 69 84	99 63 22 32 98

The above random number table is taken from Table XXXIII (III) of R. A. Fisher and F. Yates: Statistical tables for biological, agricultural and medical research, 4th edition published by Oliver and Boyd Ltd., Edinburgh, 1953.

Suppose we have a population consisting of 804 school children six years old, and we are interested in estimating the hæmoglobin percentage in these children. We need not take hæmoglobin measurements on all these children. We may select a small sample, say 20 children and study their blood for hæmoglobin. (The sample size is to be determined on the basis of the precision required or on the basis of the time and money available). These children should be selected by the method of random sampling either by drawing lots or by use of the random number table. The method of drawing lots is quite simple and need not be discussed here.

The method of using the random number table is as follows:—Every child is assigned a number in any way from 000 to 803. From the table consider all 3 digit numbers 000 to 803. If any particular number occurs as we proceed along, we keep it and say that the child with that number is to be studied. We continue this till we have 20 different children in all. The starting point may be anywhere. But once we select the starting point, the counting is continued either from a horizontal or a vertical line. Let us start from the 12th column and 7th row. The numbers are 067, *979*, 458, 263, 182, 744, 696, 692, 190, *923*, 683, 526, 009, *953*, *936*, 128, 527, 005, 483, 456, 650, 561, *869*, 092, and 107 (The numbers underlined which occurred during random sampling are omitted because they are greater than 803).

Hence the children selected by the random sampling method for hæmoglobin study will be those bearing the numbers:—5, 9, 67, 92, 107, 128, 182, 190, 263, 456, 458, 483, 526, 527, 561, 650, 683, 692, 696, and 744.

If the population is heterogeneous, then the data can be divided into groups, so that the elements within each group are more alike than are the elements in the population as a whole, in other words, the elements within the group must be homogeneous. Samples can be drawn from these groups separately by simple random sampling methods to get the desired representation from each group. This is the method of *stratified sampling*.

Stratification is resorted to in the following cases:—(*a*) If data of known precision are wanted for certain subdivisions of the population; (*b*) administrative convenience may dictate the use of stratification; (*c*) sampling problems may differ markedly in different parts of the population; and (*d*) stratification may bring about a gain in precision in the estimates of the characteristics of the whole population. The basic idea is that it may be possible to divide a heterogeneous population into sub-populations, each of which is internally homogeneous.

The total sample-size depends on the funds allotted for the survey. The sub-sample sizes, *i.e.*, the sizes of each strata may be

elected in one of several ways with the restriction that the otal sample size is equal to the sum of the strata-sample sizes.

In the case considered for hæmoglobin study suppose we know hat out of the 804 children of age six, 200 are females and 604 males. Then it would seem better to divide these 804 children into 2 groups—females and males and study them separately. Such a division of the population into more homogeneous groups is called *stratification*.

The division into strata takes into account any knowledge we may have regarding the composition of the population and hence the efficiency of sampling is increased.

Random sampling as described earlier takes a long time due to the process itself. Random tables are usually difficult to find in the field and it may take quite a lot of time to draw lots. In such cases, a scheme of systematic sampling is better.

In the case of systematic sampling we must first number the population serially and then divide the population into a number of strata where this number is equal to the sample-size. If the population size is exactly divisible by the sample-size, then the number of individuals in each strata will be equal to this quotient. If the population size is not exactly divisible by the sample size, then the number of individuals in each strata will be equal to the integral part of the quotient. Thus since the strata sizes are equal, we may number the individuals in each strata separately. Then from the first of such strata one unit is selected at random (by simple random sampling) and then from the other strata one unit each is selected in such a way that their relative position within the strata are the same as the position of the unit selected from the first stratum.

This method has the following advantages:—(*i*) It is easier to draw the sample and easier to execute without mistakes. This is of particular advantage when the drawing is done in the field. This operation is speedy, whereas simple random sampling is slow. No random tables etc. are needed; (*ii*) intuitively, systematic sampling seems likely to be more precise than simple random sampling, because it stratifies the population into strata. The systematic sample being spread more evenly over the population has sometimes made sampling considerably more precise than random sampling; (*iii*) in a systematic sample, the relative position in the population of the different units included in the sample is fixed. Hence there is no risk in the method that any large contiguous part of the population will fail to be represented.

For example, if we want 20 out of the 804 children, we proceed as follows to draw the systematic sample. The strata

size of the 20 strata will be 40 since $\frac{804}{20} = 40{\cdot}2$ and 40 is the integral part of 40·2. New we have to draw a random sample of size one from the first strata. Since the strata size is 40 this can easily be done either by using cards numbered from 0 to 39 or by using the random number tables. Suppose the random number selected is 12. Then the units selected are 12, 52, 92, 132, 172, 212, 252, 292, 332, 372, 412, 452, 492, 532, 572, 612, 652, 692, 732 and 772 because 12 occupies the 13th position in the first strata, 52 occupies the 13th position in the second strata and so on till the 20th strata.

Suppose each unit in a population can be divided into a number of smaller units or elements. A sample of n units has been selected. If units within a selected unit give similar results, it seems uneconomical to measure them all. A common practice is to select and measure a sample of the units in any chosen unit. This technique is called sub-sampling or two-stage-sampling. The technique consists in selecting a sample of units called the primary units, and the second is to select a sample of units from each chosen primary unit.

Sub-sampling has a variety of applications. Whenever any process involves chemical, physical or biological test that can be performed on a small amount of material, this is likely to be drawn as a sub-sample from a larger amount which is itself a sample. The principal advantage two-stage-sampling is that it is more flexible than one stage sampling.

Usually in blood examinations only a few drops are drawn from the body of a person. This is a sample of blood from the person and portions of the same may be used for further analysis. The few drops drawn from the body constitute the sample and portions used for further analysis constitute the sub-samples.

We have described only a few methods of sampling. There are several other methods available. For further details on these as well as on the method of analysis involved in each case reference may be made to "Techniques of Sampling" by W. G. Cochran, Wiley and Sons Inc:, New York (1953).

DIGESTIVE UPSETS

Watch what you eat when you're away from home. You can get diarrhœa, the most common symptom of stomach or intestinal irritation, by eating in restaurants where spoiled food is served.

Whenever possible, eat only in places recommended by a trustworthy rating service. Changing in diet and eating habits, different drinking waters, too many cold drinks, or sudden heat wave may also cause digestive upsets. Include some antacids in your first-aid kit. If the diarrhœa persists, see a physician.—(*Today's Health*, August 1960).

THE MODERN CONCEPT OF URINE FORMATION WAS FIRST DISCOVERED BY SUSHRUTA*

KAVIRAJ
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THE modern concept of urine formation is ascribed to Muller, Bowman or Shumlyansky by western medical men. This is wrong, these scientists by their laborious work and untiring efforts, only demonstrated to the world the true conception of urine formation.

It was Lord Dhanvantri who discussed the process involved in urine formation with Sushruta; it was much the same as we know it to-day. Sushruta in his surgico-medical thesis known as *Sushruta Samhita* has treated the subject exhaustively furnishing clear details about the working of the kidney and the role played by the nephrons. His description is so elaborate that the later and recent researches by the scientists of Europe and America drew largely from the ancient Indian physiologist and his memorable work.

Sushruta knew:—that man has two kidneys, each having a cortex and a medullary part, that each kidney has several nephrons; each nephron has a glomerulus and a tubule; each glomerulus is concerned with the filtration of blood and each tubule reabsorbs some important material; that the nephrons are very numerous, several hundred thousands in number; that they form pyramids which secrete or excrete urine to the calyces and thence to the pelvis of the ureter. Sushruta also knew that there are two ureters and that there is a bladder which is filled by the ureters. He also knew the existence of an urethral passage and thus he had a thorough knowledge of the formation and passage of urine from the kidneys to the external urethral orifice.

This knowledge of the concept of urine-formation was totally forgotten by later Ayurvedic doctors. The later commentators of the Samhitas had only a large vocabulary of Sanskrit words but did not follow the histological complications and instead of the real meaning of the word used by Sushruta, a funny meaning was given which was condemned outright by the students of modern medicine who did not care to dive into the precise meaning of the text. In one place, what was a clear description of *vrikka* was thought to be *twakka* as the manuscript was not closely followed in the context of the anatomical description.

The kidneys.—The kidneys have been described by Sushruta under the name *Vrikka*, (वृक्क). *Vrikka* has always been used by

* Specially contributed to the ANTISEPTIC.

him in the plural as (वृक्कौ) signifying that they are two in number. Charaka has also made mention of वृक्कौ in connection with the counting of the various viscera in abdomen or *Koshtha*. *Vrikka* therefore must refer to the kidneys, there is no other viscus in the abdomen which is dual in number. All other viscera are mentioned and named quite correctly and only the kidneys remain, which is denoted by the term *vrikka*. The conception and the description of kidneys by Sushruta are further dealt with later.

Nephron.—This is called by Sushruta as *Mutrashaya* (मूत्राशय).

मूत्राशयो मलाधारः प्राणायतनमुत्तमम् । सु. नि. ३१२४

This *mutrashaya* is the seat of the formation of a *mala* or excretion called *moothra* or urine. It is also the seat of *Prana* or life. If this unit stops working altogether as in anuria when the function of the nephrons is stopped, life will become extinct. Although the term *Mutrashaya* is mentioned in the singular number, its relation to the thousands of tubules, gives us an idea of several nephrons (*vide infra*).

Renal cortex.—Just as a nephron has a Malpighian corpuscle consisting of a Bowman's capsule and the glomerulus and lie in the cortex of the kidney and receive blood from renal vessels, so is the case with *Mutrashaya* also.

नाडीभिरुपनीतस्य मूत्रस्यामाशयान्तरात् ।

This quotation from Sushruta in *Nidansthan* Chap. 3 gives us the clue. Here the word *Amashaya* (अमाशय) means the cortex of the kidney. This *Amashaya* receives blood which contains the material from which urine is formed. In this *Amashaya* there are several afferent vessels called नाडी (it is plural depicting numerous vessels) these नाडीs bring urine-forming fluid (उपनीतस्य).

Glomeruli.—Two varieties of nephrons or glomeruli are described: one is जाग्रत: or active and the other स्वप्त: or passive. They are the superficial nephrons (superficial glomeruli) occupying the outer two-thirds of the renal cortex and the other juxtamedullary nephrons (juxtamedullary glomeruli) which occupy the inner one third of the cortex. The latter alone work in stress otherwise they remain inactive. The whole working has been described by Sushruta as:—

जाग्रतः स्वप्तश्चैव स निःस्यन्देन पूर्यते ।

Filtration.—The underlined half of the above Sanskrit verse is very important as giving an indication of how the *mutrashaya* (here called by the word स) or nephron or glomerulus part of the nephron produces urine. It is done by (निःस्यन्दन) *Nihsyandan* meaning filtration. So the meaning of

glucose first into glycogen which it can store. When the muscles are hungry for sugar, the glycogen is converted back into glucose, released into the blood.

Fats make the fewest demands on the liver, by being a threat to its well being. Fat accumulation can cause disease in this intricate and sensitive organ, so the liver stores very little of it, checks the rest for wholesomeness and sends it to "Fat depots" throughout the fleshy parts of the body. This is the liver's method of providing against the risk of starvation; if starvation threatens, the liver recalls the fats, converts them to glycogen, then to glucose for ready release as energy.

Three pints of blood flows through the liver every minute in two separate supplies: one from the heart, and the other from the intestines. The liver is considered a queer organ, for few other organs have two supplies and no other large organ uses secondhand unpurified blood delivered to it from a neighbouring organ!

The supply from the heart is the normal flow of oxygenated blood needed by all organs in the body. The other source is incoming food carried by the slow-moving portal vein.

As soon as food is swallowed, it is acted on by digestive enzymes and emulsified into a rich liquid. The nutrients in this liquid stays for a while in the intestines till it meets tiny veins. These whisk it away, packed with nourishment to the large portal vein which leads straight to the liver. Liver cells all look alike, when seen through the microscope.

Besides eliminating toxins and poisons and sorting out carbohydrates, proteins and fats, the liver is a vitamin centre. A, B_1, B_2, C, D and E the well-known ones are all stored in its interior. But recently two more have been added to the list, *viz.*, Vitamins B_{12} and K. In prenatal life, making blood is one of liver's jobs. After birth, the liver delegates this function to the bone marrow.

From four tons of animal liver a fraction of an ounce of B_{12} can be obtained. If a single grain of table salt were taken and divided into hundred parts, a daily amount of B_{12} equal to one of those hundreth parts would be more than enough to restore a patient with pernicious anæmia to good health. And from then on, the same minute quantity would only have to be taken about once a month, as maintenance dose.

Vitamin K is another precious substance that was tracked down to the liver in the year 1939. It is an essential part of a complex chemical that ends up by making blood to clot. It works in partnership with another substance found in the liver, heparin that acts in another direction as an anticlotting chemical. In balance the mixture of these two and other fluids keeps

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"*ascaron*"—a mixture of albumoses and peptones, is found in the body fluid of the worm. This "*ascaron*" has an inhibitory effect on pepsin and trypsin, consequently leading to non-digestion of protein. It is not clear however, whether this action has any deleterious effect on the appendix. But the abdominal pain, digestive disturbances associated with ascariasis may sometimes be too vague to simulate chronic appendicitis.

The five cases with Ascaris ova in the lumen did not show any pathological changes in the wall, nor was there any history of acute exacerbation. It might be that these ova were carried by a current of semisolid fæcal stream and found their way into the appendix.

The adult *Trichuris trichiura* is usually found in the cæcum and the appendix with its anterior end embedded in the mucosa. Occasionally the head of the worm may bury deeper into the submucous tissue. With such destruction of the lining mucous membrane, organisms like *E. Coli* and *Streptococcus faecalis*, normally present in the appendicular lumen may enter the deeper tissues and produce an inflammation depending on the infectivity of the content. Mackie *et al* (1958) described that ordinarily there is no marked tissue reaction, although liquefaction of the cells in the immediate proximity of the parasite may occur and secondary bacterial infection may set up an inflammatory process. Moreover several authors described that appendicitis may occur in infestations of *Trichuris trichiura*. Adult worms inhabiting the appendix may give rise to symptoms of acute appendicitis. Pain and discomfort referred to the lower quadrant of the abdomen, particularly in the region of the cæcum—the favourable site of these parasites, may be constant, associated with nausea and vomiting. This may simulate appendicular dyspepsia.

Of the 13 cases where the worm *Trichuris trichiura* or its ova were present in the appendiceal lumen, 3 showed histological changes suggesting subacute inflammation and thinning of the wall, while in 3 others congestion of the serosa and infiltration of a few polymorphonuclears were the chief features. Others did not reveal any gross pathological change.

The female gravid *Enterobius* (*Oxyuris*) *vermicularis* is usually found in the cæcum and the appendix. When the entire body becomes full with eggs, it usually migrates to the perianal region to deposit the eggs in that area. It is thought to produce no pathological lesions in its normal course, but mature worms penetrate the mucosa and encyst in the submucosa of the appendix, usually in a lymphoid follicle and thus open the way to infection. Such catarrhal inflammation may occur in 2% of cases. Ujiie (1935) found definite pathological changes

caused by *E. vermicularis* in 20 (6·3%) out of 330 appendices examined. Harris and Brown (1925) demonstrated *E. vermicularis* in 22 specimens out of a series of 121 cases of operated appendices. They also found subacute and chronic inflammatory changes in the wall of the appendix. From these observations these workers concluded that these worms produced acute lesions in children and subacute or chronic cellular response in adults. Recurrent and chronic appendicitis and appendicular colic in children may also result from *E. vermicularis* in the appendix. These authors further observed that these parasites which encyst in the lymphoid follicles usually do not excite any exudative response but produce degenerative changes in that area. The exudative element which is sometimes found is attributed to secondary bacterial infection. Thus according to these authors actual intramural invasion by these worms down to the musculature with even destruction of tissues along their route of transit is definite evidence of disease production. Harris and Brown (1925) further stressed that "when *Oxyuris* occurs in a diseased appendix they are in most cases the existing cause of the pathological change found."

In our 2 cases where ova of *E. vermicularis* were found deep in the wall of the appendix, none showed any exudative response and the actual worm was not found. These ova must have possibly been expressed from the encysted worms though they were not found in our sections. There were evidences of chronic inflammatory reaction and fibroblastic proliferation around these ova. In one appendix, subserosal collections of these ova showed tubercle-like lesions on the surface. Anderson (1957) described 12 cases of *Enterobius* granuloma in the appendix. This typical granulomatous lesion, localized in the submucosa shows a central necrotic area in which the remnant of the worm can be identified. This is surrounded by a zone of lymphocytes, eosinophils and epitheloid cells, with connective tissue at the periphery. It is also known that occasionally *E. vermicularis* gains access to the peritoneal cavity by way of the uterus and the fallopian tubes and produce granulomatous nodules on the peritoneal surface which resemble tuberculosis or carcinoma.

Other causes of appendicular symptoms of helminthic origin are also described in the literature. *Taenia saginata* may, on rare occasions, obstruct the appendix by its proglottides, leading to acute appendicitis. *Schistosoma japonicum*, which is an inhabitant of the intrahepatic part of the portal venous system, mesenteric veins, draining the ileocæcal region and the rectal plexus of veins, may produce manifestations of *hepatolienal* fibrosis, appendicitis or dysentery, during the time of laying eggs.

Table II

S. No.	Age	Sex	Clinical history	Histopathology
1	32 years	M.	Tubercle-like lesions in the serous coat —Chr. appendicitis?—T.B.?	Ova of *E. vermicularis* in submucosal, muscular and subperitoneal coat. Chronic inflammatory cells in the wall.
2	21 years	M.	Pain over the abdomen—4 years. Appendix slightly congested. Chronic appendicitis?	Ova of *E. vermicularis* in the submucosa. Surrounding tissue shows fibrosis.
3	24 years	M.	Pain over the abdomen—3 years. Chronic appendicitis?	A section of female *T. trichura* and fair number of ova. No gross pathology in the wall.
4	20 years	F.	Pain over the epigastrium,—aggravated after food,—relief after vomiting. Appendix elongated, thickened. Chronic appendicitis.	*E. vermicularis* in the lumen. No gross pathology in the wall.
5	39 years	M.	Occasional pain over the lower abdomen —3 months. History of acuto appendicitis—settled down with treatment. Tenderness over right iliac fossa—Chronic appendicitis.	Ova of *T. trichiura* in lumen. A few polymorphs in the wall.
6	30 years	F.	Pain over the right iliac fossa 6 months. Chronic appendicitis.	Ova of *T. trichiura* in the lumen. No great pathology in the wall.
7	36 years	F.	Pain over the abdomen 10 years. All the organs were found normal at laparotomy except the appendix—Chronic appendicitis?	Ova of *T. trichiura* in lumen. Appendix completely thinned out.
8	27 years	F.	Pain over the abdomen 6 years. Chronic appendicitis?	Ova of *T. trichiura* in the lumen. No gross pathology in the wall.
9	42 years	F.	Pain over the lower abdomen 6 years. Chronic appendicitis?	Section *T. trichiura* and ova in lumen. No gross pathology.
10	40 years	M.	Pain over the abdomen 3 years (duodenal ulcer). Gastro-jejunostomy and appendicectomy performed.	Ova of *T. trichiura* in the lumen. Congestion of serosa.
11	35 years	M.	Pain over the abdomen and acid eructation —10 years (gastric and duodenal ulcer). Gastro-jejunostomy and appendicectomy performed.	Ova of *T. trichiura* in the lumen. Congestion in the serosa.
12	20 years	M.	Partial gastrectomy and appendicectomy for gastric ulcer.	Section of *T. trichiura* with ova in the lumen. Large number of eosinophils, lymphocytes and a few polymorphs in all coats. Subacute inflammatory changes in the submucosa.
13	26 years	F.	Dysmenorrhœa—2 years. White discharge P.V. and occasional fever—1 year. Ovary showed corpus luteum cyst.	Plenty of ova of *A. lumbricoides* in the lumen. No gross pathology in the wall.

Table II—(*Contd.*)

S. No.	Age	Sex	Clinical history	Histopathology
14	20 years	F.	Dysmenorrhœa—4 years. Sterility 6 years. Ovary showed follicular cyst.	Ova of *A. lumbricoides* in the lumen. No gross pathology in the wall.
15	23 years	F.	Pain over the lower abdomen and back on exertion. Constant pain in the lower extremity, leucorrhœa and dysmenorrhœa.	Ova of *T. trichiura* in the lumen. A few polymorphs and eosinophils in the submucosa. Muscle wall thinned out. Subacute inflammatory change in serous and submucous coats.
16	35 years	F.	Pain over the abdomen 1½ years, Mixed stone in the gall bladder. Fæcal concretions in the appendix. Omentum adherent to the fallopian tube.	Ova of *T. trichiura* and *A. lumbricoides* in the lumen. No gross pathology in the wall.
17	38 years	F.	Occasional pain over the abdomen—4 years. Appendicectomy with biopsy from omentum—Tuberculosis?	Ova of *A. lumbricoides* in the lumen. Congestion and fibroblastic poliferation in the serosa, a few polymorphs infiltration in all coats—subacute inflammatory change.
18	25 years	M.	Pain over the abdomen—4 years. Chronic appendicitis.	Ova of *T. trichiura* and *A. lumbricoides* in lumen. No gross pathology in the wall.
19	29 years	M.	Pain over the abdomen—2 years. Chronic appendicitis.	Ova of *T. trichiura* in the lumen. No gross pathology in the wall.

We have found that 234 cases (41·2%) of the appendices removed did not show any pathological change on histological examination. Of the total 568 cases, 105 were associated with other operations, *i.e.*, hernial repair, removel of ovarian tumour, fibroid uterus, testicular growth etc. This gives a total of 129 appendices (28%) which failed to demonstrate any histopathological lesions although they have been removed from clinically supported cases of appendicitis. The question of diagnostic error in appendicitis as revealed from the histological examination of the resected specimens have drawn the attention of several workers. Mauldin's studies revealed a 34% incidence of error and the figures of Hays, Jaffe and Wells, ranged between 30 and 35% of normal appendices removed with primary diagnosis of acute appendicitis. Recently Thoroughman (1957) in a study of 644 cases, clinically diagnosed as acute appendicitis found that in 23% the pathological diagnosis was normal appendix and no other condition was found in other organs during operation.

The question now arises whether these worms and ova possess any pathogenic properties either direct or indirect, or are merely a harmless transient or resident of the appendicea

lumen. It is difficult to evaluate the causal relationship between these parasites and clinical appendicitis from this study. We have found that some of the appendices which contained these worms and ova, demonstrated a lesion of subacute or chronic character, and this way true in all cases where *E. vermicularis* and in some cases where *Trichuris trichiura* were found. Thus it seems likely that they possess a positive pathologic role in the causation of the appendicular lesion. At the same time *T. trichiura* and *A. lumbricoides* and their ova have been found in some appendices where there were no symptoms at all attributable to the appendix.

There exists a broad divergence of views relating to the ætiological relationship of *E. vermicularis* with appendicular lesions. Some consider the parasite as a predisposing cause, occasionally blocking and subsequently favouring the invasion by pathogenic organisms, or alternatively with the entrance of these worms into the wall of the appendix, pathogenic organisms are carried mechanically, which set up an inflammation there. While others believe that the parasite is capable of producing the lesion by itself and conclude that there is probably a classic type of *Oxyuris* appendicitis, designating the condition as "*Appendicopathia oxyurica*," as even in the absence of actual histological evidence of any inflammatory change, *Oxyuris* may at times give rise to the clinical picture of acute appendicitis. It is also probable that irritation of the mucosa by these worms (*T. trichiura* and *E. vermicularis*) affixed to it may result in appendicular symptoms in some cases. That the *E. vermicularis* produces pathological changes in the appendix seems indisputable. Their attachments to the mucosa, the hæmorrhagic ulcerations occurring at times about these attachments and the actual intramural invasion of the parasites to the musculature and serosa with chronic inflammatory change and fibrosis indicate the capacity of *E. vermicularis* to produce pathological changes in the appendix and thus afford definite evidence of disease production. These changes usually provoke a clinical and pathological picture representative of a subacute or a chronic form. That these worms (*Trichuris trichiura* and *E. vermicularis*) may occur in the lumen of a normal appendix does not negative the fact that they are capable of producing the actual disease of this structure either directly or indirectly. Whether they may remain in such a structure indefinitely without provoking any pathological change is open to question, although it is conceivable that certain of these structures may not be vulnerable to the parasite.

Summary.—Five hundred and sixty eight appendices were studied histologically; 17 of then showed *T. trichiura* and *A. lumbricoides* and their ova in the lumen. Two cases showed ova of *E. vermicularis* embedded in the wall of the appendix. The associated pathological lesions in the organ

are described. The ætiological relationship between these helminthic infestations and symptoms of appendicitis has been discussed.

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BRONCHIAL ASTHMA

The treatment of bronchial asthma necessitates immediate control of probable food or inhalant and occasional drug allergies as indicated by preliminary initial history. Rare infectant allergies need later consideration. Food allergy is indicated by the pathognomonic history of cyclic attacks decreased or absent in the summer, especially in children, and by a similar or equivalent history in adults and elderly persons. It is also indicated by perennial asthma, at times with cyclic exaggeration, and also by a history of food disagreements and dislikes.

Because of the fallibility of the skin test, especially in food allergy, test-negative diets usually fail to relieve asthma due to this cause. Thus, if food allergy is suspected, immediate ordering of our cereal-free elimination diet is nearly always advisable. This should not be delayed until the fallible skin-testing is finished. Without the initial exclusion of cereals as well as of milk, egg, fish, nuts, and other foods, our control of symptoms of bronchial asthma due to foods would have decreased.

Inhalant allergy is usually indicated by the patient's history. Immediate environmental control is important. In pollen allergy, efficient home-made or commercial filters are valuable. Desensitization to those inhalants which cannot be eliminated from the patient's environment is important.

With this initial study and control of specific allergies, the immediate use of drugs, corticoids, ACTH, and indicated fluids and electrolytes to control severe or moderate symptoms is imperative. Practically all articles on the treatment of bronchial asthma are devoted nearly entirely to the indications and use of these medicaments, with inadequate or no attention to inhalant and especially to food allergy.—(*J.A.M.A.*, 16-9-1960).

FLU DEFORMITIES

Coffey and Jessop analyzed the incidence of congenital deformities in children born to mothers who had influenza during their pregnancy. The incidence of congenital abnormalities was 2·4 times higher in the maternal-influenza group as compared to a control group. The abnormalities were almost entirely of the central nervous system, and the commonest was anencephaly. The risk of mal-formation was greatest if the infection took place in the first trimester.—(*Lancet*, *2*: 935, via *G.P.*, August 1960).

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REQUIREMENTS FOR AN EFFICIENT ANTI-LEPROSY CAMPAIGN IN THE STATE*

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THE advent of chemotherapy has ushered in a new era of hope and amelioration to the sufferers from Hansen's disease, which up till then had been considered incurable, and its victims despised as outcastes. Chemotherapy has evolved a new and cheap drug—sulphone—which has been shown to be effective in the treatment of leprosy. More than that, it is hoped that with the planned and controlled use of this and allied drugs, it would be possible to control the spread of the disease in endemic areas, of which there are many in our country. Just how this new drug acts in the amelioration is not clearly known, but it brings about a considerable reduction in the total number of the infecting organism (B. lepræ) and a breaking up of the individual bacilli. It has been used in global anti-leprosy campaigns with significant success. In India there are over two million sufferers from this disease a fourth of them being infective and there are good prospects of effective campaigns and control work being able to deal successfully with the problem during the Third Five-Year Plan period.

Any plan or campaign of public health: promotion in a country, should be framed and directed to suit the particular needs and limitations of that country. The socio-economic factors of the country, the financial and social implications of the programme and the nature and extent of development of public health among its people and the administrative apparatus available; all these influence the planning of the programme to be adopted. Thus, a rich country with high standards of living and a well-developed public health system will need only to intensify the work on particular lines which would involve large capital investment and heavy recurring expenses. But for an underdeveloped country like ours where economic conditions are not very favourable, there should be quite a different approach and a thorough reorientation of the several methods required for a speedy economic and yet effective control of the problems.

In applying this dictum to anti-leprosy work in our country, we have to visualize possible adverse factors and try to overcome them; institutional treatment through leprosy sanatoria will not bring about epidemiological control of the disease. The available accommodation in these institutions is totally inadequate to meet the needs of the millions of sufferers; it is therefore impossible to tackle the problem in that way. It would obviously

* Specially contributed to the ANTISEPTIC.

be better to reduce the infectivity of many, than to attempt to render a few non-infective. The emphasis should therefore, be laid on prompt detection of cases of leprosy in its early stages and giving effective treatment to the maximum number of patients through the existing dispensaries in and near the inspected area.

The futility of spasmodic and sporadic efforts in this work is being recognized and the importance of organized epidemiological control is gaining momentum.

In this context, it is worth while considering the basic requirements for efficient and successful anti-leprosy work in the State. As already stated, the basic requirement is a well devised and sound plan of the proposed activities. Such a plan should be drawn up by experienced workers in the field, who are far sighted and who can 'deliver the goods.'

The most important item is the case-finding programme, *i.e.* to launch an intensive and extensive campaign of methodical and systematic examination for the presence of leprosy in the entire population in every endemic area of the state. Case detection must be entrusted only to well-trained para-medical workers. This work must be repeated after a number of years to cover the average incubation period of leprosy; the surveys must be regularly conducted, consistent with changes in the local population. Each para-medical worker should be given a particular area and the work of a group, say a dozen, of para-medical workers must be strictly supervised by a trained medical officer.

The next item is to establish a number of treatment and diagnostic centres, that would cover all these endemic areas, so as to afford suitable treatment to the largest possible number of patients in the respective areas. Patients who are irregular or non-cooperative should be regularly contacted and made to take the treatment regularly. Early and stabilized cases, may be treated in the general dispensaries, to which the required drugs should be supplied in adequate quantities. As there is a general dearth in the number of doctors, the routine treatment of the safe and stabilized cases will have to be entrusted to the trained para-medical personnel under the general supervision of the medical officer-in-charge of the groups.

In order to implement these two essential needs, a suitable programme should be organized for training four different types of medical and para-medical workers.

I. The training of leprosy specialists.—These persons must have worked in this field for several years before they can qualify for the training, which being an intensive one should be conducted in a central place where different types of anti-leprosy

work could be studied under competent experts in the treatment of this disease.

After training, the specialists should be placed in charge of organizational, administrative, and also research work and placed in charge of central institutions for sometime. One specialist may be put in charge of several treatment and diagnostic centres spread over several districts to guide and advise the field staff.

II. Training of the doctors in service and of general practitioners.—All medical men in Government service should be given a compulsory minimum training for 1 to 3 months in leprosy work. Every doctor in service must be compelled to do leprosy work for a minimum period of two years. The training for these may be given in the regional or zonal training centres. Special allowances must be given to the doctors for working in the field. General practitioners in endemic areas should be given such training and encouraged to treat early and safe cases, also keeping a look-out for new cases in their daily practice. Such of them as show a keenness and zeal for this work may be provided with a free supply of necessary drugs.

III. Training of the para-medical worker.—For case detection and follow-up of cases of leprosy, trained social workers are needed, one for every twentyfive thousand of the population in endemic areas. Suitable persons with the right type of mental outlook will do well after a training for nine months. In areas where qualified medical men are not available, the routine treatment work may be entrusted to such trained social workers who will work under medical supervision. Training for this category of workers should be given in the regional languages; and they should not be deputed to any other work as this will make their lose their zeal and earnestness for this work. These trainees should receive while under training, a good perspective of the community-problem and the rural aspects of leprosy work. Every community-development block in the endemic areas should have a trained para-medical worker and anti-leprosy work should be integrated with general health-promotion and sanitation work in the block-areas. The other types of para-medical workers are the laboratory technicians and physiotherapists for the diagnostic centres and laboratories and for dealing with the deformities in early cases and helping in pre- and post-operative work.

IV. The existing sanatoria need reorganization and upgrading, so as to ensure a quick turn-over of the patients. Only infective cases, requiring special medical care, should ordinarily be admitted, and made non-infective. Selected non-infective cases with complications may also be admitted. Each sanatorium should be properly manned with trained staff, and

there should be a chain of out-patient clinics all round to undertake detection work in the surrounding areas. Rehabilitation and education centres on a small scale should be started as *annexes* to the sanatoria where suitable vocations may be provided to the inmates with cooperation from industrial firms. Every sanatorium should have a visiting team of specialists, comprising an ophthalmologist, a physician, a surgeon and a radiologist who would attend to the special needs of the patients. The sanatoria should be made attractive enough to make the patients feel that they are not in perpetual isolation.

The next important requirement is to make treatment of leprosy a part of the routine work of all the dispensaries located in endemic areas. This is most important in view of the enormity of the problem and also because unless it is treated on a par with other illnesses, social ostracism will continue to hold sway.

Education of the masses in the causation, spread and control of leprosy is another important item in this programme and should be launched in all endemic areas along with other types of field-work. In all the block areas the village-level workers should be entrusted with this basic programme of educational propaganda.

Rehabilitation of leprosy patients is another very important desideratum. Rehabilitation of a leprosy patient means much more than the finding of a shelter for him; it implies the restoration of the individual to a useful, profitable vocation in life. In this great task the joint and cooperative efforts of leprosy workers, social workers, the State and the private industries are needed. In our country particularly, it would be best if the rehabilitation and after-care centres are decentralized and preventive rehabilitation is also considered. At the same time, the children of the infective and crippled patients should be properly cared for, by keeping them in a general childrens' home away from the leprosarium. A favourable environment for the growth and development of the child should prevail in such homes.

Research in leprosy should be adequately encouraged. Its scope is enormous and rightly conducted, it will give a fillip to all anti-leprosy work in the country. The scope and usefulness of surgery in leprosy is daily increasing. Newer techniques of correcting deformities and improving the functional ability of the patients are being devised. The correction of deformities is no doubt a poor second best to the prevention of the deformity but so long as there are a large number of deformed patients in India, the need for such surgery is great and pressing. Proper incentives and facilities should be provided to orthopædic and plastic surgeons to take to reparative surgery in larger numbers.

LIVER FUNCTIONS AND LIVER DISEASE*

RASIKLAL C. DHRUVA,
Amreli, (Bombay State)

VER disease is very often wrongly diagnosed; and n when diagnosed properly y diet and rest are prescribed. Attempts to transmit the ease to experimental animals have failed.

Persons suffering from liver disease complain of headache, usea, loss of appetite and spots before the eyes.

The liver is a wedge-shaped organ placed at the top and to e right of the stomach, and is the heaviest single organ in the dy. We can cut away up to seven eighths of the liver, before gns of impaired function begin to show.

Surgery on the human liver is still believed to be dangerous xcept for the removal of surface growths.

Research has shown that the heart and the muscles are the ost heavily worked organs in the human body; the place of ride actually belongs to the liver.

Among the functions of the liver, bile secretion is one, and he liver produces bile at the rate of about-half-a-gallon a day nd passes this greenish-yellow bitter tasting fluid, to be stored n the gall bladder from where it is released to the intestine at meal times.

Bile has two duties to perform; one is to help the liver in its role as guardian of the body. The liver watches for incoming poisons, intercepts them before they reach the general circulation and gets the bile to carry them away for disposal. The other duty is to emulsify fats into a milky fluid for easy absorption; without the help of bile the absorption of fats in the body cannot take place.

The liver is a very intricate chemical mechanism which deals with the food we eat, in such a way that we can readily absorb it. Nothing can pass from the stomach into the blood stream without undergoing this process. If any one function can be singled out as being the most important, it is the glycogenic function of the liver, aided by the hormone insulin derived from the pancreas.

Carbohydrates, proteins and fats are the three essential foods that the human tissue needs most. The liver can convert all of these into the sugar when required. Carbohydrates being largely sugars, are utilized first. If the supply from this source is enough, the liver will conserve the proteins and fats for other work.

As the liver which has to hold materials until it can find use for them and as it cannot store sugar as glucose, it processes

*Specially contributed to the ANTISEPTIC.

glucose first into glycogen which it can store. When the muscles are hungry for sugar, the glycogen is converted back into glucose, released into the blood.

Fats make the fewest demands on the liver, by being a threat to its well being. Fat accumulation can cause disease in this intricate and sensitive organ, so the liver stores very little of it, checks the rest for wholesomeness and sends it to "Fat depots" throughout the fleshy parts of the body. This is the liver's method of providing against the risk of starvation; if starvation threatens, the liver recalls the fats, converts them to glycogen, then to glucose for ready release as energy.

Three pints of blood flows through the liver every minute in two separate supplies: one from the heart, and the other from the intestines. The liver is considered a queer organ, for few other organs have two supplies and no other large organ uses secondhand unpurified blood delivered to it from a neighbouring organ!

The supply from the heart is the normal flow of oxygenated blood needed by all organs in the body. The other source is incoming food carried by the slow-moving portal vein.

As soon as food is swallowed, it is acted on by digestive enzymes and emulsified into a rich liquid. The nutrients in this liquid stays for a while in the intestines till it meets tiny veins. These whisk it away, packed with nourishment to the large portal vein which leads straight to the liver. Liver cells all look alike, when seen through the microscope.

Besides eliminating toxins and poisons and sorting out carbohydrates, proteins and fats, the liver is a vitamin centre. A, B_1, B_2, C, D and E the well-known ones are all stored in its interior. But recently two more have been added to the list, *viz.*, Vitamins B_{12} and K. In prenatal life, making blood is one of liver's jobs. After birth, the liver delegates this function to the bone marrow.

From four tons of animal liver a fraction of an ounce of B_{12} can be obtained. If a single grain of table salt were taken and divided into hundred parts, a daily amount of B_{12} equal to one of those hundreth parts would be more than enough to restore a patient with pernicious anæmia to good health. And from then on, the same minute quantity would only have to be taken about once a month, as maintenance dose.

Vitamin K is another precious substance that was tracked down to the liver in the year 1939. It is an essential part of a complex chemical that ends up by making blood to clot. It works in partnership with another substance found in the liver, heparin that acts in another direction as an anticlotting chemical. In balance the mixture of these two and other fluids keeps

caused tubercle-like lesions on the surface of the organ which aroused suspicion of a tubercular lesion.

Discussion.—A study of the literature shows that various helminthic infestations in the appendix may simulate symptoms of appendicitis—acute or chronic. They are: *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, *Taenia saginata* and *Schistosoma japonicum*. In the 19 cases presented here, ova or the worm of *Ascaris lumbricoides*, *Trichuris trichiura* and *Enterobius vermicularis* were found in the histological sections of the appendix.

Fig. 1. H. & E. X 180.

Fig. 2. H. & E. X 450.

Fig. 1 and 2 shows a group of *E. vermicularis* ova embodded in the lymphoid tissue of the appendix

Though the adult *Ascaris lumbricoides* worms are usually found in the jejunum, they may wander up and down to any accessible part, more so after an anthelmintic, like carbon tetrachloride or tetrachlorethylene. The worms may invade the lumen of the appendix, which may be packed with eggs and cause symptoms of appendicitis. One of the most frequent complications of ascariasis is enteritis. This may be confined to a single loop of the gut and if suitably localized, the pain may be mistaken for appendicitis. Rogers *et al* (1952) stated that "in the tropics *Ascaris lumbricoides* must be thought of as a possible cause of the symptoms of intestinal obstruction, bile-duct obstruction and of pain in the appendix region." In Colombo, Fernando described acute abdominal symptoms in children due to A. lumbricoides mimicking appendicitis. A toxic product

glucose first into glycogen which it can store. When the muscles are hungry for sugar, the glycogen is converted back into glucose, released into the blood.

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Original Articles

MEDICAL ASPECTS OF DIABETES MELLITUS*

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Some of the more important features of diabetes mellitus will form the subject of this article. Prevention of diabetes would appear to be the more pressing problem today, as the incidence of this disease has been on the increase, in both sexes. Only a third of the total number of cases that die of diabetes comes to our notice.

The detection of diabetes can be made by the family doctor and by the sufferer himself through simple, tests on his urine. Several mild cases may remain undetected for many years.

Two methods are in use for the investigation and detection of this disease:—(1) the glucose-tolerance test and (2) the cortisone glucose-tolerance test which will enable the detection of a pre-diabetic as also the future diabetic states. Cortisone acetate is administered orally and the blood-sugar level is estimated. A value of 140 mg.% at 2 hours is the critical level; and 160 mg.% at one hour and 140 mg.% at 2 hours indicate a positive response.

Heredity plays a large part in the causation of diabetes.

Curable forms of diabetes.—Diabetes mellitus also appears along with diseases like Cushings disease, phæochromocytoma, acromegaly and hyperthyroidism. Treatment of the main disease very often results in the diabetes disappearing.

*Based on a lecture delivered before the Nellore Branch of the Indian Medical Association in Oct. 1960.

Obesity and diabetes.—Obesity is an important factor in precipitating diabetes and this is largely a preventable cause.

Factors influencing the incidence (and course) of diabetes. —Nervous: Worries and nervous tensions are of importance also infections, arteriosclerosis and trauma. Diabetes can be induced by (*a*) surgical removal of the pancreas; (*b*) injection of alloxan resulting in destruction of beta cells; (*c*) administration of anterior pituitary extract and (*d*) prolonged administration of glucose.

Endocrine factors.—(1) Removal of pituitary decreases the severity of the diabetic syndrome and injection of anterior lobe extract gives rise to hyperglycæmia and glycosuria; (2) injection of adrenal cortical extract gives rise to hyperglycæmia and glycosuria; (3) thyroid influences carbohydrate metabolism and also causes glycosuria and hyperglycæmia; (4) Glucagon; 2nd pancreatic hormone gives rise to clinical diabetes mellitus and (5) gonads, sex hormones play a part.

The appearance of glucose in the urine depends upon (1) the level of glucose in the arterial blood, reaching the glomerulus; (2) the rate of glomerular filtration; (3) the rate at which the filtered glucose is re-absorbed by the tubules.

Pathology of diabetes:—Insulin:—(1) helps in the storage of sugar as glycogen in the liver and muscles; (2) enables the tissues to burn sugar; and (3) prevents the formation of sugar from proteins in the liver.

Sugar not stored, accumulates in the blood and is excreted in the urine and not absorbed by the renal tubules. Renal lesions in diabetes are due to an accumulation of glycogen in the renal tubules.

Identification of glycosuria.—The diagnosis of diabetes in all cases of glycosuria, is made by a complete urine analysis and by the glucose-tolerance test. A specimen of urine which reduces Benedict's re-agent does not mean that it is from a case of diabetes. For some reason or other sugars like fructose, galactose, maltose, lactose and pantoses (*not* sucrose) manifest themselves in the same way with the Benedict's test. False positive reactions are obtained after the administration of drugs like aspirin and penicillin parenterally. We may distinguish glycosuria by using glucose oxidase, an enzyme which attacks only glucose.

Diagnosis of diabetes:—Persons with glycosuria whose venous blood-sugar is either 130 mg. per cent fasting or 170 mg. per cent at other times of the day are diagnosed as diabetics. It is safer to err in diagnosing a case to be diabetic than non-diabetic. Very often we have to change the diagnosis from diabetes to unclassified glycosuria and *vice versa*. Potential

diabetics are those whose glycosuria is closely related to the diet, who easily become sugar-free with slight restrictions, but whose blood-sugar is below 130 mg. per cent fasting and never quite reaches 170 mg. per cent after a meal.

The unclassified glycosurias.—(1) Alimentary glycosuria, and (2) miscellaneous: Classical symptoms closely follow the onset of angina of effort but E.C.G. does not show any evidence of myocardial ischæmia and after control for diabetes, the effort pain does not recur.

Emotional glycosuria.—Barach (1950) quoted the popular saying "In Wall Street, when stocks go down, sugar goes up." About 25% of the patients attribute their diabetic state to overwork, domestic worries and financial problems; and so anxiety states are of ætiological significance.

Trauma.—Transient glycosuria may be due to an excess in the production of diabetogenic hormone in response to stresses.

Infection.—Staphylococcal infections may provoke glycosuria and hyperglycæmia.

The physician must take pride in preventing the incidence of diabetes in his practice. Obese patients should be frankly told that they are voluntary candidates for diabetes just as heredity predisposes in certain others.

Symptoms of diabetes:—*Onset*:—The date of onset of diabetes is usually difficult to ascertain in adults, while in children it is far more easily assigned to a definite month, week or even day. If the onset has been from a week and more to two months it is considered to be 'gradual'; and if it occurred during six days it is 'rapid'. An onset in 24 hours is 'sudden'.

Diabetes is often detected during routine medical check-up of persons, undergoing examination for life-insurance and sometimes in middle aged adults who come for treatment with pain in the joints, especially shoulder and knee and also for balanitis; in these cases diabetes should be kept in mind and the urine examined for the presence of sugar. The urine of middle-aged ladies who come with manifestations of emaciation, weekness and leucorrhœa, must also be examined for the presence of sugar.

Symptoms:—Loss of strength, polyuria, polydipsia and polyphagia are the commonest symptoms. Signs and symptoms referrable to the skin are found in over 30% of cases. Pruritus of the vulva when frequent demands exclusion of diabetes mellitus. Loss of weight is common but the patients don't recognize it; a gain in weight occurs occasionally at the onset of the disease both in adults and children. Peripheral neuritis is observed in about 20% of cases. Polydipsia is a common symptom and patients often give a history of taking large quantities of water. Polydipsia often precedes coma.

Treatment:—The diabetic should be made to learn the importance of diet, exercise, insulin and other medications. Evidence of focal sepsis when found must be eradicated before doing the glucose-tolerance test.

Preliminary diet:—A safe diet for the patient should consist of a few staple articles of foods, low in calories with restriction in fat, moderate in protein and a carbohydrate-content of 100 to 150 grammes:—One slice of bread for a meal, one orange, half a glass of milk, an egg and a small portion of lean meat or fish at each of the 3 meals; also 3% carbohydrate vegetables, 4 large portions; of cereals ½ portion and an ounce of butter during the day.

The normal diet in diabetes:—30 calories per kg. of body weight: carbohydrates 150 g. = 600 calories; proteins 70 g. = 280 calories; and fats 70g.=650 calories. Cereals are rich in potassium. Adults are allowed protein at the rate of 1·75 to 1 gram per kg. of body-weight.

Insulin therapy:—The obese diabetics free from any acute complications do not need insulin therapy. They do well with diet restriction. Insulin should be given to all diabetic children and to all thin adult diabetics. Ten out of 100 patients getting insulin will achieve good results with a single dose of intermediate acting insulin-globin, N.P.H., or lente. For practical purposes, the effects of these 3 insulins are identical. The single dose is given preferably an hour before breakfast.

(1) Mild diabetics—obese patients need no insulin; (2) relatively mild diabetics—one dose of an intermediate insulin 1 hour before breakfast, *i.e.* 14 units of globin (N.P.H. or lente) insulin; (3) moderately severe but relatively staple cases of diabetes—a mixture of N.P.H. and regular insulin 15 mts. before breakfast *i.e.*, 12 units of regular insulin to which are added 40 units of N.P.H. insulin and (4) cases of severe and labile diabetes—a mixture of N.P.H. and regular insulin, 15 mts. before breakfast and a small dose of an intermediate insulin after supper, *i.e.*, 16 units of regular insulin added to 60 units of N.P.H. insulin 15 mts. before breakfast and 10 units of N.P.H. insulin after supper.

In cases of diabetic coma, infections and after surgical operations, patients should be given larger doses of soluble insulin.

Role of exercise:—Exercise is important as it lowers the glycosuria and blood-sugar by the utilization of sugar in the muscles, provided that insulin is available at the same time.

Oral hypoglycaemic agents.—In 1951 reports came from Germany that certain sulphonamides exerted a hypoglycæmic effect, which was definite enough to be helpful in the treatment of diabetic patients.

Carbutamide BZ 55:—This agent lowers the blood-sugar in normal individuals and in certain middle-aged and elderly diabetic patients with relatively mild diabetes whose insulin requirement is below 40 units a day. It is of no value for children and for adults with the unstable juvenile type of diabetes, in ketoacidosis and coma, during infections particularly with fever and also during and following major surgical operations. The toxic effects are allergic skin rashes, anorexia, nausea, vomiting, fever, leucopænia and agranulocytosis. This drug is however, not in use at present.

Tolbutamide D 860:—We get the substitute of a methyl for an amino-group in the para-position of the benzene ring. It is less hypoglycæmic, it is not antibacterial and it is less toxic than carbutamide. The dosage schedule is: 3 grams daily for 2 days; 2 grams daily for 2 days and 1 gram daily for a prolonged period. The side-effects are few.

Mode of action.—(1) Damage to the alpha-cells of the pancreas and inhibition of production of glucagon; (2) increased utilization of glucose by the peripheral tissues through a direct insulin-like action; (3) insulin secreting pancreas must be present for the sulphonyl urea compounds to act; and (4) production of insulin from the beta-cells of the pancrease.

The recent concept is that insulin secretion is increased, and a consequent glucose uptake and utilization by peripheral tissues. Tolbutamide along with insulin decreases hepatic glucogenesis. The blood glucose decreases as a result of an increased transfer of glucose to the tissues.

Only mature type patients respond to sulphonyl-urea, *i.e.*, patients who are forty years or more and whose insulin requirement is less than 40 units per day. It is useless in cases of juvenile diabetes, keto-acidosis and coma, infections, and surgical complications. It is not wise to use this compound in the case of diabetics with neuropathy and retinopathy. Patients with atherosclerosis, occlusive disease of the coronary, peripheral and cerebral arteries respond well to the sulphonyl-urea compounds.

Other hypoglycæmic agents are (1) Chlorpropamide; (2) Metahexamide; and (3) Biguanides. Chlorpropamide in doses of 0·25 to 0·5 gram daily lowers blood-sugar just like other compounds. This compound is now being tried in the Madras General Hospital. The oral sulphonyl-urea compounds are useful in obese diabetics who do not adequately respond to the dietetic regime.

Hypoglycaemia due to insulin.—The blood-sugar falls below 60 mg. per 100 cc. Following an injection of insulin, the individual develops certain symptoms which include sweating, nervous

irritability, tremor, faintness, hunger, headache, numbness tingling in the tongue or lips, rapid heart action, double vision and unsteady gait. In severe attacks unconsciousness may occur. In all cases of coma with marked sweating and plantar bilateral extensor, hypoglycæmia must be thought of.

Treatment:—Five to 10 g. of glucose orally; glucose intranasally and adrenalin 1 cc. of 1 in 1000 solution can be given. All diabetics should carry an identification card in their pockets.

Tumours of the islets of Langerhans may also produce repeated attacks of hypoglycæmia. Whenever marked hypoglycæmia with values below 60 to 50 mg. per cent regularly develops upon fasting, the presence of an islet-cell-tumour must be thought of until otherwise diagnosed.

Diabetic acidosis and coma.—It is a complication resulting from insulin deficiency and ketosis due to a failure of diabetic control. The CO_2 combining power of the blood-plasma is 20 volumes per cent or less. Coma is caused by insulin-deficiency or failure to give insulin, infections, resistance to insulin action, shock, gastroenteritis and thyrotoxicosis.

Signs and symptoms:—The patient complains of headache, restlessness, anorexia, weakness, nausea, vomiting and drowsiness; he should be advised to go to bed whenever he feels indisposed; his bowels must be emptied by an enema and large doses of quick-acting insulin must be given. The patient gets abdominal pains and vomiting, breathing becomes laboured, and emits a fruity odour; his drowsiness, proceeds to stupor and passes on to coma.

Signs.—Unconsciousness or semi-consciousness, a dry skin, flushdown face and dehydrated tissues. The eye-balls are soft, the mouth and tongue are dry and the patient vomits. Abdominal signs resemble those of acute abdomen; the extremities feel cold and the body-temperature falls below normal. Diabetic coma comes on slowly whereas insulin hypoglycæmia comes on suddenly after injection. The skin is pale and moist in insulin hypoglycæmia what it is dry in diabetic coma.

Treatment:—Before taking the patient to the hospital, in cases of diabetic coma, 20 to 40 units of insulin should be given by the family doctor. Immediately after admission in hospital, the urine must be examined for sugar, acetone, albumin and casts. Blood-sugar estimation, CO_2-combining-power of the plasma, N.P.H. nitrogen, blood-count and serum-potassium estimation must be carried out.

Insulin:—50 to 100 units of crystalline insulin must be given, *s.c.* for adults. P.Z. insulin *must not be* given. In severe cases, soluble insulin should be given intravenously. If the blood-sugar exceeds 300 mg. per 100 cc. and if blood CO_2 content is

9 milli volumes per litre the dose must be repeated. In children, 20 to 40 units of insulin are given. If the blood-sugar is 600 to 1000 mg. give an additional 200 units (Lawrence-rule is insulin dose is roughly 1/10th blood-sugar).

Give gastric lavage with warm water. Normal saline 2000 cc. must be given I.V. The patient must be kept warm. Potassium intravenously is indicated when blood or E.C.G. indicates hypokalæmia. Fluids are given by mouth in the form of tea, coffee, orange juice, 100 to 120 cc. per hour. Abdominal distention must be relieved by enema. Dehydration and loss of electrolytes are two of the most important clinical features of diabetic coma and should be countered by giving 1500 to 2000 cc. of physiological salt solution, *without glucose*, because glucose may increase loss of potassium from the serum.

Circulatory stimulants.—We give Epinephrine 0·3 to 1 cc. for extreme collapse and in medical wards *nor*-adrenalin drips in 5% glucose saline.

Vitamins and antibiotics:—Penicillin is given to combat infections, also large doses of vitamins B-complex and C.

Allergy and diabetes.—Some patients show untoward response to insulin due to impurities in theinsulin rather than to the insulin itself. Local reaction is greater with P.Z. and N.P.H. types of insulin. The patient complains of stinging, burning and itching sensations over the site of injection. Urticaria is common and some go into anaphylactic shock. It may be due to the insulin which is a protein or due to the protamine or the globin content.

Treatment:—(*a*) People who show allergic reactions spontaneously overcome this effect; by continuing the insulin for several weeks they get spontaneous desensitization; (*b*) changing the brand of insulin; (*c*) a low carbohydrate diet; (*d*) oral hypoglycæmic agents; (*e*) use of denatured insulin which is obtained by immersing unmodified insulin-containing-vial in boiling water for 30 minutes; (*f*) use of antihistaminic agents; (*g*) desensitization; beginning with small doses of diluted insulin and increasing rapidly, using crystalline insulin. The initial dose is 1/1000 units *s-c.* 1/500–1/250.

Complications of diabetes.—Caused by:—(1) Derangement of metabolism, (2) vascular damage. The eye complications are (*a*) cataracts (*b*) retinopathy; hæmorrhages, exudates and micro-aneurysms. Careful control of the diabetes definitely mitigates the severity of retinopathy.

C.V.S. complications.—Involvement of venules, capillaries and arterioles. Diabetes increases the intensity, extent and incidence of atherosclerosis. One theory is that the effect of hyperglycæmia may be responsible for it.

Changes in the circulating lipid and protein fractions are related to vascular diseases in the diabetic.

Prevention and treatment:—(1) The early and continuous use of insulin; (2) the use of a regulated diet; (3) daily check-up of urine and periodic blood-sugar estimations. Diet is very important in diabetes and elevated blood lipids are kept up by proper administration of insulin. The patient should get 25 to 30% of the total calories in fat supplies.

Hormones.—Oestrogen may be tried for the prevention of atherosclerosis, premarin 2·5 to 5 mg. per day. Oestrogen therapy may give rise to feminizing side-effects in males and so must be used with caution.

Hypertension.—Systolic hypertension in females has proved less serious. Diabetes itself produces (1) hypertension of the renal type because of the premature development of arteriolar diseases in the kidney. (2) Diastolic hypertension of the essential type. Treatment of diabetes prevents the elevation of the diastolic pressure due to renal arteriolar diseases. Salt retention is very useful.

Renal diseases.—*Diabetic nephropathy*:—The syndrome of diabetes, gross albuminuria, hypertension and intercapillary glomerular sclerosis have steadily increased in importance. A combination of arteriolar sclerosis, acute and chronic pyelonephritis, inter-capillary glomerulosclerosis and arteriosclerosis is seen with the greatest frequency.

Coronary atherosclerosis.—This is fairly common in diabetic patients past 40 years of age. The angina in diabetes is predominantly one of exertion.

Coronary insufficiency.—Patients get severe pain like occlusion and congestive failure sets in quickly.

Myocardial infarction.—Female diabetics have an almost equal incidence with the male. Prognosis is worse in diabetic patients. Clinical problems arise when myocardial infarction and diabetic ketosis occur together with shock and dyspnœa. Uncontrolled diabetes with ketotic or non-ketotic acidosis after myocardial infarction is an absolute indication for the use of insulin. In fact, large doses of it are indicated in order to prevent insulin-resistance.

Prevention of CT.—(1) Continuous diabetic control; (2) weight-reduction; (3) reduction of hypertension; (4) reduction of dietary fat; (5) moderate exercise, giving up of smoking; œstrogen replacement in women at and following menopause.

Infection.—The causes for lowered resistance to infection in uncontrolled diabetes are still not apparent. It is related to malnutrition, a lowered glycogen-content of the liver, dehydration and acidosis.

Diabetic neuropathy.—May be defined as an acute or chronic degenerative condition of the peripheral nerves, autonomic nervous system, or central nervous system peculiar to diabetes. It usually involves the nerves supplying the lower extremities and vibration sense is usually affected. We get bilateral foot drop and ataxia.

Clinical course:—Pain gets worse at night, postural hypotension and tachycardia are characteristic findings in diabetic neuropathy, indicating an involvement of the autonomic fibres by the neuritic process. Lesions in the feet, and amyotrophy are found to occur. Neuropathy may occur following diabetic coma. Autonomic neuropathy may simulate the effect of sympathectomy. We get increased protein in the cerebrospinal fluid in diabetic neuropathy. Usually the involvement of the peripheral nerves is bilateral with the sensory fibres suffering greater damage than the motor fibres.

Diabetic neuropathy.—May take the form of:—(1) the painless foot ulcer; (2) the Charcot-joints seen in diabetic pseudotabes; (3) irritative nerve lesions with deficient peripheral circulation and (4) ischæmic neuropathy of the posterior root ganglia. Neuropathy results from the abnormal metabolism of unregulated diabetes. Arteriosclerosis has also been mentioned.

Treatment:—Diabetes must be controlled by insulin and by diet. Carbohydrates 150 to 200 g.; proteins 90 to 120 g.; vitamins B_1, B-Complex, B_{12}, parenterally; salicylates, and aspirin may be given in doses of 5 to 10 grains.

Charcot-joints.—"Neurotrophic bone changes occur in the foot as a complication of diabetes.

Diabetic nocturnal diarrhoea.—"Diarrhœa of undetermined origin is called diarrhœa of diabetes."

Urinary complications.—Pyelonephritis, cystitis and urinary tract culculi may occur.

Disorders of the skin.—These may be either infectious or metabolic in origin.

Staphylococcal infections are common and the resistant staphyloccous is a problem which is frequent when antibiotics alone are used. Pruritus ani *et* vulvæ, intertrigo and vaginitis are frequent symptoms of uncontrolled diabetes. The commonest metabolic skin diseases which involve the subcutaneous fat are known as "Insulin lipodystrophy" and other lesions as 'xanthosis.'

Tuberculosis and diabetes.—The diabetic is particularly susceptible to pulmonary tuberculosis. A delay in diagnosis of tuberculosis in diabetes, usually results in an acute course with rapid caseation, cavitation and pneumonic consolidation. The underweight diabetic whose diabetes is poorly controlled and

who has been exposed to contact with a case of active tuberculosis is likely to develop active pulmonary tuberculosis. The prognosis depends upon prompt diagnosis and treatment with streptomycin and P.A.S. Every diabetic must have an X-ray of his chest taken at 3 to 12 months' intervals. A diabetic should avoid contact with and exposure to a known case of active pulmonary tuberculosis. Plenty of vitamin C must be taken. Death in the tuberculous diabetic is due to uræmia, diabetic nephropathy or coronary occlusion.

Juvenile diabetics. are those who are afflicted with the disease while still below 15 years of age; five to 10% of cases are of this type. Heredity plays a prominent part in these cases. A prediabetic state would appear to be recognizable in the juvenile population. The glucose-tolerance test will establish the diagnosis. The fundamental principle in the management of juvenile diabetes is the regulation of both insulin and diet, so as to enhance both physiological and chemical controls. Quick-acting insulins, regular and semi-lente, should be used. For routine and general use, the intermediate-acting insulins will do. Regular insulin must be given in diabetic-coma, infections and after surgery. Oral antidiabetic compounds should *not* be used in treating juvenile diabetics. Juvenile diabetics will also have complications similar to those of adult diabetics.

THE ORIGIN OF THE FÆCAL FAT IN STEATORRHŒA

In a normal person on a normal diet the fat content of the fæces does not exceed 5 grams. The excretion of considerably larger amounts of fat in steatorrhœa has hitherto been ascribed to deficient fat absorption. Experiments in man and rats with iodine-labelled olive oil have provided evidence that only a small proportion of the fat in the fæces comes from ingested, unabsorbed fat; the greater part originates from endogenous fat metabolism. Although intestinal bacteria may be involved in the production of fæcal fat, it appears that most of it is secreted by the intestinal mucosa, and that this secretion of fat is abnormally raised in steatorrhœa. —(*Munch. Med. Wschr.*, *101* : 2119, via *German Med. Monthly*, August 1960).

LIVER DAMAGE FROM ORAL ANTI-DIABETICS DRUGS

This investigation was prompted by the observation that some diabetics developed jaundice during sulphonylurea treatment. The case material of the out-patient diabetic clinic was divided into 3 groups, those receiving (1) carbutamide, (2) tolbutamide, (3) insulin, either alone or in combination with a diet. In all 3 groups the incidence of liver damage rose with the length of treatment, but only in the carbutamide-treated group was there a satistically significant rise in hepatic lesions. Tolbutamide appears to be the safer drug.—(Zur Frage, *Munch. Med. Wschr.*, *100* : 2121, via *German Med. Monthly*, August 1960).

APPENDICULAR SYMPTOMS OF HELMINTHIC ORIGIN*

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THE appendix is a cul-de-sac without a through direct passage to the intestinal canal: it opens into the cæcum postero-inferior to the ileo-cæcal valve by a small opening, guarded sometimes by a valve of mucous fold. This organ was for long considered to serve no useful purpose; on the contrary, some authorities believed it to be a harbour for infective organisms and so a great source of evil. Its submucosa contains a considerable amount of lymphoid tissue, which acts as in the tonsils, as the first line of defence against swarming hosts of bacteria. This predisposes to inflammation.

Till the middle of the last century, sources of afflictions of the right iliac fossa were thought to be of cæcal origin. With the advances in the field of pathology and of surgical ventures during the latter half of this century the appendix was proved to be an established and notorious offender. The term "appendicitis" was coined by Fitz in 1886.

Inflammation of the appendix has the same features and follows the same course as inflammation elsewhere. Its importance is due to its frequency as a serious surgical condition with a significant mortality. Spread of infection beyond the appendix rather than the lesion in the appendix itself is the factor which causes this mortality. The full story of the ætiology of appendicitis is not yet known, though various factors have been incriminated. The essential thing in causing the wall of the appendix to react with inflammation is the invasion by bacteria—the commonest being *E. coli* and various species of *streptococci*, *i.e.*, organisms commonly found in the intestines of man. But it is not clear whether these organisms gain access to the wall of the appendix by direct invasion of the mucosa or through the lymphatic and vascular routes. Obstruction of the appendicular lumen and interference with its vascular supply are the important features in pathogenesis. They probably act by breaking down the resistance of the appendiceal wall to invasion by the potential pathogens from the lumen.

In tropical countries, helminthic infestation of the intestines is fairly common and may present a variety of clinical pictures. Metchnikoff (1901) was the first to lay stress on the relationship between intestinal parasites and appendicitis. The occurrence of various species of worms in the appendix has been

*Specially contributed to the ANTISEPTIC.

frequently described in the literature and in some cases they simulate the clinical picture of appendicitis, acute or chronic. There are several published reports, in which the examination of an appendix removed from a case suspected to be appendicitis, revealed none of the usual histological evidences of inflammation, but only the presence of worms and ova in the lumen or the wall. Considerable interest has centered round the possible role played by these parasites in the production of symptoms of appendicitis, particularly in children. There is still some difference of opinion about it, and it is evident from the literature that this subject has received little attention.

We have attempted in this paper to correlate the clinical symptoms attributable to the appendix with the occurrence of worms and ova in this organ, based on the histological findings of the resected appendices and to determine the causal relationship, if any, between them.

During the last 10 years from 1949 to 1958, five hundred and sixty eight resected specimens of appendices, sent for routine pathological diagnosis, were subjected to histological examination in the Department of Pathology of the Assam Medical College. Sections were taken from the sites where pathological lesions were suspected most, without any attention to the possibility of getting any worm or ova. These appendices were removed from 3 types of patients, the diagnosis of which was based entirely on the presenting clinical evidence:— (*a*) Cases with symptoms and signs of acute appendicitis; (*b*) cases where the symptoms and signs suggested a chronic appendicular syndrome; and (*c*) cases where appendicectomy was performed as a routine procedure along with other operations, *i.e.*, gastrectomy, cholecytectomy, hysterectomy etc., in the absence of any symptoms and signs attributable to the appendix.

RESULT:—The pathological lesions found in the 568 appendices examined are summarized in Table I, on *page 13*. No pathological change was found in 234 or (41·2%) of the 568 cases; 38 (6·6%); showed only congestion in the wall without any evidence of inflammatory exudate; 72 (12·7%) showed acute appendicitis as evidenced by the presence of congestion, œdema, exudate containing a large number of polymorphonuclear leucocytes in all the coats, specially the submucous and serous coats. Thirtyone cases (5·5%) were classed as subacute appendicitis because little exudative change was present but showed slight congestion and infiltration of lymphocytes, eosinophils, macrophages and a few polymorphonuclears; 174 cases (30·7%) showed evidence of chronic appendicitis with varying amounts of fibrosis and infiltration of lymphocytes, eosinophils into the wall without any exudative changes.

TABLE I

Pathological findings in the 568 resected appendices

	No gross pathology	Simple congestion	Acute appendicitis	Sub-acute appendicitis	Chronic appendicitis	Worms or ova	Total
No. of cases	234*	38	72	31	174	19	568
Percentage	41·2%	6·6%	12·7%	5·5%	30·7%	3·3%	

* 105 appendicectomies were associated with surgery of other abdominal organs. This leads to a total of 125 appendices with no demonstrable lesions, although they were removed from clinically supported cases of appendicitis. So the corrected percentage of normal appendices removed is 22·5%.

In 19 or (3·3%) of the 568 cases, sections of worms or their ova were detected in the appendix. In 2 of them ova of *Enterobius vermicularis* were found embedded in the wall of the appendix, while in the other 17 cases they were inside the lumen. Of these 17 cases, ova of *Trichuris trichiura* were found in 8, sections of *Enterobius vermicularis* in 1, ova of *Ascaris lumbricoides* in 3, ova of *Ascaris lumbricoides* and *Trichuris trichiura* in 2, while the remaining 3 showed sections of *Trichuris trichiura* along with a number of their ova.

These appendices were removed from 10 female and 9 male patients whose ages varied from 20 to 42 years. Eleven cases were operated with clinical diagnosis of chronic appendicitis having a history of pain over the abdomen for 3 months to 10 years. Seven appendicectomies were performed along with other operations, *i.e.*, gastrectomy, cholecystectomy and hysterectomy. One case was suspected to be tuberculous from its gross appearance during laparotomy. The clinical history and histological findings of these 19 cases are summarized in Table II, on *page 17*.

In addition to the presence of worms and ova, the lesions in the wall of the appendix were as follows:—

Ten showed no pathological change at all; 2 showed only serosal congestion; 4 showed evidence of subacute inflammation and one showed a thinned-out wall with fibrosis. Of the 2 cases with ova of *Enterobius vermicularis* in the wall, one showed ova deep in the submucous tissue, arranged solitarily or in groups with fibrosis around them. In the other, ova of *E. vermicularis* were found to be embedded in the submucous and subserous walls with chronic inflammatory changes around them. No trace of the actual worm was found in sections taken from different parts of the appendix. These subserosal infiltrations might have

caused tubercle-like lesions on the surface of the organ which aroused suspicion of a tubercular lesion.

Discussion.—A study of the literature shows that various helminthic infestations in the appendix may simulate symptoms of appendicitis—acute or chronic. They are: *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, *Taenia saginata* and *Schistosoma japonicum*. In the 19 cases presented here, ova or the worm of *Ascaris lumbricoides*, *Trichuris trichiura* and *Enterobius vermicularis* were found in the histological sections of the appendix.

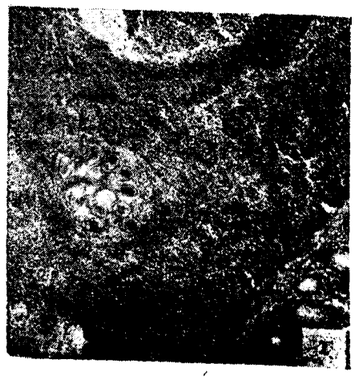

Fig. 1. H. & E. X 180.

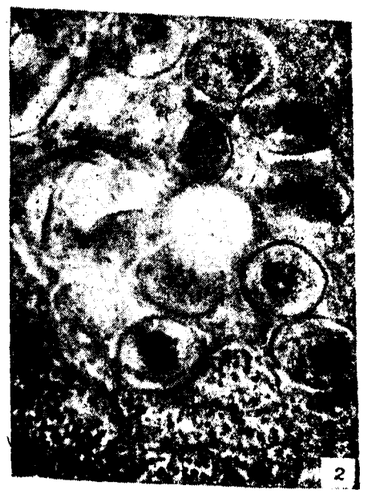

Fig. 2. H. & E. X 450.

Fig. 1 and 2 shows a group of *E. vermicularis* ova embedded in the lymphoid tissue of the appendix

Though the adult *Ascaris lumbricoides* worms are usually found in the jejunum, they may wander up and down to any accessible part, more so after an anthelmintic, like carbon tetrachloride or tetrachlorethylene. The worms may invade the lumen of the appendix, which may be packed with eggs and cause symptoms of appendicitis. One of the most frequent complications of ascariasis is enteritis. This may be confined to a single loop of the gut and if suitably localized, the pain may be mistaken for appendicitis. Rogers *et al* (1952) stated that "in the tropics *Ascaris lumbricoides* must be thought of as a possible cause of the symptoms of intestinal obstruction, bile-duct obstruction and of pain in the appendix region." In Colombo, Fernando described acute abdominal symptoms in children due to A. lumbricoides mimicking appendicitis. A toxic product

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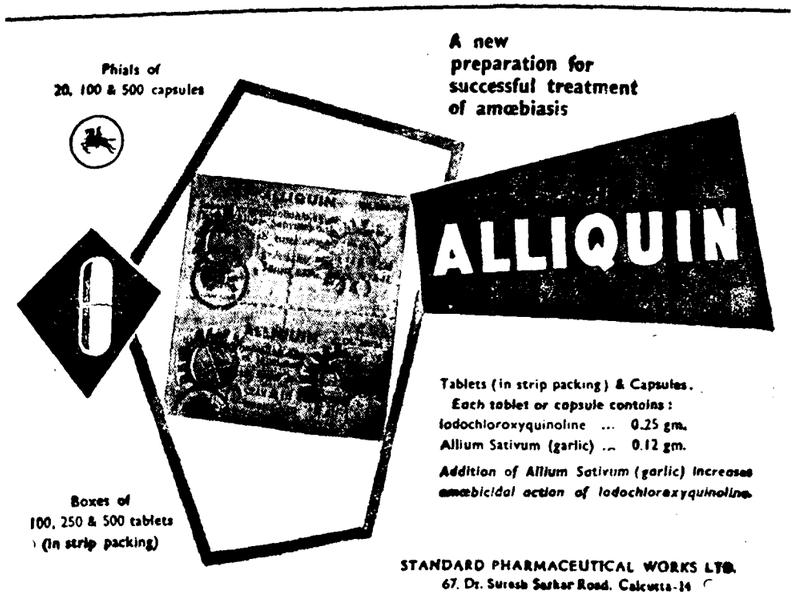

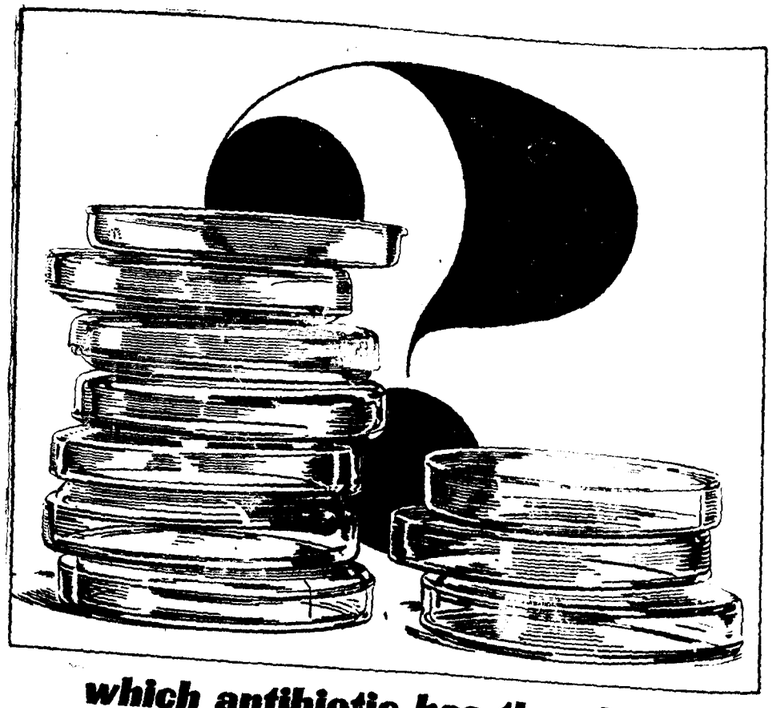

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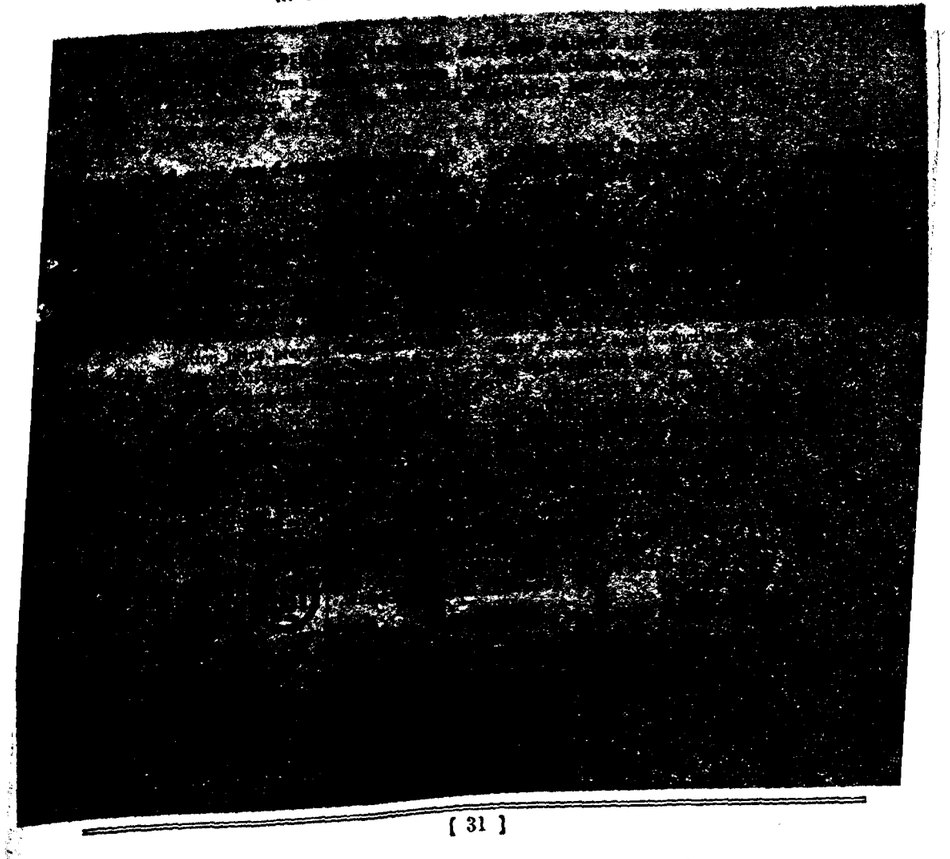

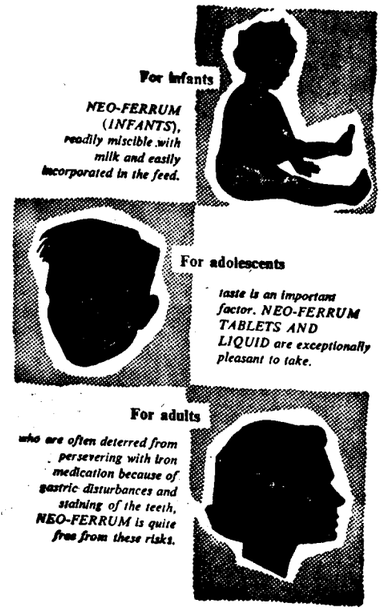

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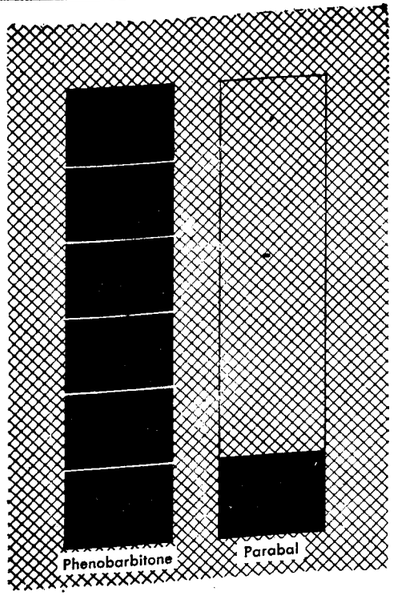

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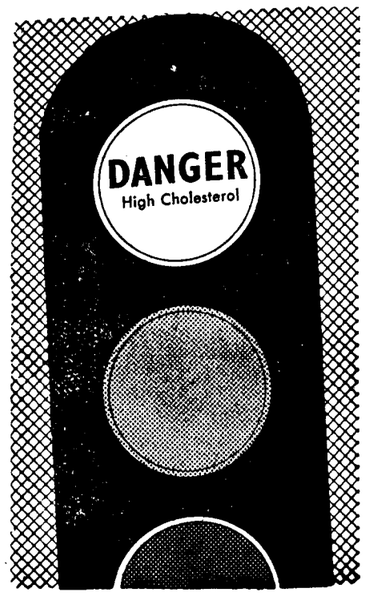

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Original Articles

CONGENITAL PYLORIC STENOSIS*

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THE surgical treatment of congenital pyloric stenosis has achieved unexcelled success, yet the disease is in relatively scientific obscurity, particularly in our country. Babies with congenital pyloric stenosis continue to die, even without being diagnosed, and what is more without being given treatment in a large number of cases. The fundamental problems of the disease still remain unsolved. Therefore, we believe their assessment on the basis of knowledge and experience gained by us as the background will be of interest to the readers, since there has not been much published work on the subject in our country.

Between 1955 and September, 1961, there were 17880 admissions in the Children's Surgical Wards of the Patna Medical College Hospital; 880 of these were patients with congenital anomalies. And in this list, we had only 6 with congenital pyloric stenosis, giving an incidence of 1 in 3000 of surgical admissions for children's ailments. We propose to describe these six cases in detail, before commenting on them.

CASE 1 :—G., a male baby, 35 days old, was referred on 11-4-1955 by Dr. G. Sahay, of Buxar as a case of congenital pyloric stenosis for surgical correction. On admission the baby showed loss of weight, dehydration, projectile nonbilious vomiting, gastric contraction, palpable pyloric tumour and constipation for three weeks. The baby was the second child of the parents, normally delivered, and was on the mother's

*Specially contributed to the ANTISEPTIC.

breast. Subcutaneous saline, 250 cc. was given daily in the thighs and Ramstedt's operation was performed by a right upper paramedian incision on 13-4-1955 under general anæsthesia with gas, oxygen and ether. Feeding was started 3 hours after the operation and was followed according to a schedule. The vomiting persisted in a mild form for a day. The baby was discharged cured on 22-4-1955.

This child was followed up and is now an intelligent young boy with average growth and no complaints. A skiagram of the stomach taken after a barium-meal on 12-9-1961 revealed no abnormality.

Case 2:—M., a female baby, 37 days old, was referred on 30-8-1956 by Dr. T. N. Banerjee, as a case of congenital pyloric stenosis for surgical correction. On admission, the baby was emaciated, and suffered from dehydration, projectile nonbilious vomiting, gastric contraction which was worse after feeds, palpable pyloric tumour and constipation. The child started vomiting from the second day of birth. She was the 5th issue of her parents and was breast-fed. Preoperatively she was given glucose saline and gastric lavage. Ramstedt's operation was performed on 2-9-1956 by a right upper paramedian incision. In the post-operative period feeding was given according to a schedule. She vomited for a day but the vomitus contained bile. She was discharged cured on 10-9-1956. The follow-up showed that she is *now* (five years later) a healthy child with good growth and no complaints.

Case 3:—X, a male baby, 30 days old, was referred on 6-11-1959 by Dr. L. S. N. Prasad, with projectile vomiting for 5 days. On admission besides nonbilious projectile vomiting the baby showed gastric peristalsis and a pyloric tumour could be felt. He was constipated and was having Eumydrine drops This baby was the first issue of the family after normal delivery Ramstedt's operation was performed on 10-11-1959 uuder general anæsthesia through a right paramedian incision. During operation the duodenum was perforated which was repaired with intestinal catgut. In the post-operative period, Ryle's tube aspiration was carried out, but the feeds were started according to a schedule. The baby had to be treated for high fever with Achromycin 25 mg. intramuscularly every 6 hours. He was discharged cured 3 weeks later on 28-11-1959. This child is now doing well.

Case 4:—A male baby, 33 days old, was referred on 11-10-1960 by Dr. G. Sharan, as a case of congenital pyloric stenosis for surgical treatment. The baby on admission presented the following clinical features:—projectile nonbilious vomiting of 12 days' duration, visible gastric contraction,

palpable pyloric tumour, constipation and loss of weight during the previous 7 days.

The baby was the first issue of the parents and was breast-fed. He started vomiting on the 21st day after birth first as eructations which in a few days became projectile. The vomitus consisted mostly of milk. Eumydrine drops gave no relief, about 5 years previously, a female baby (Case No. 2 M., *supra*) of the same family and a cousin had been operated for the same trouble.

Normal saline 150 cc. was given subcutaneously daily and the baby was operated (Ramstedt's operation) on 14-10-1960 by a right upper paramedian incision. The baby was discharged cured on 24-10-1960.

The child has since been growing normally with no complaints.

Case 5:—Z., a male baby, 75 days old, was referred on 28-1-1961 by Dr. S. P. Ram. The child had vomiting for past one week. On admission the baby had nonbilious projectile vomiting. Gastric peristalsis was observed particularly while feeding but no pyloric tumour could be felt. There was no constipation and no appreciable loss of weight. The baby was the first issue after normal delivery and was on his mother's breast. He was put on Eumydrine drops and feeds were regulated. The vomiting became less frequent and in about two weeks' time there was occasional vomiting. He gained weight. The baby was transferred back to have medical care and attention. He is now well and growing normally.

Case 6:—Y., a male baby, 11 days old, was referred on 24-7-1961 by Dr. G. Sharan, with nonbilious projectile vomiting and visible gastric peristalsis of 5 days' duration. He was the first issue of the family, after normal delivery. On admission, the baby was lusty and used to vomit after taking feeds. The vomitus did not contain bile. There was visible peristalsis in the epigastrium which was more pronounced after feed. He was constipated. The baby was put on Eumydrine drops and the feeds were regulated. The vomiting gradually diminished both in number and in force and after a week it was infrequent.

The baby was transferred back to medical care. He is doing well and is growing normally.

Aetiology:—The cause of this disease is still unknown and its pathogeny obscure. There are however certain observed facts which cannot be disputed.

Several authors have noted its familial occurrence. In our series, Cases 2 and 4 were from the same family. Patient No. 2 was the first cousin of the father of patient No. 4. Judged by the frequency of familial incidence a genetic factor probably plays a

role in the ætiology of the condition. Further valuable evidence in favour of a hereditary aetiology is the incidence of the disease in twins. In cases of uniovular twins, both as a rule, are affected.. Sheldon (1938) believes that the evidence of twinning incidence is strong proof that congenital pyloric stenosis has a genetic basis. It must be added, that from information available the exact mode of inheritance of the hereditary factor cannot be stated though Carter and Powell (1954) assume that the disease depends upon a dominant gene which finds full clinical expression in one out of every five boys and one of every twenty-five girls.

The intra-uterine development of the babies with congenital pyloric stenosis shows no significant deviation from the normal. The course of pregnancy and delivery reveals nothing unusual. This disease occurs more frequently in male babies than in the female babies. In the reported series from 80 to 90% incidence was in the males. In our series there were five males and only one female baby, giving an incidence of over 80% for males.

Of the six cases reported here, four were first-born, one was the second and another was the 5th child. Ford *et al* (1941) have also recorded that there is an absolute preponderance of first-borns among infants suffering from congenital pyloric stenosis. Wood and Smellie's (1951) series reveal that there is about 50 per cent more risk of pyloric stenosis in the first-borns than in the later babies.

Very little information is available about racial distribution of the disease. In our series all children were from Hindu families but our list is much too small to be able to draw conclusions of value as regards race incidence. Lanman *et al* (1933) could find no evidence of the influence of racial factors in their series. Only a few cases have been reported from Italy and the disease is uncommon in negroes (Donovan, 1932), while the Anglosaxon and Teutonic races are very susceptible.

Pathology :—The essential pathology lies in the stomach particularly in the pyloric canal, while the general wasting and the pathological processes developing terminally are all secondary thereto. The entire pyloantral region shows a shining, grey-white, spindle-shaped thickening of a cartilagenous consistency. This swelling loosely termed a tumour, is about an inch long and half an inch wide. The gastric mucosa is normal except for some evidence of gastritis due to retention from obstruction. The muscular coat of the entire stomach wall is thickened and the lumen of the viscus may be dilated. Essentially there is a gross thickening of the musculature of the pyloric canal, ending abruptly at the pylorus, but fading away gradually proximally. Microscopically the increase in the volume of the pyloric musculature is due to hypertrophy.

Metenheim (1934) states that it is due to both hypertrophy and hyperplasia. The inner circular fibres are prominently involved, although the longitudinal layer also shows a lesser degree of similar changes. The connective tissue of the muscle-coat, elastic fibres of the submucosa and to a lesser degree the muscularis mucosæ also share in the hypertrophy. These changes are limited to the pyloric canal, the pyloric ring (pylorus) itself being uninvolved. It is a progressive change becoming more pronounced with increasing duration of symptoms advancing in the long axis of the canal (Cameron, 1925). The increase of the muscle-volume within the confines of an adherent and unstretchable peritoneal covering, transforms the limp and relaxed pylorus into a hard and solid tube. Another effect of the muscle swelling is the protrusion of the thickened pyloric segment into the duodenal lumen, much as the cervix projects into the vagina. The tension within the thickened pyloric muscular coat compresses the vascular branch and lends a pale, bloodless appearance to the component tissue. The consistency of the muscle turns crisp and gritty but as the disease progresses, the muscle becomes again soft and more vascular. Accumulated evidence based on observations recorded during operations enables a classification to be made of cases of congenital pyloric stenosis into three groups :—(Twistington Higgins, 1950).

(a) Group 1 :—Comprises infants operated on up to the third week from birth. Clinically the pyloric tumour is small and elusive. At operation it is soft and vascular ; though it cuts easily, the texture is loose and bleeds freely. The extent of the hypertrophy is obviously much less than that seen in the later cases, and the appearance would rather suggest, a developing stage with rapid growth and great vascularity.

(b) Group 2 :—Consists of infants operated on between the fourth and ninth weeks and constitutes the great majority of cases. Clinically the tumour is readily palpable and at operation it is large, firm and avascular. The muscle is very thick, cuts cleanly, and the cut surface is pale and bleeds little. The appearance suggests hypertrophy and its height-muscle bundles packed tightly and blood-vessels squeezed out—autodevascularization determining the atrophy and resolution.

(c) Group 3 :—Comprises cases operated on between the third and fourth months of life. At operation the tumour is still large but has become leathery in consistency. It cuts with some difficulty and bleeds more freely than at any other stage. The muscle tends to adhere to the mucosa and considerable separation may be necessary to free the mucosa sufficiently well. The appearance indicates resolution. We know that in cases in which recovery is complete, all traces of hypertrophy usually have disappeared.

The above grouping would go to indicate that the disorder proceeds in a definite cycle in which hyperplasia reaches a maximum and then subsides as natural recovery occurs. Whatever may be the underlying cause, it has been clinically observed that the disease once past the first 3 months of life, shows spontaneous healing. Sharan (1961) reported a case of congenital pyloric stenosis which was cured by medical care and attention. The treatment, however, had to be continued for four months.

CLINICAL FEATURES :—The initial incident is vomiting in a lusty baby; its onset is commonest between the second and fourth weeks, occasionally earlier. In our series, patient No. 2 started vomiting on the 2nd day of her life while patient No. 5 started on the 68th day of his life.

The vomiting first follows a feed, usually without warning. This recurs and becomes forceful in a few days. Some feeds are retained, but from time to time a single large projectile vomit occurs, which becomes more severe and reaches a point where it starts with the first gulp of a feed. An important characteristic of the vomitus is the absence of bile. The confirmatory physical signs are well-marked—visible gastric peristalsis and the palpation of a pyloric tumour. Gastric peristalsis was seen and felt in all our six cases while pyloric tumour could be felt in only four.

Despite the vomiting, the baby becomes hungry and takes feeds with avidity, but constipation, oliguria, dehydration and loss of weight ensue in proportion to the severity of the vomiting.

Problems in diagnosis.—The essential confirmatory sign is the feeling of the tumour, and unless this is unmistakably felt, the diagnosis must remain in doubt. Statistics which tend to disregard this essential diagnostic sign are unreliable (Twistington Higgins, 1950). In our series of six, pyloric tumour as already stated, could be felt in only four which was confirmed on operation. The two cases where pyloric tumour could not be palpated were not taken up for operation and both responded well to medical measures.

Vomiting in early infancy may arise from feeding difficulties, from swallowing of air, or even as a result of intracranial birth-injury, but in all these cases the vomiting is irregular in its incidence and the clinical picture lacks precision. Vigorous gastric peristalsis is not seen and no pyloric tumour is felt. In duodenal obstruction the vomiting dates from birth and the vomitus contains bile. The pyloric tumour is not felt. It is a simple matter to eliminate the possibility of infectious vomiting on the grounds of absence of high fever and dyspeptic stools. In the presence of the typical findings—persistent projectile vomiting, visible gastric peristaltic waves, palpable pyloric tumour,

loss of weight, and constipation—no other disease should confuse the diagnosis.

However, at this stage, the clinical term pylorospasm needs clarification. It is believed that pylorospasm is a form of pyloric obstruction due to a purely neurogenic dysfunction, presumably spasm, of the pyloric musculature. The diagnostic criteria appear to be :—transitory character of the obstruction, the less violent, less persistent and usually nonprojectile character of the vomiting, less common in males, late onset and in its generally less malignant course. Holt (1917) claims that this condition exists only as a transitory state and is incapable of giving rise to a disease picture of importance. We think that it is a mild form of congenital pyloric stenosis. But for the absence of a palpable pyloric tumour, the signs and symptoms of pylorospasm show no essential quantitative difference from those of congenital pyloric stenosis. If there is any difference, it is only one of degree. The difference between pylorospasm and congenital pyloric stenosis is not of any importance from the point of view of pathology but it may have some significance from the therapeutic point of view. The benign form of congenital pyloric stenosis which not infrequently is called pylorospasm, may respond well to medication whereas the more severe ones will always need surgical correction.

Choice of treatment.—The treatment of choice at the present day is surgical. A well-ordered early operation offers the prospect of cure in two weeks approximately in 98 per cent of such infants. Statistics of non-operative treatment cannot compare with this figure (Higgins, 1950). The period of hospitalization is prolonged and the mortality rate is higher in medically treated cases. Robertson (1940) believed in operating every case in which a diagnosis of congenital pyloric stenosis is made. We operated on 4 of the six cases; in these 4 cases pyloric tumour could be felt. The two cases in which pyloric tumour was not felt improved on medical measures alone. All six cases were cured.

We suggest that one should recognize the two main types of the disease. *First*, the severe type in which besides projectile nonbilious vomiting, and gastric peristalsis, a palpable tumour is felt and the *second* type, a relatively mild one with projectile nonbilious vomiting, gastric peristalsis but no palpable pyloric tumour. The first type is eminently suitable for surgery whereas the second one could do well with medical measures. In the second type when medical measures fail or when the infant is fast losing weight even under medical treatment, operative surgery should be promptly resorted to.

The operation.—In all six cases of our series, we performed the Ramstedt's operation.

The baby's general condition served as our guide for decid ing on the pre-operative measures. Replacement of fluid wa done in proportion to the degree of dehydration and chlorid loss. Normal saline or 5% glucose saline was routinely given the thighs of our patients. On an average the babies require 2½ ounces per pound of body weight in 24 hours.

All patients were operated under general anæsthesia with mixture of nitrous oxide, oxygen and ether, which gave ad quate relaxation with no ill-effects. The operation was do with a right upper paramedian incision about 2" in length. T gave us an easy approach to the pyloric tumour and left behi a strong scar. After the pylorus was delivered into the wou it was fixed with the left finger and thumb, and the incision w given on its antero-superior aspect along with "bloodless lin cutting only the peritoneum and just entering the muscle la with the right hand. The muscle was further separated w dissecting forceps until the mucosa bulged into view. gastric end presented no difficulty but the duodenal ends nee special care. The pyloric vein bled when this end was reached. Perforation of duodenal mucosa occurred in one case (No. 3) which was repaired with chromic intestinal catgut and the baby recovered.

The peritoneum and the posterior layer of the rectus sheath were closed with continuous catgut sutures. The anterior rectus sheath was also stitched with continuous catgut stitches. The skin was stitched with interrupted thread stitches. During the post-operative period the babies were closely watched, and feeding was started 3 hours after operation in all cases according to a schedule. The skin stitches were removed on the eighth day. And the patients were discharged a few days later.

Table I

Showing the schedule of feeding adopt during the post-operative period

Hours after operation	Feeds
3	2 drachms of 5% glucose in water
5	2 dr. ,, ,, ,,
7	2 dr. ,, ,, ,,
9	3 dr. ,, ,, ,,
11	3 dr. (Breast milk 50% glucose 50% water) 5%
13	4 dr. ,, ,,
15	4 dr. ,, ,,
17	6 dr. ,, ,,
19	6 dr. ,,
21	1 oz. ,,
24	1 oz. ,,
27	1 oz. 2 dr.
29	1 oz. 2 dr.
32	1½ oz. ,,
35	1½ oz. ,,
38	2 oz. (breast mi
41	2 oz. ,,
44	Baby put to br feeds given 3 after. Breast rly there-

Results.—As stated *supra*, 4 out of 6 cases we upon; and all were discharged cured. The only c perated was duodenal perforation in No. 3 which healed. A lication e babies