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CONTENTS

INTUITION AND SCIENCE

"THAT is a case of leukæmia. This is undoubtedly a case of bronchiectasis" said the learned physician as he strolled down the length of his ward on the day after admission. He was followed by a great crowd of students, many of whom turned their admiring and devoted gaze upon him mightily impressed by the great wisdom, sagacity and erudition which enabled this disciple of Hippocrates to make such a swift and certain diagnosis of a patient's ailment without any need for a detailed anamnesis or a proper physical examination. It is true that often he was correct. It was equally true that often he was wrong. When he was correct his disciples admired him all the more and when he was wrong they put it down to human fallibility and were not so tactless as to bring it to his notice. But is this modern medicine? Is this the method of teaching? Is the criterion of an able physician the ability to stroll down the ward and make a "spot diagnosis" without even having a word with the patient? Yet, we find that this unscientific trend is rampant in many a teaching hospital.

It is true that such an attitude impresses both students and the patient. If one is more often right than wrong it is because long practice of the art gives the physician an intuitive power to diagnose correctly as soon as he sees the patient. However this factor should not be allowed to dominate medical practice. True it may play a small role, but only a very minor one at that, in practice. All sound diagnosis of disease is made by detailed anamnesis and careful examination. Of these two methods which contribute to reach accuracy in diagnosis, taking a detailed and careful history is of far greater importance than physical examination.

How often we find that in spite of the most elaborate investigations we miss the obvious diagnosis? We find in retrospect that had we only stopped to listen to what the patient had to say and to have the patience to take a detailed history and make a thorough physical examination we may have reached a correct conclusion without subjecting the patient to elaborate and sometimes dangerous methods of investigation. The value of recording accurate history is not widely appreciated.

Take for instance, a common complaint like pain. It is possible by interrogating the patient about his pain, very often to make a fairly precise diagnosis. The manner in which this can be done is most admirably written by that most eminent and distinguished of physicians, the late John Ryle in his book *NATURAL HISTORY OF DISEASE.* This is the way in which he analyses pain. What is the character of the pain? How severe is it? What is its situation? At what depth from the surface is the pain? What is its exact localization or extent of diffusion? What are the paths of reference? What is the duration of the pain? What is its frequency? At what special times does it occur? What makes the pain worse and what makes it better? What associated symptoms are experienced with the pain? By such detailed questioning it is often possible to get a fairly strong and reasonable hint as to what the cause of the patient's trouble is. Not only with pain, but

with all the other symptoms detailed questioning should be valuable. Too often in these modern times we appear to be in great hurry and have no time whatever to listen to what the patient has to say. We are more anxious to get the work done and we tend to be only too ready to prescribe. It is this very haste that sometimes leads to great disasters and which results sometimes in the patient being submitted to unnecessarily expensive and useless investigations. Obtaining the proper history and enquiring into the symptoms, is a lengthy process. Indeed it is an art. In normal circumstances history taking would occupy more than three quarters of the time which we give to any patient. A physical examination is often the least important part of the examination although from time to time in the simpler forms of disease, examination by itself provides a ready answer.

If it is important to be thorough in history taking it is of equal importance to adopt a systematic approach in physical examination also. It is in the realm of physical examination and the performance of such special investigations as may be necessary that the difference in approach between the general practitioner and the specialist becomes most evident. It works out something like this. Provided the specialist is not a self-dubbed expert but a man who has spent a great part of his professional life time systematically acquiring knowledge in his special field of interest, he is able readily to distinguish between what is normal and what is abnormal.

Take for instance, the case of newly qualified doctor who has just been posted to a gynæcological unit. He is completely bewildered when he elicits physical signs in the first few gynæcological examinations. Yet, he has a sound book knowledge of anatomy and pathology and can describe the structure and the function of the internal genitalia in great detail. He even has some basic knowledge of the various diseases which affect these organs. Yet, after he has examined the patient he finds himself totally at a loss. He feels sufficiently encouraged if he is able to locate the cervix and to discover in which direction it points and becomes quite self-confident when he is able to palpate the uterus. Yet contrast this to the approach of a specialist in gynæcology. I can recall an incident when the great master of gynæcology the late Wilfred Shaw of St. Bartholomews' Hospital was performing a vaginal examination on a patient during one of his teaching rounds. He declared before the class much to the astonishment of all, that the disease from which the patient suffered was most probably a calculus lodged in the lower part of the left ureter. The way in which he made this dramatic discovery by vaginal examination was undoubtedly like this. In his early days he must no doubt have considered the genitalia structure by structure and said to himself, "Is it normal or is it abnormal? If it is abnormal what is wrong with it? Is the anterior vaginal wall normal? Is the left vaginal wall normal? Is the posterior vaginal wall normal? Is the right vaginal wall normal? Are the other peri-vaginal structures such as the bladder and the urethra, rectum and anal canal, Douglas's pouch and the soft tissue and bony structures normal? Is the levator and the pelvic floor tone good? Is the anterior fornix normal? Is the left fornix normal? Is the posterior fornix normal? Is the right fornix normal? Is the cervix normal? And finally are the other para-cervical structures such as the ureter, the cervical arteries and the parametrium normal?

By such a systematic approach he discovered that everything was normal except in the region of the left ureter where he could feel a small ovoid hard structure. Having already obtained a detailed history with discretion and discrimination he had come to the conclusion that the type of pain which the patient was experiencing was being caused by some lesion in the lower urinary tract. By putting these things together he was able to arrive at a moderately sound diagnosis by vaginal examination that a left ureteric calculus was probably present. The correctness of this diagnosis was subsequently confirmed by radiology. Is there anything magical about the diagnosis?

If we are to set about an examination in this fashion it would take us sometime before we could complete it. Yet, by going through the same process again and again like Wilfred Shaw and the illustrious gynæcologists who have preceded him, we too may be able to make a speedy examination and to recognize what is normal and what is not. The gynæcologists who lack this particular type of training or the general practitioner who has not specialized in gynæcology may also come to conclusions by performing a vaginal examination but their findings will not be as valuable as those of the specialists.

It is high time that we discarded the notion that anything other than a careful anamnesis and systematic examination can help towards sound diagnosis. It is true that very often even after these two processes we have to go in for special methods of investigation to help us. There is nothing wrong in this; but the modern trend to rush in for such tests straightaway is to be condemned. When we have narrowed down the diagnosis to one of two or three conditions, it is true that there is an element of intuition which is acquired by long practice, observation and experience which helps us to lean more towards a particular diagnosis. This factor is a very minor one.

One cannot but condemn, therefore, those physicians in big teaching institutes who use the methods of 'spot diagnosis' to impress their students and their patients. Medicine is a scientific study and those who are not prepared to accept this should have no place whatever in a teaching institute however great a physician they may think themselves to be and however lucrative may be their private practice.

Diagnosis of amebiasis. Annotations, *Lancet*, Great Britain, 1:247-248, January 30, 1954.

Diagnosis of amebiasis is based upon identification of amebæ or cysts of *Entameba histolytica* in the feces. Differentiation of this type of organism from other intestinal amebæ is not at all difficult if (1) specimens are fresh, and (2) the organisms are reasonably numerous. The problem of identification is more difficult if the reverse conditions, i.e., degeneration or sparsity of amebæ or cysts, prevail. As there are obvious difficulties here, other methods have been worked out to make diagnosis easier. Staining methods have been developed to distinguish between trophozoites and cysts of intestinal amebæ from fecal material. A flotation method for culture and concentration of cysts is helpful when only small numbers of *Entameba histolytica* are present. A method of revealing fluorescence only with this type of organism employs a globulin fraction of an antiserum conjugated with a fluorescein derivative. As the standard of identifying the desired organisms is based wholly on presence or absence of fluorescence relatively untrained workers could employ the test. Even where the number of amebæ or cysts present is extremely low, the fluorescence should make identification certain, as long as no other fluorescent material is present in the feces.

The Improvement of the Protein Quality of White Rice by Lysine Supplementation

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THE improvement in nutritive quality of the protein of a food or feed attainable by amino acid supplementation is dependent upon many factors. Certain principles governing successful supplementation have evolved as a result of many studies carried out in recent years. Such principles include the recognition of the essential amino acid requirement of the species or individual which is to benefit from the improved protein and the amino acid composition of the food to be improved. The key step, then, involves supplementation of the food with the first limiting essential amino acid to the extent of bringing the total amount of the first limiting amino acid in balance with the second limiting amino acid according to the species' requirements. While this procedure assures a protein of superior nutritive quality, the organism consuming it will obtain benefit from the improvement only when the diet includes energy from non-protein sources in an amount sufficient to assure utilization of the balanced portion of the protein for tissue synthesis and repair.

Application of these sound principles has been rewarding in several instances, e. g. in studies on the lysine supplementation of bread (Rosenberg and Rohdenburg, '52) and on the methionine supplementation of corn-soybean oil meal diets for the growing chick (Baldini and Rosenberg, '55). In the present work it has been demonstrated that the protein quality of white rice can be significantly improved by the addition of relatively small amounts of lysine as the sole supplementary amino acid. This is in agreement with the concept that lysine is the first limiting amino acid in white rice (Mitchell and Block, '46) and that only small amounts of supplementary lysine are necessary to balance this amino acid against the second limiting amino acid according to the rat's requirements as stated by Rose ('37) and modified by Rama Rao, Chalam Metta and Johnson ('57).

EXPERIMENTAL PROCEDURE

Five growth experiments involving the supplementary value of lysine on rice diets have been carried out with weanling animals from our colony of hooded rats. At 21 days of age litter mates were distributed among the various treatments so as to assure equal average weight per group. The animals were housed individually in cages with raised screen-bottoms, and food and water was supplied *ad libitum*. Individual weekly records were kept on weight gains of the animals and the amount of food consumed. In all experiments but one (Experiment 5) six male and six female animals were assigned to each treatment. The studies were carried out during a growth period of five weeks. Experiment 5 was started with 20 male and an equal number of female weanling rats per treatment. In the latter experiment ten animals of each sex and each treatment were sacrificed after the initial five-week growth period for determinations of liver fat, liver protein and liver glycogen. The remaining animals were kept on their respective diets for further growth studies until they were mature.

The composition of the basal rice diet used in all experiments is shown in Table 1. Precooked, air-dried rice was ground to 20—40 mesh and all vitamins and minerals known to be required by rats were added to the ration. In Experiments 1, 2 and 3, 1% diammonium citrate was included in the diet. Substituting graded levels of L-lysine. HCl* for the same levels of diammonium citrate resulted in isonitrogenous diets throughout the experiments. In the other three experiments diets containing 91% rice were used and the L-lysine. HCl replaced equal amounts of rice. Since earlier exploratory experiments have indicated that the protein content of rice was increased slightly by cooking, causing an increase in the growth rate of rats and in the dietary protein efficiency, precooked rice was used throughout this

* Du Pont L-lysine. HCl ("Darvyl") containing 95% L-lysine. HCl and 5% D-lysine. HCl.

study. In the last experiment parboiled rice and raw, long-grain rice were compared with precooked rice.

RESULTS

In Experiments 1 and 2 graded levels of L-lysine. HCl were added to the basal diet. The design of these experiments is seen in Table 2, which also gives the total gain of the animals and the efficiency of food utilization. Supplementation of the rice diet with 0.05% L-lysine. HCl improved the growth of the male animals 37% and 32% in the two experiments. Supplementation with a smaller amount, 0.025% L-lysine. HCl, was considerably less beneficial, and supplementation with larger amounts of lysine did not give further improvements. In fact, the improvements in gain and feed efficiency obtained with 0.05% L-lysine. HCl were not maintained when larger amounts of lysine were supplied. The female rats behaved very similarly as seen from Table 2, maximum benefit being obtained when 0.1% L-lysine. HCl was added to the diet.

In order to obtain further information on the improvement of the quality of rice protein attainable with lysine supplementation, a diet very similar to that described, but without the added diammonium citrate, was used. A preliminary study (Experiment 3) was carried out to determine what contribution diammonium citrate might make to the nutritive value of the rice diet. This diet, therefore, was fed to groups of male and female rats and other groups of animals were fed similar diets in which the diammonium citrate was replaced isocalorically with cerelose or glycine. As seen from Table 3, there was no difference in the performance of the animals on these three diets. It was concluded, therefore, that under the conditions of this experiment the animals receiving the basal rice diet did not benefit from added diammonium citrate for the purpose of tissue synthesis.

The next experiments then employed the basal diet containing 91% of precooked rice together with graded levels of L-lysine. HCl as seen in Table 4. In Experiments 4 and 5 highly significant responses to L-lysine. HCl supplementation were obtained, best gains and feed efficiency being observed at a level of 0.10% supplementary L-lysine. HCl for both males and females. Ten of the original twenty males from Experiment 5 and an equal number of females were kept on the same diets for further studies. The growth curves for the groups of animals on the basal diet and on the diet supplemented with 0.1% L-lysine. HCl, as described earlier, are seen in Figure 1. Although it appears that, by reducing the number of animals, unintentionally a slight bias was introduced in favor of the lysine-supplemented groups, nevertheless the improvement in growth rate due to lysine supplementation is consistent throughout the entire experiment. The slopes of the response curves of the males as well as of the female rats are very similar to those recorded for rats of the same strain maintained on lysine-supplemented bread diets (Rosenberg and Rohdenburg, '52).

The design and results of Experiment 6 are seen in Table 5. The precooked rice diet (7.75% protein) was compared with a similarly compounded diet of parboiled rice (8.25% protein) and of raw, long-grain rice (6.38% protein) in feeding experiments with male and female weanling rats. Considerable differences were found in the nutritive value of the three types of rice studied. All three diets, however, were improved by supplementation with 0.1% L-lysine. HCl.

Liver fat and liver protein were determined in the animals from Experiments 2 and 5. Three male and three female rats per group were killed with pentobarbital sodium with mephenesin at the end of the five-week growth period. Their livers were removed, frozen with dry ice, lyophilized and ground. Fat and protein in the pooled samples were determined by the AOAC procedures ('55). For the determination of liver glycogen, ten animals of each sex and each treatment of Experiment 5 were killed with pentobarbital sodium with mephenesin. The livers were removed and approximately 1 g. samples taken for glycogen assay by the method of Carroll *et al.* ('56).

As seen in Table 6, lysine supplementation of the rice diets caused a reduction in liver fat and an increase in the liver protein. Although the changes in fat and protein concentration, caused by the amount of supplementary lysine found optimum for growth, are substantial, supplementation with larger quantities of lysine produced further changes in liver fat and liver protein towards the levels obtained with the stock diet. There was no apparent effect of dietary lysine supplementation on liver glycogen concentration.

DISCUSSION

In all five experiments a pronounced improvement was observed in the growth rate of rats maintained on 90% rice diets when the first limiting amino acid, lysine, was brought into balance with the second limiting amino acid, threonine, by supplementation with L-lysine. HCl. Best balance was achieved with approximately 0.10% L-lysine. HCl. As the basal rice diet contained about 0.25% lysine, [analyzed microbiologically (Rosenberg and Rohdendurg, '51)], a total of 0.33% lysine produced optimum balance. At the end of the five-week experimental period the improvement in weight gain due to lysine addition ranged from 32% to 50% for the males (average 41%) and from 27% to 58% for the females (average 44%). This substantial improvement in weight gain was accompanied by an average saving of 20% of the feed consumed (range 15% to 27%) per unit of gain. These results suggest that proper supplementation of rice diets with lysine might be of great benefit to humans.

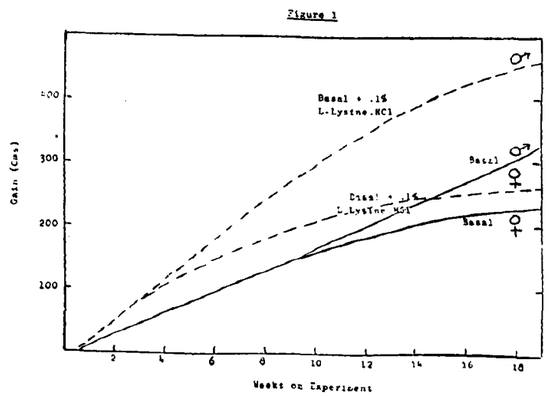
The addition of larger than optimum amounts of lysine to the experimental rice diet did not permit the rats to grow as well as when the optimum amount of L-lysine. HCl, 0.1%, was added. Supplementation with twice the optimum amount, namely 0.20%, resulted in a growth response which in many experiments was very similar to that obtained with the basal rice diet without any lysine supplementation. The latter result confirms similar observations from other laboratories (Harper *et al.*, '55). In view of the highly significant growth response at the 0.1% level of lysine supplementation, it must be concluded that high levels of lysine overbalance the amino acid pattern. The consistency with which higher levels of lysine depressed growth may well explain why other workers did not find a growth response for lysine.

The growth response attainable by supplementation of rice diets with small amounts of lysine was not noted by earlier workers probably because of their different experimental approach. Pecora and Hundley ('51) added to the experimental rice diets various essential amino acids in the amount suggested by Rose ('37) for the growing rat. Supplementation with 2.0% DL-lysine. HCl, equivalent to 0.8% L-lysine, did not improve the diet. These investigators, however, made the important observation that the combination of lysine plus threonine produced approximately a threefold increase in growth. They discovered in later experiments that the amounts of added lysine and threonine could be reduced to one-fifth without reducing the benefit obtained from the full supplements. These results have been confirmed and extended by various investigators. Harper *et al.* ('55) tested not only the effect of the lysine-threonine combination at the reduced level, 0.20% L-lysine. HCl and 0.24% DL-threonine, but tested the effect of each amino acid separately. At these levels, no growth response was obtained from either lysine or threonine alone, but the combination gave the results found by the earlier workers. Harper *et al.* ('55) investigated specifically the deposition of liver fat in rats fed various rice diets. Although a slight reduction in liver fat from 28% to 25.7% was obtained when 0.2% L-lysine. HCl was added, this was not considered to be meaningful. The reduction in liver fat due to lysine supplementation of rice diets in the present study (Table .) is somewhat more pronounced. Although the results of the two experiments are not identical as far as the absolute amounts of fat found in the livers are concerned, the trends are the same. The observation that liver fat decreases with increasing amounts of lysine supplementation and that this effect does not parallel the effects on growth is a confirmation of the work of Harper *et al.* ('55).

SUMMARY

The nutritive value of the protein of white polished rice can be improved significantly by supplementation with the first limiting amino acid, lysine, in amounts sufficient to bring this amino acid in balance with the second limiting amino acid.

Figure 1



In five experiments, male and female weanling rats were fed diets containing 90% precooked white polished rice supplemented with graded amounts of L-lysine. HCl. Substantial improvements in growth rate and in efficiency of food utilization were obtained with 0.05%—0.10% L-lysine. HCl supplementation. This growth response was accompanied by a decrease in the amount of fat and by an increase in the amount of protein deposited in the liver.

TABLE 1

Composition of Basal Diet

Ground rice	90.0%
Vitamin Mix § 1 *	1.5
Salt Mix § 351	3.0
Crude Soybean Oil	3.0
Cod Liver Oil	1.5
Diammonium Citrate (or rice)	1.0
Total	100.0%

* At 1.5% level, Vitamin Mix § 1 supplies per 100 gms. diet :

Choline chloride	150.0 mg	Vitamin B_{12} (0.1% triturate)	1.500 mg
Inositol	75.0 mg		
PABA	75.0 mg	Thiamine	0.750 mg
a-Tocopherol acetate	7.5 mg	Pyridoxine HCl	0.750 mg
Niacin	3.0 mg	Menadione	0.375 mg
Ca Pantothenate	3.0 mg	Folic acid	0.075 mg
Riboflavin	1.5 mg	Biotin	18.750 ug

TABLE 2

Improvement of Rice Diet by Lysine Supplementation

5-Week Rat Growth Data

% L-Lysine. HCl Supplementation to 90% Rice Diet	MALES			
	Gain in grams		Feed/Gain	
	Experiment 1	Experiment 2	Experiment 1	Experiment 2
0.00	51.1 ± 4.16[a]	62.5 ± 6.68[a]	8.12 ± 0 42[a]	7.41 ± 0.51[a]
0.025	— —	67.8 ± 7.16	— —	6.70 ± 0.36
0.05	70.1[b] ± 3.79	82.5[b] ± 4.41	6 56[b] ± 0.33	5.82[b] ± 0.19
0.10	63.8 ± 6.50	76.6 ± 12.71	7.12 ± 0.70	6.17 ± 0.56
0.20	51.3 ± 4.66	72.0 ± 5.78	7.84 ± 0.74	6.17 ± 0.26
0.30	— —	72.0 ± 4.72	— —	6.05 ± 0.34
0.40	49:6 ± 3.33	— —	7.14 ± 0.42	— —
0.80	52.6 ± 4.50	— —	6.55 ± 0.27	— —

TABLE 2—(Continued)

% L-Lysine. HCl Supplementation to 90% Rice Diet	FEMALES			
	Gain in grams		Feed/Gain	
	Experiment 1	Experiment 2	Experiment 1	Experiment 2
0.00	61.2 ± 5.33	71.1 ± 3.47	7.33 ± 0.32	6.62 ± 0.14
0.025	— —	84.1 ± 4.98	— —	5.88 ± 0.07
0.05	70.5 ± 3.51	69.6 ± 6.73	6.81 ± 0.28	6.70 ± 0.33
0.10	88.0[b] ± 7.83	90.4 ± 10.31	5.74[b] ± 0.25	5.58[c] ± 0.24
0.20	70.8 ± 8.35	76.3 ± 12.36	6.42 ± 0.33	6.60 ± 0.73
0.30	— —	73.8 ± 6.20	— —	6.40 ± 0.51
0.40	70.0 ± 8.81	— —	6.14 ± 0.36	— —
0.80	57.8 ± 5.11	— —	7.15 ± 0.59	— —

a = Standard deviation of the mean

b = Significant difference (t-test)

c = Highly significant difference (t-test)

TABLE 3

5-Week Rat Growth Data

Supplement to 90% Rice Diet	Experiment 3			
	MALES		FEMALES	
	Gain in gms	Feed/Gain	Gain in gms	Feed/Gain
1% Diammonium Citrate	55.9 ± 5.60[a]	7.27 ± 0.75[a]	60.1 ± 4.59[a]	6.75 ± 0.28[a]
1% Glycine	59.7 ± 6.77	7.31 ± 0.72	62.2 ± 5.01	6.46 ± 0.29
1% Cerelose	60.0 ± 7.52	7.19 ± 0.67	60.5 ± 4.57	6.67 ± 0.31

a = Standard deviation of the mean

TABLE 4

5-Week Rat Growth Data

% of L-Lysine. HCl Supplementation to 91% Rice Diet	MALES Gain in grams Experiment 4	Gain in grams Experiment 5	Feed/Gain Experiment 4	Feed/Gain Experiment 5
0.00	85.2 ± 6.74 [a]	82.6 ± 4.05 [a]	6.02 ± 0.264 [a]	5.82 ± 0.139 [a]
0.05	100.6 ± 8.64	106.2§ ± 3.79	5.30 ± 0.292	4.98§ ± 0.112
0.10	121.8§ ± 7.60	117.8§ ± 9.09	4.79§ ± 0.117	4.81§ ± 0.176
0.20	— —	92.8 ± 5.84	— —	4.93§ ± 0.145
	FEMALES			
0.00	93.0 ± 6.55	81.3 ± 3.11	5.40 ± 0.210	5.79 ± 0.111
0.05	112.8 ± 7.16*	114.0§ ± 4.93	4.80* ± 0.087	5.03§ ± 0.149
0.10	132.4§ ± 8.30	122.7§ ± 6.01	4.56§ ± 0.121	4.68§ ± 0.138
0.20	— —	115.0§ ± 7.35	— —	4.61§ ± 0.178

a = Standard deviation of the mean
* = Significant difference (t-test)
§ = Highly significant difference (t-test)

TABLE 5

Lysine Supplementation of Diets from Precooked Rice, Parboiled Rice and Raw Long-Grain Rice

Experiment 6, 5-Week Rat Growth Data

% of L-Lysine. HCl Supplementation to:	MALES Gain in gms	Feed/Gain	FEMALES Gain in gms	Feed/Gain
Precooked Rice Diet				
0.00	79.5 ± 5.66 [a]	6.02 ± 0.22 [a]	84.6 ± 8.83 [a]	5.81 ± 0.45 [a]
0.10	115.3 ± 13.55 [b]	4.84 ± 0.35 [b]	110.0 ± 12.56	4.69 ± 0.32
0.20	83.7 ± 8.72	5.55 ± 0.37	123.6 ± 10.69	4.32 ± 0.13
Parboiled Rice Diet				
0.00	68.3 ± 14.71	6.60 ± 0.25	77.7 ± 6.71	5.77 ± 0.23
0.10	102.3 ± 12.08 [b]	4.89 ± 0.23 [c]	117.0 ± 5.38 [c]	4.50 ± 0.08 [c]
0.20	83.4 ± 8.76	5.14 ± 0.35	114.2 ± 20.54	4.66 ± 0.39

TABLE 5—(Continued)

% of L-Lysine. HCl Supplementation to:	MALES Gain in gms	Feed/Gain	FEMALES Gain in gms	Feed/Gain
Raw Long-Grain Rice Diet				
0.00	39.2 ± 3.69	9.80 ± 0.59	43.0 ± 4.54	8.82 ± 0.61
0.10	54.2 ± 5.54 [b]	7.23 ± 0.41 [b]	67.5 ± 10.91	6.09 ± 0.84
0.20	42.2 ± 2.56	8.44 ± 0.75	51.5 ± 6.13	7.95 ± 1.09

a = Standard deviation of the mean
b = Significant difference (t-test)
c = Highly significant difference (t-test)

TABLE 6

Effect of Lysine Supplementation on Liver Fat and Liver Protein of Rats Fed Rice Diets

% L-Lysine. HCl Supplemented to Basal Diet	Liver Fat in % of Dry Weight Experiment 2* Males	Females	Experiment 5* Males	Females	Liver Protein in % of Dry Weight Experiment 2* Males	Females	Experiment 5* Males	Females	Liver Glycogen in mg./ % of Fresh Weight Experiment 5** Males	Females
0.00	22.04	24.56	31.98	40.83	47.36	44.62	36.24	35.42	3213	2851
0.05	19.01	—	—	—	46.44	—	—	—	—	—
0.10	—	17.87	23.44	36.71	—	53.72	46.19	39.04	3448	2806
0.20	—	—	18.51	32.51	—	—	55.54	42.93	2371	3141
0.30	14.38	16.70	—	—	59.74	56.78	—	—	—	—
Stock Diet	9.86	10.08	—	—	67.10	68.01	—	—	—	—

* Values determined on pooled livers from three animals per sex and per treatment
** Average values of determinations on ten animals per sex and per treatment

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AN INTERESTING CASE OF ACROMEGALY

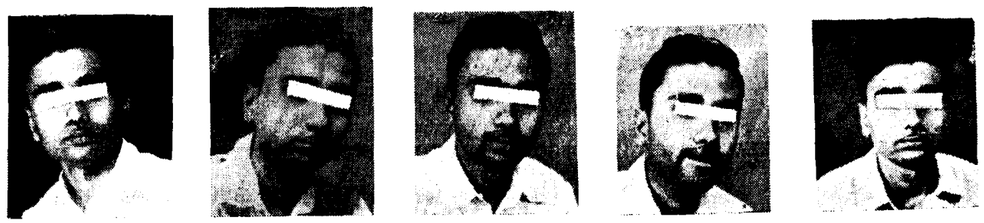
BY DR. R. K. PAL, D. SC. (Edin), M. SC., M. B. (Cal.) M. R. C. P., F. R. S. E.; F. N. I.
CALCUTTA

SRI U. K., aged about 22 consulted a compounder (not a qualified medical practitioner) for low blood pressure, slow pulse, subnormal body temperature and small genitalia, who prescribed for him 18 tablets of thyroid extract of ½ gr. each daily. After taking the full dose for one day he complained of nausea, anorexia, giddiness and muscular weakness on the second day but still he persisted on taking the full dose for another two days when he became extremely weak with sleeplessness and shakiness of hands and felt as if his jaw bones were 'coming down after getting loosened'. So having been much afraid he cut down the daily dose of thyroid extract to only 4 tablets a day when the acute symptoms gradually subsided and he continued to take this latter dose for two months. In the meanwhile he became very much emaciated, complained of feverishness, palpitation of heart, tremors in hands and his friends and relations noticed that his chin was becoming slightly prognathus with somewhat flattening of his naturally prominent zygoma and mandibular angles, when he consulted a qualified doctor who immediately stopped the medicine altogether and according to the doctor's report 'inspite of this and full rest his symptoms continued and not only his chin became more elongated but also his eye-brows and nose became more prominent and his fingers more elongated with clubbing, even after another month's complete rest after the stoppage of the thyroid extract.' (Pictures 1, 2, 3, & 4 show the change over of the normal square-cut face into an elongated one gradually with the progress of the condition).

At this stage as a specialist I was consulted when the pulse and respiratory rates were 90 and 21 respectively per minute, B. P. was 154/90, body temperature 98.4° F. and body weight 8 stones 2 lbs. only. Owing to the gradual changes in facial contour with prominence of most of the *acros* except the ears the case was diagnosed as one of acromegaly for which injections of testosterone propionate, 25 mg. on alternate days were prescribed. After one month injections were given twice a week for another month, when the following improvements were noticed (as will be evident from the picture. No. 5):— any further prominence of the supra-orbital ridges, nose, fingers and toes was not only arrested but also the chin and supra-orbital ridges appeared to be much less prominent although the zygoma remained as flattened and mandibular angles as less prominent as before. The gastrointestinal symptoms, headache, palpitation and tremor of hands disappeared and although he gained about 4 lbs. of weight he was still feeling far from strong. He has been since advised to continue the same injection at least once a week for another 3 months.

The points of interest in this case are:— No acromegalic changes were detected by the patient himself nor noticed by his friends and relations before the excessive dose of thyroid extract was taken by him, which seemed to have either initiated or rather accelerated the hitherto dormant acromegalic process due to secretion of an excessive quantity of growth-promoting hormone in an adult after the closure of the epiphyses of bones. So the question naturally arises how could an excessive dose of thyroid medication produce or accelerate acromegalic changes? Excessive thyroid feeding causes parathyroid hypertrophy (Wiggers, 1949) and hence is likely to cause changes in bones due to hypercalcæmia and negative cam balance and jaws are sometimes affected along with long bones, which were not present in this case. But in a large percentage of cases of acromegaly goitre develops with symptoms of hyperthyroidism (Youmans, 1957) yet there is no reference available as yet to say that the converse is also true and hyper-thyroidism or excessive doses of thyroid extract also can lead to acromegalic changes.

According to Riddle (1937) the growth-promoting, adrenocorticotrophic and lactogenic hormones are secreted by the acidophil cells of the adeno-hypophysis and the basophil cells of the same gland are responsible for the secretion of the gonadotrophins as also TSH or thyrotrophin, the secretion of the latter being regulated by the amount of thyroid hormone present in the blood. Again it is a known fact that gonadotrophins and somatotrophin are antagonistic to each other, so that the former while



(1) (2) (3) (4) (5)

(1) Before commencement of thyroid medication, (2) Three days after taking 18 tablets a day, (3) One month after commencement of thyroid medication, (4) Acromegalic face on first consultation, (5) After 2 months treatment with testicular hormone (improved)

accelerate the closure of the epiphyses of bones stopping further growth, the other can accelerate growth by prolonging the period of nonclosure of the epiphyses. So the initiation or stimulation of the acromegalic changes (in an adult) may be possible only if excessive thyroid hormone circulating in the blood not only depresses the TSH secretion but also the activity of the basophil cells as a whole, thereby depressing the secretion of the gonadotrophins too. However this is but a round about way of trying to explain things which is otherwise difficult to explain. I shall be glad if some of my expert colleagues of the medical profession can suggest any other better explanation.

According to Wiggers (1949) in acromegaly overgrowth of bone first affects the lower, then the upper jaw and malar bones and later supra-orbital ridges are enlarged; this was exactly the case with this patient. Further the very fact that it has been possible to arrest the acromegalic process in its initial stage by administration of the testicular hormone leaves no doubt that the case was one of acromegaly.

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The male climacteric and the postclimacteric state. Goldzieher, M. and Goldzieher, J. W., *Geriatrics*, U. S. A., 8: 1 – 10, January, 1953.

The male climacteric, defined as the phenomena attending the normal decrease in sexual function in the male, is characterized by a series of symptoms. Some of the most frequent are subjective nervousness, fatigue, insomnia, excitability, depression, nuchal aches, headaches, flushes, tachycardia and palpitation, and decreased memory and ability to concentrate. Other symptoms include vertigo, constipation, psychosis, paresthesias, and chills and pains of various types. Reduced lubido and potency appear in about 75% of cases; impotence in 50%. Factors other than hormonal influences may affect libido and potency; these include emotional, nervous, and metabolic influences. Insufficiency of testosterone secretion plays a major part in the phenomena of the male climacteric. Recognition of the male climacteric is impeded by the fact that most of the usual symptoms, even the loss of libido and potency, may also appear in neurotic or psychoneurotic patients. Laboratory methods in themselves cannot suffice to establish the presence of the male climacteric syndrome, and the clinical symptoms, being subjective, require confirming evidence. The only really reliable test is a therapeutic one: testosterone should relieve the symptoms with very little delay if the male climacteric is truly involved. Eighty patients were studied in this series, 28 of whom showed the customary clinical symptoms of the male climacteric. All showed some response, 24 being greatly improved, at least, or entirely relieved of their symptoms, at best, while the other 4 showed some-though not a full-response. There were 19 patients with symptoms resembling those of the male climacteric, and in this group were a number of psychoneurotic persons. Fourteen of them failed to respond to testosterone administration; the remaining five did show some improvement. Finally, there were 33 patients, aged 60 to 80 years, who did not show the characteristics of the male climacteric syndrome; such symptoms they did have could be associated with senescence rather than with the climacteric. Thirteen were treated with testosterone; 12 responded satisfactorily, one showed a partial response. In postclimacteric individuals evidence of hormonal deficiency can be shown regardless of the presence of subjective symptoms. Cases of hormonal deficiency are likely to be accompanied by a metabolic disorder. Although such patients may be asymptomatic, substitution therapy is recommended, unless there is a clear-cut contraindication. Testosterone provides both diagnosis and treatment of the male climacteric syndrome.

The Role of Rehabilitation in a Programme for Handicapped Children

Dr. HELEN M. WALLACE, M.D., Dr. JEROME S. TOBIS, M.D., Dr. ROBERT S. SIFFERT, M.D., Dr. MARGARET A. LOSTY, Dr. R. N. CAROLINE H. ELLEDGE, M.S.W.

Chronic disease is as important and rehabilitative programmes are as necessary in children as they are in adults. There is reason to fear that children have sometimes been kept in institutions too long. The development of departments of physical medicine and rehabilitation, the use of consultants in this field, the multidisciplined approach, the integration of programmes for children with those already existing for adults, and the facilities provided by recent federal legislation are significant steps toward the solution of this problem.

BY and large, rehabilitation of the chronically ill has been most closely identified with the care of the adult. Younger persons with chronic illness, although a frequent subject for special types of care, have not generally been included in programmes of rehabilitation. The advances made in the field of rehabilitation of the adult during recent years, partly as a result of the impetus of World War II experiences are equally applicable to the handicapped child. In the broadest sense, rehabilitation is the process by which the patient may attain the maximum physical, psychological, social, educational and vocational restoration in the community.

Recognition of the importance of rehabilitation in the care of patients with chronic illness has recently occurred through the extension of two important pieces of federal legislation—the Hill-Burton Act and the Vocational Rehabilitation Act. The anticipated end-result of the extension of these two federal legislative acts will be the opportunity to provide well constructed and well equipped physical resources and to provide the many persons with professional skills necessary for the management, care, and rehabilitation of the patient's physical, vocational social, educational and psychological needs. Particularly because of these two acts, with their potential influence on patient case, personnel engaged in crippled children's programmes have a unique opportunity to improve services for handicapped children. Perhaps the first question that comes to mind is: How can these newer concepts of rehabilitation be used and applied for the benefits of handicapped children? While details may vary from community to community, depending on present local resources of personnel and physical facilities, certain principles can probably be laid down.

EMPLOYMENT OF A CONSULTANT

Just as it is important to have expert medical consultants, such as the orthopedist, ophthalmologist, and otologist, for each of the specialties involved in a handicapped children's programme, it is important to employ a consultant in physical medicine and rehabilitation to outline and co-ordinate more modern concepts of rehabilitation. His role might include (1) evaluation of the physical medicine and rehabilitation services; (2) assistance in the development of physical medicine and rehabilitation services; (3) assistance in the development of standards for a department of physical medicine and rehabilitation in institutions; and (4) assistance in the training of personnel on the staffs of health departments, crippled children's agencies, and institutions in rehabilitation methods and techniques.

In New York City the handicapped children's programme has employed such a consultant for the past two years. He has played a large role in educating the handicapped children's team in rehabilitation methods. He has evaluated departments of physical medicine and rehabilitation at the hospitals surveyed, he has consulted on special problems arising in the programme in relation to physical medicine and rehabilitation, and he has participated in training programmes and in hospital conferences in interpreting concepts of rehabilitation as they relate to the practical care of handicapped children. As rehabilitation becomes a larger part of the programme his role will increase. In fact, specialists in physical medicine and rehabilitation have been regular members of the orthopedic advisory committee to help the programme in development and evaluation of these aspects of total care.

For example, in New York City, a recent survey of 24 hospitals caring for orthopedically handicapped children disclosed that 14 had a department of physical medicine and rehabilitation. Of the 14 hospitals with a department of physical medicine and rehabilitation 8 were found to be well organized and equipped. Seven hospitals had a separate rehabilitation in-patient service, and eight had a separate out-patient service. In nine hospitals, the physical medicine and rehabilitation department staff had periodic staff conferences. Twenty-two of the 24 hospitals had at least one physical therapist, but 10 had no occupational therapist, 10 had no speech therapist, 8 had no psychologist, 6 had no teacher and 21 had no recreation worker. In nine hospitals, medical rounds were made by a physiatrist; the visits varied in frequency from "daily" to "rarely". In 15 hospitals, no such rounds were made. It seems evident from this survey material that there is wide variation in the quality and quantity of physical medicine and rehabilitation services afforded orthopedically handicapped children. One of the major functions of the consulting physiatrist to the department of health has been to work with the hospitals to assist them with the further development of their services.

REHABILITATION TRAINING PROGRAMME

As in any new field, there is a certain body of knowledge developed and there are certain techniques used that may be helpful and that, therefore, should be disseminated to professional personnel working with patients. This is true for rehabilitation, and it applies equally well both to the staffs of crippled children's agencies and health departments. For example, from reports based on surveys of hospitals and convalescent homes in the metropolitan New York City area, children are being kept in institutions too long, and, in general, the programme for children has not been one of active rehabilitation. Perhaps with the newer knowledge of rehabilitation techniques and the teaching of activities of daily living, such as feeding, dressing, toilet care, bowel and bladder control training, wheel chair transfer, ambulation and gait training, these programmes can become much more dynamic and positive for patient care. This same principle should be equally applied to patients at home who are visited by public health nurses, with the specific purpose of assisting the patient to develop maximum self-sufficiency wherever he is. Such a rehabilitation training programme should in our opinion, be developed on a multi-disciplined team basis, for both the faculty and the trainees. One tangible plan might be that each health jurisdiction have atleast one person, possibly a physician or public health nurse, who had had special training in the field and who would be the resource staff person for improvement in patient care in the specific field.

The field of physical medicine and rehabilitation is a new medical specialty that concerns itself with the care of children with neuromuscular and musculo-skeletal disorders. This medical specialty, as does medicine generally in the care of the chronically ill, provides symptomatic treatment directed toward improving the function of the patient without influencing the underlying disease process. Thus it seeks to improve motor power whether the weakness results from a lower motor neuron disease, such as poliomyelitis, or an upper motor neuron disease, such as intracranial damage. In this field disease is looked upon as more than the specific pathology and the social and psychological effects of the disability upon the total function of the patient are considered. Because all these factors and more must be considered in the total care of the patient, there are many disciplines involved in the rehabilitation of the handicapped child. The professional staff, including such specialists as the pediatrician, orthopedist, psychiatrist, ophthalmologist, neurologist, physical therapist, occupational therapist, psychologist, speech therapist, vocational or educational counsellor, social worker and nurse, functions as a team under the direction of the physiatrist. There is one additional unnamed member of the team whose participation is essential—the patient himself. By the very nature of rehabilitation care, the patient must be an active participant. In medical care of acute conditions, the success of treatment does not depend essentially upon the co-operation of the patient. If a child has pneumonia, the outcome will depend upon the antibiotic prescribed and the nursing care given, not on whether the child is co-operative. But in rehabilitation, the success of treatment requires the active participation of the child because of two major factors. 1) Rehabilitation is primarily a learning or relearning process on the part of the patient—the learning of new and greater skills. 2) The necessary increase of motor power is dependent upon active exercises that the patient himself must perform.

MULTIDISCIPLINED APPROACH

Rehabilitation of many handicapped children and adults usually requires a battery of skills as well as a large number of medical specialists in addition to the patient himself and his family. To produce a truly effective programme that will result in the rehabilitation of the patient, these skilled persons must have an understanding of the contribution and the role of each of the other professional groups and must be able to work closely together in order to provide the services the patient needs when he needs them. The multidisciplined approach should result not in a replacement of one type of professional worker by another but rather in a supplementation of one by the other. This should apply to the stage of the initial evaluation of the patient, periodic reevaluations, continuous supervision, and counselling of the patient and his family.

The paramedical members of this team have many roles, each of which complements the other. The physical therapist improves the patient's motor power by exercise, teaches ambulation and applies physical modalities to relieve pain, reduce inflammation and increase range of motion. The occupational therapist improves the dexterity and power of the patient's upper extremities by giving him meaningful work. She also teaches the patient self-care techniques, such as feeding and dressing himself. The rehabilitation nurse complements the role of the occupational therapist by continuing the self-care activities on the ward. The educational or vocational counsellor evaluates the child's educational or vocational capacities and aptitudes and aids in the plans for his future training and study. The psychologist evaluates the child's intellectual and emotional profile and assists other therapists in creating the optimum conditions for the patient's learning of new techniques of rehabilitation. The speech therapist assists the child with speech and language disorders in order to help him attain his maximum potential. The social worker relates the family and home situation in the treatment planning. The group worker applies recreation programming as a physical and social therapeutic activity for the child. The teacher contributes to the over-all evaluation and educational goals of the child.

INTEGRATION WITH ADULT PROGRAMMES

Because of the country's aging population, chronic illness has become one of the major public health problems, and health departments are now planning and developing rehabilitation programmes and services for adults with chronic illness. By and large, however, chronic illness does not magically begin at the age of 21 years. Many principles learned in the rehabilitation of handicapped children are equally applicable to adults, and many services developed for one age group can be and should be utilized and modified for the rehabilitation of the other age group. Services for the rehabilitation handicapped children and adults must be co-ordinated and integrated. The artificial separation of the under 21 and over 21 age groups merely confuses community planning and results in duplication of efforts, funds and services. Failure to apply the knowledge gained in one age group to the other age group causes repetition of errors in the trial-and-error method. It is important, therefore, that there be close integration of chronic disease rehabilitation programmes and services for both children and adults.

CONSIDERATION OF LONG-TERM CARE

Rehabilitation of the handicapped child is frequently not accomplished on a short-term basis. As is true of any chronically ill patient, child or adult, long-term care is often essential. Frequently long-term care has meant for the child, at least, long-term institutional care. It should more properly imply the necessity of continuity of care, supervision and rehabilitation wherever the child is—in an in-patient service, in an out-patient department, at home, in school, in jobtraining, or at camp. This principle of continuity of long-term care must include provision of the multi-disciplined team in the various settings listed above as well as provision for the easy flow of patients, when they are ready, from one setting to another and provision for the rapid interchange of full information from one setting to another. Otherwise, it is possible and probable that some patients will become fixed in one setting, which may be appropriate at one time but inappropriate at another time. It is also true that lack of interchange of information usually results in the expenditure of efforts and funds for duplicating evaluation. This may be discouraging to the patient and his family as well as being wasteful of the community's resources.

EVALUATION OF RESULTS AND DEVELOPMENT OF PRIORITIES AND STANDARDS

The principle of evaluation of results is important for

for the individual patient, for the administrator of a crippled children's programme and for the director of any community service in future planning. Studies are necessary to develop even such basic data as the rehabilitation results in the individual patient for a given period of time, the most effective and successful techniques in certain types of disabilities, and the cost of rehabilitation per patient for each diagnostic group by individual institutions. Other such necessary studies include the duration of in-patient care and the reasons for prolonged in-patient stay long-term longitudinal studies of the handicapped, comparing results in those who have had the opportunity for comprehensive rehabilitation care with those who have not; the results of prolonged in-patient care compared with an alternate community method, such as an organized home care programme; the reasons for vocational success and failure among the handicapped in order to provide leads for further development of community services; and retrospective studies of adults who have been handicapped by conditions arising in infancy and childhood and who are now receiving public assistance. Such studies are essential if medical advances are to be made in improvement of methods and if fiscal authorities and the public are to be convinced of the value of rehabilitation programme.

In the early stages of any rehabilitation programme, priorities must be established, since there are usually insufficient personnel and funds to serve all patients. The development of a priority system may be carried out on the basis of diagnosis or degree of diability. A priority list developed for one community will not necessarily be applicable in all phases to another community. The community's existing resources, available personnel and the public and professional interests are key factors in deciding any priority system. Also, carefully worked out standards are essential to serve as guides to participating institutions and agencies in their planning and developing good services. They will also be of help to accrediting groups in approving adequate acceptable services for a payment programme.

DEVELOPMENT OF COMMUNITY SERVICES AND RESOURCES

In the development of community services and resources, a fairly complete knowledge of existing services and resources and of current gaps or lacks in patient care is necessary. This quantitive and qualitative knowledge should include such details as the hospitals and convalescent homes; the resources for the homebound group of children; the services provided for the children at school, especially the high priority groups in special classes or schools; the vocational resources, including sheltered workshops; the recreational programmes; the transportation facilities; the long-term residential or custodial services; and the foster home and child welfare services. It is likely that in most communities at the present time 'pieces' of services are now available and that undoubtedly there are many good or potentially good resources that can be further developed and improved with guidance, financial support, consultation and patience.

Two examples will be used to illustrate this principle: the hospital resources and the convalescent resources. Once a knowledge of the hospital resources has been acquired, it is likely that it will be found that a minority of the hospitals have active and well developed rehabilitation programmes. The principles that might apply in such a situation are as follows:— 1) General and not specialty hospitals would participate in the programme in the beginning. 2) The initial selection would be of those hospitals that serve a teaching function in connection with medical and other professional schools, from the viewpoints of patient care, training of personnel, and research. 3) Diagnostic services on the one hand would be integrated with treatment and rehabilitation services on the other hand; this step might mean either the affiliation and joint staffing of detached diagnostic clinic services with hospitals or the physical relocation of detached diagnostic clinic services in hospitals with joint staffing. 4) There would be the development of a generalised rehabilitation programme within the hospital. This programme ideally would not be completely separate one but would be one that would be closely integrated with other clinical departments so that rehabilitation techniques could be applied early; such a principle would apply to both in-patient and out-patient care. 5) There would be the development of certain specialized services in the hospital; for example, services for patients with hearing impairment, cleft palate, convulsive disorder, and mental retardation as well as for the traditionally accepted groups of patients, such as those with orthopedic, cardiac, and visual defects. 6) Assistance and guidance would be given to the hospitals in the recruitment of personnel, the training of personnel, and the development of programme policies. 7) There

would be continuity of care including supervision and follow up, between the hospital in-patient service and out-patient service and the home through the development of broad home care programmes or the more limited public health nursing referral and follow up.

The second example selected—that of convalescent care in the traditional convalescent homes—is more controversial and therefore more interesting. Once a working knowledge of the community's convalescent homes has been acquired, several principles might be raised such as: Is convalescent care as it has been traditionally given in the past necessary at the present time? What kinds of children are presently in convalescent homes, what are the reasons that they are there and how many can be discharged home? Is a particular convalescent home fulfilling as essential community need at this time? Can a dynamic and active rehabilitation programme be provided in a convalescent home currently located in a semirural setting, with its difficulties of recruitment and retaining of well-trained personnel of close medical supervision, and of parent visiting? What are the alternatives that a community might provide that might mean better and more prompt rehabilitation care, better psychological care, and possibly even lower cost to the community? What are the current facts about the present capacity, census and length of stay in convalescent homes? The first essential principle that should apply to this somewhat controversial subject, in an effort to answer the foregoing questions, is that of fact-finding. Other principles, which undoubtedly fall into the general area of better co-ordinated and broader community planning of rehabilitation services, will stem from the original one of fact-finding.

RELATIONSHIP TO NEWER FEDERAL LEGISLATION

Two types of federal legislation were extended recently that are of great significance to programmes for handicapped children: 1) the Hill-Burton Act, which will make available new funds for construction and equipping of rehabilitation centers, diagnostic centres, chronic disease services, and nursing homes, in addition to the funds presently appropriated for general hospital construction and 2) the Vocational Rehabilitation Act, which will make funds available for special projects, training of personnel, and research. It would seem essential that administrators and clinicians concerned with the programme for handicapped children work closely with the state and local agencies responsible for the carrying out of new federal legislation.

PURCHASE CARE

Rehabilitation of patients is costly; for example, the per diem cost of in-patient care in a large rehabilitation service in New York city is $. 25 for a child and $. 30 for an adult. Even though there is a considerable amount of funds available for the rehabilitation of patients, from both official and voluntary sources, funds will always be wanting. These two sources of funds, official and voluntary, should not be looked upon as competitors of each other, both are essential. This principle can work in a variety of ways, such by grants to agencies or services, complete payment of salaries, joint payment of salaries, purchase of equipment, research projects and experimentation and training of personnel. The important principle is that the two major sources of funds work together to develop rehabilitation services as rapidly as possible with well-trained personnel wherever they are needed. The second principle is that of the purchase of care on a cost basis. If one accepts the fact that rehabilitation is economically sound as well as socially desirable even though it is costly then someone must be prepared to pay the bill. Logical sources, in addition to the patient and his family, are the categorical voluntary agencies, and governmental agencies, including the crippled children's programme. It is a fallacy that by paying less than cost, if cost is calculated on sound formula, one is saving money. If the cost of care is not met in some way, then services are automatically decreased by reduction of personnel. This means that some essential services will not be provided and that rehabilitation may not be as effective or as complete. In any event, by not meeting the costs of rehabilitation it is the patient and the community who pay the price, and the principle of purchase of care on a cost basis is a vital one.

SUMMARY

Some principles in the possible role of rehabilitation in services for handicapped children may be based on experience in a large crippled children's programme in an urban area. These principles include the employment of a consultant in the field of physical medicine and rehabilitation as a staff member of the crippled children's agency the need for the establishment of a training programme in rehabilitation to disseminate the newer knowledge developed in the field to personnel working directly with patients, the use of the multi-disciplined team approach to meet the broad needs of the patients, and the need to integrate rehabilitation services for children with those for adults. It is necessary to recognise the need for long-term follow-up and supervision of patients and for flexibility of services and policies. Evaluation of results of services to the individual patient is important, and methods for such evaluation must be devised. Additional principles are those of development of knowledge regarding present resources and currently unmet needs of patient care and purchase of care on a cost basis. Newer extensions of federal legislation, such as the Hill-Burton Act and the Vocational Rehabilitation Act provide excellent opportunities to develop, expand and improve services for patients with chronic illness, both children and adults.

(Continued on page 23)

Theses of Reports Presented at the First U.S.S.R. Conference of Neurosurgeons in Leningrad

I

New Conceptions Regarding the Mechanisms of Nervous Regulation of Blood Circulation in the Brain

By B. A. DOLGO-SABUROV
LENINGRAD

CREATIVE development of the neuron theory, as a basis of modern conceptions of the structure and function of the nervous system requires that investigations should not be confined merely to examining the biological characteristics of the neurons or the character of their interrelationship, as well as, their relations with the innervated substrate (in the area of effectors and receptors). It is a well known fact, that it is necessary to have maximal blood supply, as a required condition for the activity of the nervous cell with its intensive metabolic process. A neuron cannot live outside its environment, that is, without the neuroglia and capillaries.

The conception of physiology (Academician K. M. Bykov's school) that during reflex action there are always reflex changes in the vascular beds, which provide blood circulation in the neurons, had to be morphologically founded. The evidence acquired from a study of the most intimate topographical relations of the neurons with the blood vessels, which take place in the brain parenchyma (according to B. N. Klosovsky, for instance), is not sufficient for explanation of these processes.

Our investigations show that ramifications of axons of afferent conducting systems in the brain and spinal cord *in man* and in certain animals terminates in *synapses* not only on the nerve cells and their dendrites (the so-called axosomatic and axodendritic), as acknowledged a long time ago, but, likewise, on the capillaries surrounding them.

These axovasal synapses, discovered by us, apparently provide conduction of nerve-impulses to the vascular beds of the nerve centres, causing reflex changes in their blood supply. These structures are thus indispensible components of interneuronic and neurovascular relationships and, probably, serve in regulation of circulation in the capillary beds of brain parenchyma, providing its nutrition.

Afferent and efferent conducting systems of the brain form extensive synaptic apparatus by ramification of their fibers. This apparatus belongs not merely to neurons, but, likewise, to capillaries which surround them. Thus, since synaptic structures are common both to neurons and capillaries, the simultaneous transmission of the nerve-impulses to the neurons and to the apparatus, which supplies them, becomes clear. The rapid processes which take place in the brain are possible only in these circumstances, since they require the most favourable conditions for blood supply of the brain tissue.

(Continued from page 22)

(Courtesy: J. of A. M. A., Sep. 1956.)

New conceptions of neurocirculatory relations in the brain clarify the understanding of the mechanisms of blood circulation in the brain not only in a healthy organism, but also provide prospects for investigation of these processes in various pathological conditions.

II

Functional Morphology of the Pia Mater of the Brain and its Participation in Certain Pathological Processes

By M. A. BARON
MOSCOW

Two interrelated systems exist in the pia mater of cerebral hemispheres of the brain: a system of perivascular channels and a system of subarachnoid cells. These systems are absolutely different in their structure, function and significance in pathology.

A) THE SYSTEM OF PERIVASCULAR CHANNELS

The perivascular channels were discovered by scientists as far back as in the 19th century. Their existence was considered to be doubtful and they were almost forgotten. However, at the present time these channels were revealed by modern macro-microscopical methods of investigation and were studied in experiments in vivo.

These channels have their own wall and present a well formed bed, where the main streams of the cerebrospinal fluid are flowing. The cerebrospinal fluid enters the subarachnoid cells which surround the channels through the small openings in the walls of the channels.

If large spores of lycopodium are introduced into the cisterna magna of a live dog and the exposed brain is simultaneously observed, the movement of spores within the channels may be seen with the aid of stereoscopical microscope. If a mixture of particles of different size is introduced into cisterna magna (such as lycopodium spores, yeast or suspension of carmine) fractionation of these particles takes place in the channels. The spores of lycopodium remain in the lumen of the channels, while smaller particles of carmine and a part of yeast cells escape into the subarachnoid cells. In non-physiological conditions, particularly when pressure of the cerebrospinal fluid is increased, communications between the channels and the subarachnoid cells become wider. In such case, the large spores of lycopodium, likewise, escape into the subarachnoid cells.

One may judge the character of the movement of cerebrospinal fluid in the channels and the subarachnoid cells (i. e. in different parts of subarachnoid space) by the movement of particles introduced into the cerebrospinal fluid. The cerebrospinal fluid makes continuous oscillating movements which are synchronous with respiration and pulse. These oscillations are absent in the subarachnoid cells. As soon as the particles escape from the channels into the subarachnoid cells their oscillations stop. The progressive movement of cerebrospinal fluid was observed in experiments. It moves much faster in the channels than in the subarachnoid cells. It has been established, that cerebrospinal fluid in the channels does not always flow in one direction. Depending on conditions of circulation of cerebrospinal fluid in the pia mater the direction of flow in the channels may become reversed in adjacent periods of time. Permeability of different channels for cerebrospinal fluid is always changing.

It was revealed by examination of pathological necropsy specimens that the perivascular channels are the main routes of metastasis of certain brain tumours. It may be clearly seen on specimens of total preparations of completely isolated pia mater (which allows 3-dimensional microscopy) that permeation of tumour cells or their groups from the channels into the subarachnoid cells is only secondary.

Air introduced into the subarachnoid space in encephalography spreads and fills only the system of perivascular channels. As a rule, it does not get into the subarachnoid cells even if the pressure is greatly increased. Thus, it may be concluded that the corresponding craniograms represent the condition not of the whole subarachnoid space, but only of the system of perivascular channels.

Besides being the main route by which the cerebrospinal fluid flows, the channels have another very important function which is connected with drainage of the cerebrospinal fluid. A new and probably the fundamental route of drainage of the cerebrospinal fluid was experimentally established in 1948—1953 by I. A. Alov at the laboratory where the author of this article works. It drains through the arachnoid mater of the whole brain into the subdural space. It was, likewise, demonstrated that the "subdural fluid," which appears in this way, is absorbed by the vascular network of the dura mater. At the present time the same was proved in man. This data is supported by the accumulation of hæmoglobin in the histiocytes of the dura mater in cases of subarachnoid hæmorrhage, which is not complicated by hæmorrhage into the subdural space.

It was, likewise, revealed that the drainage of the cerebrospinal fluid takes place only where the perivascular channels are adjacent. There are no subarachnoid cells in the biological membrane, which separates the lumen of the channel from the subdural space and therefore its permeability is different. Thus, it is the cerebrospinal fluid of the lumen of the channels that is drained into the subdural space, not the cerebrospinal fluid of the subarachnoid cells.

The following experiments were carried out :—weak concentrations of vital dyes were introduced suboccipitally (about 0.5—2 mg. per kilogram of body weight).

Then a piece of chromatographic paper, moistened by warm physiological saline, was carefully applied to the arachnoid mater. In 15—30 seconds clear contours of the perivascular channels were printed on the paper. The prints show that the dye reaches the subdural space only from the channels. Adjacent areas of the same piece of paper, which are located above the subarachnoid cells, remain undyed. If this paper is replaced at short intervals one may obtain a series of prints which characterize the intensity and time of the escape of the dye as well as of the drainage of the cerebrospinal fluid.

Experiments of introduction of various dyes of

different dispersity and charge into the cerebrospinal fluid gave the opportunity to study the permeability of the above-mentioned biological membrane. It was established that this permeability is very high for all dyes. Such almost non-diffusible dyes of low dispersity, as congo red (acid), for instance, pass through the membrane together with the cerebrospinal fluid. The escape of proteins from the channels into the subdural space deserves special attention. This, likewise, concerns hæmoglobin which is easily differentiated on the prints. The most intensive permeability is shown by crystalloid dyes which are highly diffusible. But they, likewise, escape into subdural space not everywhere, but only within the limits of the contours of the channels. Only a narrow band adjacent to the channels is slightly stained. If a mixture of crystalloid dye and colloid dye is introduced into the cerebrospinal fluid, both dyes escape from the channels into the subdural space. But, as shown by the prints, the area of permeation is slightly greater in the case of crystalloid dye than that of colloid dye. Suspensions do not permeate from the channels into subdural space at all. If a mixture of Congo red and Berlin blue is introduced fractionation takes place, i. e. the picture on the print is dyed by Congo red, while the particles of Berlin blue remain in the lumen of the channel.

Only highly dispersible substances are able to permeate from the channels into the subdural space. Therefore, it may be supposed that removal of the microscopically visible products of brain metabolism from the cerebrospinal fluid, such as detritus and large molecular proteins is possible only after they are broken down, i. e. "digested" in the subarachnoid cells. After being changed into another condition these substances are able to pass through the barrier located on their way.

The appearance of droplets ("dew") of the cerebrospinal fluid on the surface of the arachnoid has been traced. This phenomenon, which is well known to neurosurgeons, takes place during convulsions or at the beginning of prolabation of the brain during surgical interference. It was established by direct observation through the microscope that these droplets appear only in those places, where the perivascular channels are adjacent to the arachnoid, i. e. where cerebrospinal fluid escapes from the channels into the subdural space in physiological conditions.

In pronounced hypertension with prolonged course, when due to changed permeability of the arachnoid it is unable to provide drainage of the surplus cerebrospinal fluid, numerous microscopical openings appear in the arachnoid above the channels, by which communication is established between the perivascular channels and the subdural space. These openings are formed not by rupture, but as a result of gradual reorganization of the arachnoid. The natural compensatory route of the cerebrospinal fluid which appears in this way to a certain extent resembles the artificial routes which are created by neurosurgeons in blocking the passage of cerebrospinal fluid.

Neglected fibrosis of the pia mater results in obliteration of subarachnoid space in those places where the subarachnoid cells are located. They are completely replaced by compact fibrous tissue, and the movement of cerebrospinal fluid in these areas is greatly disturbed. However, the perivascular channels remain unchanged for a long time. Due to that, the circulation of the cerebrospinal fluid in the channels, as well as, its drainage into subdural space continues, even in pronounced fibrosis of the pia mater.

B) THE SYSTEM OF SUBARACHNOID CELLS

Subarachnoid cells which have a honey-comb appearance, are formed by very thin membranes and include 2 components: arachnoidendothelial protoplasm, not subdivided into cells and a carcass of a membrane formed by argyrophilic and collagen fibres, which is included in this protoplasm. The fibres cross at a definite angle and thus form a so-called lattice-work, which is adapted to physiological variations of the volume of cells (A. M. Zubin). The openings in the membranes, which were described a long time ago allow the flow of the cerebrospinal fluid from one subarachnoid cell to another.

Experiments on animals and examination of the human brain showed that these membranes are the most reactive part of the pia mater, that their structure is extremely dynamic and that they are protective-trophic in function.

It has been established that new openings in the membranes may appear, they may disappear, become wider, or decrease in diameter. In this way the structure of the pia mater is adapted to the changeable conditions of the circulation of the cerebrospinal fluid.

In normal conditions the subarachnoid membranes

of identical areas of the pia mater may have different structure in people of the same age: the openings may be absent entirely (true symplasts), the membrane may have a small number of minute openings (syncytia), or these openings may be enormous in size and be subdivided only by a thin band of protoplasm.

In pathological conditions the widening of communications between the cells, i. e. the increase of the number and diameter of the openings is especially pronounced. Such condition is found in the case of certain brain tumours and, as a rule, near the foci of fibrosis. This widening of communications facilitates the movement of cerebrospinal fluid and is definitely of compensatory nature.

The foreign bodies which are experimentally introduced into cerebrospinal fluid, as well as, various cells suspended in it (such as erythrocytes, macrophages etc.) pass through the openings of the membrane. The ability of cells of medulloblastoma and of certain other tumours to pass through the openings of the membrane should be especially mentioned.

Arachnoidendothelium of the membranes is a source of formation of 3 different cellular elements:

a) Cells of arachnoidendothelium with from 1 to 15 nuclei, become isolated from arachnoidendothelial symplast or syncytium. They become rounded, drop off and are carried away by the cerebrospinal fluid. Identity of the cells liberated by the pia mater with the same cells of arachnoidendothelium which are found in cytological examination of the cerebrospinal fluid was definitely established.

b) A qualitatively new form of cells—macrophages are formed from arachnoidendothelium of the membrane. These cells play the most important role in protective-trophic function of the membrane. Macrophages are formed out of uninucleate, as well as, multinucleate areas of arachnoidendothelium. The appearance of macrophages under pathological conditions differs in several ways from their appearance in normal conditions.

c) Argyrophilic and collagen fibers appear in symplasts and syncytia of arachnoidendothelium. During a certain stage of this process symplasts and syncytium disintegrate into separate cells which are transformed into fibroplasts. This is the way of fibre formation in the cases of so-called simple fibrosis. In this condition the cells of the infiltrate are absent in the pia mater and fibrosis develops without the previous inflammatory reaction (fibrosis of the pia mater in arachnoidendotheliomas).

The cerebrospinal fluid, which slowly circulates in the subarachnoid cells flows around the enormous surface of the subarachnoidal membranes. Complex metabolic processes take place between the cerebrospinal fluid and the arachnoidendothelial protoplasm. These processes are manifested morphologically by a well developed chondriome with the abundance of various inclusions.

The arachnoidendothelium of the membranes, of the vascular beds and the arachnoidendothelium lining the inner surface of the arachnoid mater (interior covering layer) are the only structures which have the property of accumulating and treating colloidal substances present in the cerebrospinal fluid, particularly of hæmoglobin. As to arachnoidendothelium, which is lining the outer surface of the arachnoid (exterior layer)—it has no ability to accumulation whatsoever.

Destruction of the arachnoidendothelium of the membranes and its disappearance is observed in the final stage of the simple fibrosis. Its pathologically proliferated and collagenized fibrous carcass is no more included in the protoplasm of syncytia and symplasts, as it is in normal condition. The fibers are exposed and are in direct contact with the cerebrospinal fluid. In such cases of simple fibrosis the destruction of arachnoidendothelium of the membranes greatly decreases the trophic functions of pia mater.

Consequently, it may be concluded that the basic function of the cerebrospinal channels is the role they play as the main routes along which the cerebrospinal fluid circulates. Likewise, these channels take part in drainage of the cerebrospinal fluid through the arachnoid mater into the subarachnoid space. Protective—trophic function is the property of the subarachnoid cells, or more precisely of the subarachnoid membranes which form them. This function is manifested in different processes, which take place between the cerebrospinal fluid and the arachnoidendothelial protoplasm.

HEART SURGERY

A new attack on our Number 1 Killer

BY LEONARD ENGEL

A handful of youthful doctors—working against considerable opposition—have pioneered a series of breathlessly dramatic operations . . . which already are saving thousands of lives.

LIKE the Army, hospital operating rooms have rank: orderlies and student nurses at the bottom; then graduate nurses; then interns, the wet-behind-the-ears second lieutenants of the medical world; next, surgical residents and anesthesiologists, who are the first lieutenants and captains; finally, the battalion commander, the surgeon. As in the Army, however—where the major of air-borne troops outshines the mere major of infantry—there are surgeons and surgeons. In 1957 the Prince of the Operating Room, the man the big-league hospital can't afford to be without, is the heart surgeon.

Heart surgeons owe their new star-touched status to a breath-quickening fact. In the face of a decade, surgery of the human heart has graduated from the class of the unusual and unlikely, into an established practice. Operations around, on, and within the heart are being done at a rate of many thousands a year. At half-a-dozen institutions, "open-heart" surgery—with a heart-lung machine keeping the patient alive, while the surgeon works inside the heart—is being done several times a week. At still others, the heart is stopped altogether, then started again after the surgeon has finished.

The cardiac surgeon has strategems and techniques for overcoming about three-quarters of inborn heart defects and the commonest form of rheumatic heart disease. Now it seems likely that surgical remedies will even be found (indeed, may already have been found) for some cases of coronary disease. The latter—the underlying cause of coronary thrombosis and other diseases of the heart artery—is the most wide-spread of diseases of the heart, responsible currently for upwards of 400,000 deaths a year in the United States alone. All at once, heart surgery is not only remarkable; it has become a part of the everyday battle for life.

Bringing heart surgery to this point took a lot of doing. There were immense problems to be solved. There were tragic failures and brilliant successes. Above all, there were desperately sick patients pleading for help at any cost, and surgeons with the courage to plunge ahead–frequently over the open opposition of colleagues.

Just how far have the heart surgeons come, up to now? What can we rightly hope for in their strategic attack on the greatest killer in the Western world?

BAD HEARTS FROM BIRTH

Heart surgery began in a substantial way less than twenty years ago. In 1883, Theodor Billroth of Germany, one of the outstanding figures of nineteenth-century surgery, threatened professional excommunication to any surgeon rash enough to suture a heart wound. Thirteen years later, the British physician Stephen Paget predicted that the heart would never be operated on safely. Billroth's and Paget's warnings put the heart out of bounds to surgeons for nearly fifty years, except for an occasional operation (done despite Billroth) to sew up a stab wound. By the mid-1930s, though, modern methods of blood transfusion and anesthesia and other new aids to surgery were making surgeons bolder. Moreover, surgery was clearly the only possible answer to one form of heart disease.

This was the congenital kind. Approximately one child in every 125 is born with one or more defects in the architecture of the heart or the great vessels associated with it—the pulmonary artery (which carries blood from the heart to the lungs) and the aorta (which carries it from the heart to the body). Without aid, half of these babies do not make it to the first birthday, and few reach their teens.

Drugs cannot correct inborn errors in the architecture of the heart; but surgery might. The challenge of congenital heart disease was taken up at the logical place by the logical man in the logical way. The place was Children's Hospital, Boston, one of the complex of hospitals around Harvard's old but still bold-and-

pioneering medical school. The man was Dr. Robert E. Gross, pupil of Dr. William Ladd, trail-breaker in infant and child surgery.

Dr. Gross decided to begin with an anomaly of the great vessels rather than with the more difficult problem of a defect in the heart itself. Specifically, he chose "patent ductus arteriosus," an abnormal opening between the aorta and pulmonary artery. A patent ductus leads to severe damage to the blood vessels of the lungs and predisposes to dangerous infections of the heart.

Dr. Gross performed the first operation for closing an open ductus (and thereby giving these youngsters a normal circulation for the first time in their lives) in 1938. Today, the operation is part of the surgical repertory in scores of hospitals. It has been performed upon thousands of children and some hundreds of adult survivors from the pre-ductus-surgery era. *Under favorable circumstances, the mortality rate is well under the rate for major abdominal surgery.*

The striking success of the Children's Hospital surgeon stimulated, over the next ten years, the development of procedures for dealing with other defects. These procedures, however, still involved congenital defects of the great vessels or operations on the great vessels. For instance, the widely-known "blue baby" operation devised by Drs. Alfred Blalock and Helen B. Taussig of Johns Hopkins was designed to relieve the effects of a set of heart defects called the tetralogy of Fallot; but the operation is performed on arteries outside the heart. Cardiac surgeons were not quite ready to operate on the heart itself or to move on to heart diseases other than congenital heart disease.

Both steps were taken simultaneously in 1948. The new kind of heart disease taken on by the surgeons was mitral stenosis, a form of rheumatic heart disease. Mitral stenosis is the narrowing of the mitral valve, which controls the flow of blood through the left side of the heart—the high-pressure side that pumps blood to all the body (except the lungs) through the aorta. The cause of mitral stenosis is rheumatic inflammation, which welds the valve leaflets into a nearly immovable stone-like mass instead of permitting them to open and close with the flow of blood. The result is a crippling

diminution of the flow of blood, overloading of the heart, and premature death.

Early in 1948, Dr. Horace G. Smithy, Jr., of South Carolina (who was to die of rheumatic heart disease himself a few months later) successfully reopened a patient's stenosed mitral valve. In June of the same year, similar operations were performed by two other surgeons, Dr. Charles P. Bailey of Hahnemann Medical College, Philadelphia, and Dr. Dwight Harken of Harvard.

The three surgeons employed somewhat different techniques. Dr. Bailey's is the one in widest use now. To reopen the mitral valve, a small incision is made in the tip of the left auricle, the receiving chamber for blood on the left side of the heart. The surgeon inserts his finger—armed with a special knife—through the incision and into the valve inside the heart. The knife is then manipulated to open the valve.

Mitral commissurotomy (as the Bailey operation is known) sounds hair-raising. But it has been performed more often than all other heart operations together and, in expert hands, is effective and quite safe. In grade II and III stenotics (patients going downhill, but not yet wholly incapacitated by their disease), the mortality rate is about that of other major surgery (1 to 2 per cent); and *three-quarters are restored to normal or near-normal living*. In fact, in less than a decade, several score of young women—including Dr. Bailey's first successful patient—have borne babies after recovering from this operation.

OPENING UP A HEART

Within a few years of the Smithy-Bailey-Harken penetration of the heart, operations were developed for remedying a number of other defects—inborn and acquired—within the heart, or requiring an approach through it. Drs. Bailey and Gross devised separate procedures for closing atrial defects (holes in the partition between the right and left auricles, a congenital defect). Dr. Bailey worked out a method of relieving aortic-valve stenosis (a consequence, usually, of rheumatic heart-disease). Sir Russell Brock, the noted English cardiac surgeon, found a way to open stenotic pulmonary-artery valves (an inborn anomaly). There were other new cardiac surgical procedures as well.

These operations were remarkably ingenious and helped a good number of patients. But they were considerably less than ideal, for they were "closed" procedures; that is, they were carried out by sense of touch, either from outside the heart or through an incision just large enough to admit a slender instrument or one or more fingers. The surgeon could not see what he was doing or really be certain of effecting a good repair. For that reason, the results of some of these operations have been quite uneven. As we shall see, moreover, there are heart defects and injuries that *ought* to be remediable by surgery, but which cannot be dealt with by any conceivable closed operation.

What was needed was a method of draining and opening the heart and operating on it under direct vision, as any other organ in the body. Several methods of doing this now exist. But their achievement cost a long and frequently bitter struggle.

The problem, of course, is that the function of the heart may not be interrupted for more than a very few moments without disastrous consequences. Extensive investigations have shown that many tissues can survive for quite considerable periods without a continuous supply of freshly oxygenated blood. Provided it is doing no work (*i. e.*, pumping no blood), even heart muscle can probably go bloodless for fifteen or twenty minutes without harm. The brain, however, is a different matter; under ordinary conditions, the safe limit for brain tissue is under four minutes.

Curiously, among possible solutions of the problem, the last starter was the first into the operating room. This was hypothermia, the artificial lowering of body temperature. Hypothermia—which is generally carried out by placing the patient in a rubber blanket through which cold water is circulated—originated as a means of combating shock during major operations. It also lowers the demand of tissues for oxygen, so lengthens the period they may survive without oxygenated blood.

At a body temperature of 84 degrees Fahrenheit—not quite 15 degrees below normal—the blood flow can be stopped safely for eight minutes. In eight minutes, a fast operator can open the heart, make a simple repair inside, and close up and start the flow of flood again. In the hands of two surgeons in particular—Dr. F. John Lewis, until recently of Minnesoto, now at Northwestern, and Dr. Henry Swan of the University of Colorado—hypothermia has been an effective means of repairing atrial defects.

But hypothermia was not the right solution to the open-heart surgery problem. For one thing, eight minutes is not enough to deal with surprises—defects more complex than diagnostic reports had led the surgeon to expect. For another, the main pumping chambers of the heart, the ventricles cannot be opened without danger under hypothermia; thus defects in the ventricles were still beyond repair.

The problem has finally been solved by the development of heart-lung machines—astonishing devices that pump blood and also breathe for the patient. With their aid, surgeons, can operate in literally any part of the heart, and for as long as an hour.

In "The Automatic Heart" (in *Harper's* for June 1952) I gave an account of early work on heart-lung machines. I told why it had to be a heart-*lung* machine and not just a heart machine (because of the heart's anatomy, a substitute for the heart alone would be in the surgeon's way); and how, though suitable pumps were not hard to come by, duplicating the function of the lungs was difficult. I wrote especially of Dr. J. H. Gibbon of Jefferson Medical College, Philadelphia, who had virtually single-handedly opened the field of heart-lung machine research in 1935 and who, by 1952, had a device that seemed nearly ready for the operating room.

Dr. Gibbon first employed his machine for a human patient in the spring of 1953. That patient died, and so did several others before the first success. The historic successful patient was a young woman with a huge opening between the auricles (atrial defect). On May 16, as the machine whirred away, keeping her alive, Dr. Gibbon opened her heart and with deliberation and care stitched the defect shut.

Dr. Gibbon's hard luck with his other patients probably had little to do with the intrinsic qualities of his machine. Gibbon pump-oxygenators are being used with success at the Mayo Clinic today. The trouble was, most likely, the condition of his patients (all were near death before entering the operating room) and the state of the art of managing cardiac-surgery patients in 1953. The difficulties of the man who had labored so hard and so long nevertheless plunged heart-lung machine researchers into gloom. As 1954 began, nearly all despaired of ever making an effective stand-in for the heart and lungs.

But rescue was to come, with surprising speed and in astonishing form. That spring, four University of Minnesota surgeons—Drs. C. Walton Lillehei, Richard L. Varco, Morley Cohen, and Herbert Warden—went into the operating room with a bold expedient tested for months in the animal laboratory—hooking up the blood vessels of the patient to the blood vessels of a "donor" who would breathe for the patient during the operation.

The technique is called cross-circulation. It was used some forty-five times in the next dozen months. With it, the Minnesota group carried out surgical repairs, for the first time in medical history, inside the ventricles. With it, the group demonstrated also that even the sick heart can be by-passed with comparative safety.

The effect was to re-stimulate interest in heart-lung apparatus—not least at Minnesota itself, where three additional methods of by-pass were soon worked out. One was an extraordinarily simple heart-lung machine devised by Dr. Lillehei and a young Minnesota resident, Dr. Richard B. De Wall. It consists of little more than a pair of pumps (one to draw blood from the patient and the other to return it) and a few feet of plastic tubing. Oxygen is bubbled into the blood in one section of tubing; excess oxygen is removed, with the aid of an anti-foam chemical, in another section.

The Lillehei—De Wall heart-lung machine was introduced in June 1955, and has performed well in some three hundred open-heart operations at Minnesota and elsewhere to date. With this device, Drs. Lillehei, Varco, and others have carried out a lengthening list of hitherto impossible heart repairs. For example, they have repaired ventricular flaws and corrected the main defects in "blue baby" disease (rather than merely palliating them, as in the earlier Blalock operation). There have been deaths, to be sure, but few, if any, that involved the machine.

In fact, heart-lung machines as well as open-heart operations are becoming positively commonplace. In a recent run-through of medical journals, I counted seven distinct *types* of heart-lung machines—beside the Gibbon and Minnesota devices—that have been used with at least some success in recent months. It would seem that there are many ways to skin a cat, especially after a couple of fellows have showed how.

THE SURGEON'S FAITH

The most fascinating character in the drama of heart surgery is, of course, the man who does it. Cardiac

surgery is still a small enough field so that I can say I have met and visited and talked at length with a majority of the men who have made significant contributions to it.

Nearly all cardiac surgeons are young. The founding fathers—men like Dr. Gross of Boston Children's and Dr. Blalock of Hopkins—are in their fifties. The recent headliners—such as Dr. Lillehei and Dr. John W. Kirklin of the Mayo Clinic—are mainly in their late thirties or early forties. So far as I can find out, there is in the United States no heart surgeon old enough to retire

Some cardiac surgeons are flamboyant, like the two well-known Eastern heart surgeons who have entertained medical meetings for a decade with a ferocious running feud. Some are the very model of the Ivy League doctor. The other striking characteristic of cardiac surgeons, besides youth, is a strong belief in the rightness of what they are doing—which is another way of saying they have courage. There are no mice in cardiac surgery.

The heart, however, is at the center of life and the frontier of surgery. In spite of the fact that it is the patient's blood on the floor, no surgeon approaches the heart (at least for the first several hundred times) without an inward quiver of fear. Moreover, the medical doctor—on whom the surgeon depends for cases—will often be reluctant to send patients to heart surgery.

Indeed, some medical men are openly hostile to heart surgery, especially of the experimental kind. They point out that new heart operations inevitably involve deaths—sometimes a substantial number of deaths—however carefully rehearsed and studied in the animal laboratory (because experimental animals cannot be an exact equivalent of sick human beings). These men feel that it is usually better to keep the patient alive as long as possible (if only for a few months) by medical treatment than to risk immediate death in the operating room.

The wisdom of sending a given patient to heart surgery can certainly be a perplexing and painful question to decide. I mention it not to judge between heart surgeons and medical men, or to decry medical conservatism (which has its proper place), but to make

another point. To bring cardiac surgery to its present state, heart surgeons have not only had to resolve their own doubts. They have frequently had to overcome open opposition from medical colleagues and hospital officials as well.

In the Philadelphia area, there are several hospitals where Dr. Bailey—the mitral commissurotomy man—is now a power and, within limits, can do very nearly anything he wants. He faced a rather different situation eight and a half years ago.

Dr. Bailey performed his first successful mitral-valve operation on June 10, 1948. It was actually his fifth commissurotomy. The first four patients died.

These deaths led to Dr. Bailey's ouster from three of the five hospitals where he had operating privileges. Another failure would close all Philadelphia to him. To guarantee himself one more chance, Dr. Bailey resorted to a bold maneuver. He scheduled his fifth commissurotomy for the same day as the fourth, so that he could get the fifth one done before word reached the hospital of the outcome of the fourth.

To do what he did, Dr. Bailey had to believe that he was right—as he was. But all cardiac surgeons must believe strongly in what they are doing. A few minutes' conversation with any one of them makes it clear that they do.

THE OPERATING THEATER

The ingenious procedures surgeons have devised for operating in and around the heart—as well as the cardiac surgeons themselves—are only part of the story. Like other recent developments in medicine, heart surgery depends upon a complex of advances in related fields.

This kind of surgery in particular owes much to anesthesia techniques that have made it possible to open the chest safely; to modern methods of blood transfusion (sizable volumes of blood are usually needed during heart operations); and to greatly improved methods of preparing patients before operation and caring for them afterward. Above all, heart surgery would be unthinkable without means of detecting and identifying surgically correctible heart lesions—procedures like cardiac catheterization, the tube-in-the-heart method that recently won a German physician and two Columbia University professors the Nobel prize. This technique locates heart defects from pressure readings and blood samples taken through the tube.

In short, heart surgery requires many skills beside those of the heart surgeon himself. This is nowhere clearer than on the stage where the climax of the heart surgery drama takes place—in the operating room.

A heart operation is a team affair. As many as a dozen men and women will be in the operating room, especially if a heart-lung machine is to be used. There will be a surgeon or even two (as at the University of Minnesota, where Drs. Lillehei and Varco frequently work across the table from each other), and two or three surgical residents to assist the surgeons. Two "sterile" nurses are generally needed to pass instruments to the men at the table, and also a "circulating" nurse to bring in fresh supplies and take away used instruments. At the head of the operating table will be the anesthesiologist and an assistant (a resident physician studying anesthesiology); they not only administer the anesthesia, but act as "physiological bookkeepers" for the operation, keeping track of blood losses, blood and fluids administered, and so on. Last but not least, there will be another resident and perhaps a technician to man the heart-lung machine.

A heart operation usually takes between two and a half and four hours. An hour is needed to work down, layer by layer, through the muscles and tissues of the chest to expose the heart; the chest must be dissected carefully, in a way that will allow it to function normally when put together again.

Now the sac around the heart is opened, laying bare the heart itself. In healthy individuals, the heart is somewhat larger than the fist and a glistening pink in color. In patients needing heart surgery, it is often enormous (I have seen a boy with a heart as large as his lung) and a sick purplish blue in hue.

The surgeon connects the heart-lung machine to veins from which blood will be collected, and the artery to which the blood, refreshed with oxygen, will be returned. The surgeon calls, "Pump on!" Under the watchful eye of its crew, the heart-lung machine whirs into life.

In a moment, the heart is free of blood. It continues to beat, to be sure, but much less strongly. The color is lighter, too.

Let us say the patient on the table is a child with an opening in the wall between the ventricles. To expose it, the surgeon makes a long incision in the right ventricle. The defect can be seen plainly; it is nearly the size of a half-dollar—much too large simply to be sewn shut. So the surgeon shuts it with a plug of plastic sponge cut to shape and carefully stitched into place.

Then the ventricle is closed, the surgeon calls "Pump off!", and the heart-lung machine is disconnected. The surgery within the heart took fourteen minutes—about par for the repair of a ventricular defect. Only in repairing certain complex defects is it necessary to use the heart-lung machine as long as three-quarters of an hour.

What happens from now on is essentially anticlimax, though each step must be taken with deliberate and delicate care. About an hour later—literally as the surgeon ties off the last stitch to close the chest wall—the patient opens his eyes. (Anesthesia is kept light nowadays; it's safer that way.) The anesthesiologist gets the youngster (who is still groggy and feels no pain) to say a few words to make sure he is all right.

For the next twenty-hour hours, the youngster is in the post-anesthesia recovery room, where equipment and personnel specially trained in dealing with post-operative emergencies stand by continuously. Then, three days or so in the hands of private nurses experienced in nursing heart-surgery patients. Finally, three to five weeks later, he leaves the hospital, his future immeasurably brightened by a truly great feat of the healing arts. In all, some thirty or forty highly skilled individuals will have had a quite direct part at some point in the intricate process of repairing his heart.

NEW BLOOD VESSELS?

It was remarked earlier that heart surgeons are now able to repair, by one means or another, defects responsible for about 75 per cent of congenital heart disease, and to relieve narrowing of the mitral valve, the commonest consequence of rheumatic heart disease. And the horizon is widening constantly.

For instance, instead of narrowing them, rheumatic heart disease often causes heart valves to leak, *i.e.*, to allow blood to flow backwards. Considerable progress has already been made in methods of patching up leaky valves or in replacing them altogether with plastic substitutes.

Another striking recent development is "elective cardiac arrest"—stopping the heart altogether with drugs during repair, then starting it again when the mending job is done. (A heart-lung machine carries on for the patient meanwhile, as in conventional open-heart surgery.) The stopped-heart technique was introduced into the United States last spring at the Cleveland Clinic, from England, where it originated. Surgeons are still divided about its merits. Stopped-heart surgery simplifies some operations, but perhaps at an added risk.

Most exciting of recent developments, however, is the prospect that heart surgery may soon have a place in the management of the Number 1 heart-killer, coronary disease. Actually, surgical techniques for treating coronary disease already exist. The question is, do they work? Specifically, do they work well enough to warrant the hazards of a major operation?

In coronary disease, the primary difficulty is the formation of fatty deposits in the coronary arteries, the vessels which supply the heart muscle with blood; as a result, the heart muscle is deprived of an adequate supply of blood. Disability and death follow if a large enough part of the heart muscle is deprived of blood.

Logically, coronary disease ought to be dealt with by prevention rather than surgery, and much research toward this end is under way. Still, great numbers of people already have coronary disease. They cannot be ignored.

Surgeons have taken two approaches to the treatment of coronary disease. One is the provision of a new blood vessel system for the heart. This is the purpose of the well-known talc operation of Dr. Samuel A. Thompson of New York Medical College, the several procedures of Dr. Claude S. Beck of Western Reserve, and the artery-transplant operation of Dr. Arthur Vineberg of McGill University. The other surgical approach to coronary disease is the direct removal of coronary-artery obstructions. It was accomplished in man for the first time just a few months ago by Philadelphia's Dr. Bailey, who used

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NEW MOVES IN THE BATTLE AGAINST CANCER

BY PROF. N. BLOKHIN

Considerable research work is in progress in the Soviet Union on the causes and possible treatments of cancer. In the following interview some of the most recent developments are discussed by the head of the Soviet Cancer Research Institute.

What is your opinion of the virus theory of Cancer ?

So far it has been proved that only a small group of tumours in animals is caused by viruses.

Science, however, knows of other causes conducive to the formation of malignant tumours. We know it is possible to cause tumours in animals by subjecting their organisms for prolonged periods to the action of chemical substances, or, for instance, X-rays, radiation from radium or radioactive isotopes.

The state of the human organism also plays a part in the complicated process of the development of disease.

Most widely held is the opinion that the various tumour diseases encountered in man and animals do not have a single cause, that in different instances different features, which, however, cause the same biochemical changes in the tissues of the organism, may play a part in their origin. The majority of Soviet oncologists adhere to this view.

Supporters of another view assert that cancer is caused only by viruses. They hold that the chemical and physical agents known as cancerogenes are not the true causes of cancer, but only facilitate its development. I consider study of the role of viruses and the origin of tumours to be most important, as discovery of the virus nature of certain tumours in man would open up new possibilities for their prevention and cure.

It must be pointed out that the idea of the virus nature of tumours is no indication that cancer is contagious in the ordinary sense of the word. Many years of observations go to show that this disease is practically non-contagious.

CAUSES NOT CLEAR

Thus, there is as yet no complete clarity on the causes of cancer. But the working out of effective methods for its prevention and treatment continues.

The history of medicine knows many such cases. Take for instance smallpox. Medicine was given anti-smallpox vaccination long before the virus causing the disease was discovered. Use of quinine was known long before the malaria agent was discovered.

The same thing is happening as regards the prevention and treatment of cancer.

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a reaming-out technique conceived by a young San Franciscan, Dr. Angelo May.

Cardiologists and surgeons alike have been doubtful that the new-blood-vessel operations either add to the heart muscle's blood supply or help the patient. Last October, though, the American College of Surgeons heard evidence that some of these operations do promote the formation of new blood vessels and have helped carefully selected patients, disabled by coronary disease, back on their feet. "I won't say they have earned a place in the treatment of coronary disease," a distinguished cardiologist commented. "But there may well be something there and, with care, they seem safe enough. The time has come to try them on more patients in more hospitals."

As for the May-Bailey operation, at the time of writing Dr. Bailey had performed it on three patients only. Three patients are too few, and the time since operation has been far too short to answer two key questions: do reamed-out coronary arteries stay open, and are patients really helped? But Drs. Bailey and May have answered the first question about operations directly on the coronary arteries. They can be done. Thus, Drs. Bailey and May have made it more probable than ever that heart surgeons will some day have much to say about coronary disease, too.

Considerable success have been achieved in this field (although the causes of the disease are still insufficiently clear).

I would say more: that even the means which we possess make it possible to assert that *the widespread opinion, that this disease is incurable, is unfounded, that cancer can be cured.*

WHAT ARE THE METHODS OF TREATMENT?

At the moment an important element in the battle against cancer is prevention. This is carried out along two lines. Various harmful factors that, existing in man's environment, may have a detrimental effect on him through the skin, mucous membranes of the respiratory passages of the digestive tract, are studied and eliminated.

As a result, industrial cancer diseases have disappeared in our country.

The second line is by identifying and treating various chronic diseases usually called pre-cancer or pre-tumour diseases.

This term is not a happy one, for such diseases by no means always develop into cancer. But they may become a favourable ground for the development of malignant tumour which never form in completely healthy tissues.

This is why mass preventive examinations of the population, which we carry out on wide scale, and also hygienic educational and explanatory work among the population, are of such great importance.

Every person should be told that at the first symptom of tumour or pre-tumour disease it is necessary to see the doctor immediately.

Now about the process of treatment itself.

The oldest method is the surgical removal of affected tissues. Nowadays, methods of analgesia and combating post-operational complications have been so greatly improved that the complete removal of the stomach, part of the alimentary canal, etc. have become possible.

Such operations save the lives of many patients who are suffering from forms of cancer which in the relatively recent past were still considered incurable.

Other forms of the disease are being successfully treated by ray therapy, without surgical intervention.

Many instances could be cited where patients have been completely cured by these methods.

It is not difficult to foretell that in the next few years radioactive isotopes will become far more widely applied in oncology than is now the case.

In many cases oncologists have recourse to combinations of the surgical method with ray therapy.

One of the new trends is seeking means for treatment by medicines. The possibilities are being studied of using certain chemical preparations, hormones, antibiotics.

HORMONES

At the present time, for instance, we know of hormone preparations which are used in cancer of the milk or prostate glands, chemical preparations used in tumour diseases of the blood and lymphatic system, and also for certain other tumours.

Such treatments, like ray therapy, may within the next few years open up many fresh possibilities for treatment of malignant tumours.

Also of interest is the immunological trend—seeking ways to create immunity of the organism to tumour diseases. These methods are, as yet, being studied mainly in experimental laboratories.

Experiments with animals provide grounds for thinking that immunological methods may in time find a definite place in the prevention and treatment of cancer in man.

All these trends are being actively worked out by oncologists both in our country and in other countries.

COULD YOU PLEASE TELL US SOMETHING ABOUT THE CHEMICAL AND HORMONE PREPARATIONS AND ANTIBIOTICS THAT HAVE JUSTIFIED THEMSELVES IN CLINICAL USE?

In this country and abroad in recent years a number of preparations have been produced which have justified themselves when used for the treatment of certain tumour diseases.

Of the new chemical preparations I would mention novembiquine, dopan and sarcolysis, invented by L. Larionov in co-operation with the chemists V. Nemets and A. Khokhlov and today being studied in the clinic of our institute.

Novembiquine and dopan are used for the treatment of lymphogranulomatosis and tumour diseases of the blood. Sarcolysin has proved effective in seminoma, metastases of this tumour, and in certain sarcomas.

E. Vermel and G. Menshikov have obtained a preparation of vegetable origin, omain, successfully used in the treatment of cancer of the skin by using dressings of omain ointment.

It should, however., be borne in mind that all these preparations are still being studied in special clinics, and only subsequently will it be possible for them to receive wide application.

Of the foreign anti-tumour antibiotics I can mention actinomycin C, obtained by Waxman, and the Japanese preparation sarcomycin. These have a certain therapeutical action on some tumour diseases, in particular in lymphogranulomatosis, certain metastatic tumours in the lymphatic nodes.

A great deal of work is being carried out on the chemical-therapy of tumours in the United States, Britain, France and other countries.

The series of preparations evolved in other countries in the most part are close to those which are used in our country.

In some cases our preparations appeared subsequent to the appearance of analogous preparations abroad, in others the foreign preparations appeared after we had produced a similar preparation, the work apparently having been carried out simultaneously.

MAY WE HOPE THAT WITHIN THE NEXT FEW YEARS MANKIND WILL AT LAST BE GIVEN A RADICAL MEANS OF FIGHTING CANCER?

It is a mistake to think that it will be possible to find a universal medicinal preparation that will be effective in all forms and at all stages of the disease.

The result of such a view being widespread is that every announcement of a new method of ray treatment or new chemical preparation gives rise to rumours that the problem of cancer has been completely solved.

The conception of cancer embraces a large group of malignant tumours—diseases which are close to one another, but at the same time are different, and each one calls for its own methods of treatment.

Thus, some tumours prove sensitive to X-rays, others impervious to them. Chemical and hormone preparations are each used only for particular forms of tumour diseases and prove ineffective in others.

We therefore regard it as the result of lack of information on the part of individuals (sometimes even doctors) when they write asking us to send immediately this or that preparation for the treatment of a patient, of whom nothing is said other than that he suffers from cancer.

NO CURE—ALL

We get such letters from many countries—Poland, Czechoslovakia, Italy, Belgium, Israel, France and others. We naturally understand that these requests are made because the treatment of neglected forms of cancer is most difficult, and the existing methods satisfy neither the patients nor the doctors.

There are grounds for believing that the next few years will bring a great deal that is new in the treatment of cancer, but it is a matter not of inventing a single, universal preparation, but of perfecting surgical, ray and medicamental treatment, of working out the most effective combinations of these methods.

Let me say in conclusion: the results of treatment of malignant tumours are improving from year to year. Thus, for instance, cancer of the skin is now showing more than 90 per cent complete cures.

Even cancer of the stomach, with the results of treatment of which we can in no way be satisfied, shows 30 to 40 per cent of complete cures in cases in which radical operations have been performed.

If the statistics for the treatment of early forms of this

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Controlled Arterial Hypotony applied in Neurosurgery

BY V. LERMAN AND E. ZLOTNIK
(MINSK)

THE usage of new methods against hæmorrhage, loss of blood, shock and other side effects of surgical injury, is a recent major achievement in surgery. One of these methods is controlled arterial hypotony. Surgeons are showing a growing interest in this method, which enables them to expand the field of brain tumour operations, hitherto limited by insufficiently effective methods of hæmostasia and prevention of shock and œdema of the brain.

The comparative study of data, taken from medical literature and personal experience, concerning various methods of controlled arterial hypotony (phlebotomy, high spinal anæsthesy and ganglioplegical preparations) has shown that the simplest, comparatively safe and sufficiently effective method is the use of ganglio-blocking substances.

This report is founded on the study of controlled arterial hypotony caused by the injection of hexonium during brain operations in 54 cases (62 operations) of intracranial tumours.

We considered controlled arterial hypotony to be contraindicated in the presence of cardiovascular disorders, in particular disbalanced brain circulation (including changes due to age) and disorders of the breathing organs, liver and kidneys. Preoperational measures consisted of repeated transfusions of erythrocytic mass and regular injections of vitamins, glucose and heart remedies, measures calculated to improve the delivery of oxygen by the blood and the metabolic processes of the organism.

In most cases controlled arterial hypotony was rapidly brought about by intravenous injections of hexonium (6—10 milligrammes of 2 per cent solution during 20—40 seconds). We therefore applied it directly before extracting the tumours and more rarely during trepanation or the resection of the brain, made to expose the tumour. Hæmorrhage from the smaller arteries and veins was much diminished during controlled arterial hypotony (50—60 millimetres of the mercury column with a simultaneous change of the patient's position) and surgical manipulations of the larger brain arteries were made easier. There were no cases of acute œdema of the brain, caused by surgery. With prolonged oxygen inhalation, which is a necessary measure, the manifest degrees of controlled arterial hypotony were not accompanied either by any changes of consciousness and breathing, or by any changes in the electrocardiogramme. Moderate tachycardia was observed constantly.

The gradual ascent of arterial pressure began after 30—90 minutes and could, if necessary, be accelerated by blood transfusion and injections of ephedrin in drops. The brain wound was closed after checking hæmostasia, with arterial pressure not below 90 millimetres of the mercury column. Usually arterial pressure was finally stabilized at the preoperational level a few hours after the operation. We did not observe any side-effects that could be ascribed to controlled arterial hypotony.

Considerable differences were observed in individual cases where controlled arterial hypotony was applied, both as regards, effective doses and length of time. A second injection of hexonium does not have any depressive effect. Difficulties of dosage were partly corrected by changing the position of the patient's body.

Experiments on cats yielded the following results :

The results of a slight overdosage in the first injection of hexonium are difficult breathing, accompanied by a sharp fall of the arterial pressure. These can be successfully overcome by artificial breathing, blood transfusion or injection of ephedrin in drops.

After injection of the first dose of hexonium, the organism adapts itself to usually toxic quantities of the preparation, which completely loses its depressive effect. The injection of supertoxic doses caused the animals' death, preceded by symptoms of paralysed breathing and a late fall of arterial pressure.

Peculiarities of the controlled arterial hypotony process in cases of loss of blood, oxygen shortage and breathing of carbonic acid were also studied.

Controlled arterial hypotony is indicated in cases when local methods of hæmostasia are insufficient, on condition that the general state of the organism is such as to allow for the compensation of the vital functions during the period of hypotony.

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disease be taken, the results prove to be considerably better.

I must repeat: the working out of methods of early diagnosis of the disease, mass preventive examinations of the population, and wide-scale anti-cancer propagandat are of no less importance for the successful fight against cancer.

There is every indication that in the next few years medicine will achieve further, still more significant successes in oncology.

PRINCIPLES IN THE MANAGEMENT OF ANEMIAS

Wintrobe, M.M., *Bulletin of the New York Academy of Medicine*, U.S.A., 20: 6–26, January, 1954.

Etiologically, anemias may be divided into four broad categories. First, there are those resulting from loss of blood: acute and chronic posthemorrhagic anemias. Second, some anemias arise from deficiency of factors concerned in erythropoiesis, and such deficiencies may be in iron, certain elements of the B complex, proteins, and possibly ascorbic acid. The two remaining classifications are, respectively, anemias following excessive destruction of red corpuscles, and those following impaired production of such red corpuscles. Accurate differential diagnosis is essential to intelligent management of anemias. The most important therapeutic agents are iron, liver extract, B_{12} and desiccated thyroid. The use of folic acid is very limited and that of ascorbic acid has not yet been evaluated. Liver extract or B_{12} is indicated in pernicious anemia to replenish stores of antipernicious anemia factors and to provide a reserve for maintenance, and in megaloblastic macrocytic anemia in sprue, nutritional macrocytic anemia, and other conditions. The recommended dose is, for liver extract, 15 units a day in relapse until a good response is observed and 60 units every 45 to 60 days for maintenance. For B_{12} the suggested dose is 30 mcg. daily, in relapse, until a satisfactory response appears; 120 mcg. every 45 to 60 days for maintenance. The intramuscular route of administration should always be used. In pernicious anemia and sprue treatment should continue permanently. The only other truly important therapeutic agent in anemia is iron, and it, of course, is indicated in iron deficiency anemias only. The usual route of administration is the oral, ferrous sulfate or gluconate tablets of 0.325 gm. being taken three times a day with meals. Intravenous preparations may be used in certain cases where the oral route is ineffective, but it is rarely necessary to give iron parenterally. Folic acid is indicated in so-called pernicious anemia of pregnancy, megaloblastic anemia of infancy, refractory megaloblastic anemia, and some cases of sprue. The usual dose is 5 to 20 mg. per day orally. It is contraindicated in cases of pernicious anemia. Desiccated thyroid is included in the list of specific agents since it is required to relieve the anemia of hypothyroidism. It is uncertain whether ascorbic acid is really specific for anemia associated with scurvy. Blood transfusions, splenectomy, and ACTH and cortisone are non-specific agents, of considerable value in specific cases. Where anemia is due to an underlying disorder or infection, the best treatment of the anemia is the treatment of the underlying condition.

Non-Malignant strictures of Colon and Rectum

BY DR. S. P. SRIVASTAVA, M.S., F.R.C.S., F.A.C.S., P.M.S.,
Professor of Surgery, Medical College, Agra.

THE commonest cause of stricture of large bowel is carcinoma which is usually of the schirous type. No age is exempt and cases have been met with in as young patients as 16 years old. The different age groups met with in my series of cases has been published in the article of carcinoma of Rectum and anal canal, published in the Journal of Indian Medical Association July, 1955.

A series of cases of stenosis of large bowel and rectum is being presented which were due to non-malignant lesions.

The usual classification of non-malignant strictures is :—

1. Congenital
2. Spasmodic
3. Traumatic
4. Inflammatory

CONGENITAL

(a) In Atresia anovaginalis there is a narrow opening of anal canal below the vaginal orifice which requires backward displacement by operation. Six such cases were operated upon. In all cases there was a history that the fæces pass out of the vaginal orifice. On examination the atresial opening was just outside & below the hymen.

A badly planned plastic operation for atresia ani and anovaginals may give rise to stricture again requiring another plastic repair, as a badly planned colostomy needs another operation for stenosis.

(b) The congenital stricture in the anal canal occurs at the level of the pectinate line due to the partial absorption of the proctodeal membrane. The stools are pipe stem like and bleeding may occur due to development of fissure. Rectal examination shows funnel shapped anus.

Cases of imperforate anus after operation develop two types of complications :—

(a) Incontinence

(b) Stricture of anal canal.

Incontinence of fæces can be avoided if the external sphinctre muscle fibres are not damaged and the new opening of anal orifice is brought out in between the muscle fibres. The anal stricture is more commonly met with, provided the operation of suturing the rectal mucous membrane to the skin of the anal canal is not properly done.

The patient requires dilatation to be done intermittently and the occurrence of fissure is common in these cases if a constipated stool is passed.

II SPASMODIC STRICTURE

Occurs in the region of internal sphinctre due to its spasm and hypertrophy. The result is the occurrence of megocolon with dilatation of the sigmoid and later descending and transverse colon. The etiology of the lesion is not the spasm of the muscle fibres of internal sphinctre but the congenital absence of the sympathetic ganglia and aurbach's plexus in the wall of this portion of the rectum. The peristalsis stops short at this level of the bowel hence the patient suffers from chronic constipation and distension of abdomen.

I had two cases of megacolon one aged 26 yrs. old and another about 28 yrs. both of whom had a chronic trouble of passing motions on 7th or 8th day or with the help of an enema.

Barium enema showed the typical dilatation of the whole of colon. Those persons who habitually take saline purgatives may develop spasmodic stricture of anal canal due to the passage of liquid stools. Acute fissure leads to the development of a very acute spasm of anal sphinctre which may lead to fibrous stenosis of anal canal when the fissure becomes chronic.

III TRAUMATIC STRICTURE

It is the result of a badly performed operation of piles. When the White-head's method has been used

where excessive denudation of mucous membrane has been done from the anal canal and lower rectum the ulceration leads to fibrosis and stricture. Submucous injection of piles incorrectly given may also lead to ulceration followed by stricture.

Irradiation of cervix for cancer produces proctitis and stricture of anal canal or rectum. I know of two cases where a severe proctitis developed which may result in stricture later on.

IV. INFLAMMATORY

Lymphogranuloma venereum—It gives rise to a diffuse inflammatory stricture of rectum and 80% of cases occur in women.

Three of my cases were ladies of 30, 35 and 40 years respectively and one a male of 40 yrs. In the latter case stricture later gave rise to epidermoid carcinoma. Two ladies aged 35 and 40 yrs. had multiple fistulae in the perineum discharging pus and so was the condition in a male also, who developed epidermoid carcinoma over the external openings of these fistulæ. The lady aged 30 yrs. complained of difficulty in the passage of passing stools due to a dense stricture in the middle third of rectum. The biopsy from the area of the strictures showed chronic inflammatory tissue. There were no fistulæ in the perineum in this case.

Bersud found in 64% of cases positive serological evidence of syphilis but he did not consider syphlis had any role in the origin of the disease. Similarly he found 45% with accompanying infection of gonorrhoea and 14.5% with chancroid infection. The Frie's test is positive in cases of lymphogranuloma. Actino-mycosis can also give rise to a diffuse stricture extending down to the anus accompanied by induration of buttock and sinus formation.

Inflammatory strictures are very rare in the colon.

There were two cases of tubercular stricture of transverse colon with ulceration of the mucous membrane and fibrous stenosis, in the Surgical department.

Both were young women of 20 and 25 yrs. old respectively. In one case the lesion was situated in the proximal third of transverse colon while in the other it was in the splenic flexure. The lymph glands in the transverse mesocolon and the omentum were tuberculous and the peritoneal surface of the bowel showed tubercles on microscopic examination in one case. The lesion in the splenic flexure was also confirmed by biopsy.

The mucous surface showed ulceration with small multiple polypoid growths in the surrounding mucous membrane.

Both cases were admitted as cases of chronic intestinal obstruction. The obstruction was relieved by conservative treatment and barium enema done after relief of acute construction showed the site of stricture and stoppage of the enema at the splenic flexure and mid-transverse colon respectively. Resection of the tuberculous stricture of the bowel was done by Paul Mickuliez operation of exteriorisation and resection.

Tuberculosis of the ileo-caecal region along with fibrosis in this region gives rise to obstructive symptoms with the formation of a lump in the right iliac fossa.

I had 17 cases of Chrone's disease out of which one was in region of transverse colon and one in the splenic plexure while in the rest were in the ileo-caecal region or terminal ileum. All these cases had symptoms of chronic obstruction with alternating constipation and diarrhoea and visible peristalsis in the abdomen. Barium enema showed a filling defect in caecal lesions, and stricture with obstruction to the passage of the barium in lesions of the colon. Ten cases had a lump in the right iliac fossa which was excised by right hemicolectomy. On histological examination the diagnosis of Chrone's disease was made.

In seven cases short circuit operations were done when the patient was not fit for resection. The patients got marked relief even after this conservative operation.

The diagnosis of cases of Chrone's disease from ileo-cæcal tuberculosis who came with palpable lump in the right iliac fossa is not possible clinically or radiologically. It was only possible to diagnose Chrone's disease by histological examination and negative staining results for acid fast bacilli. There were no areas of caseation met with in this disease and there was fibrosis with characteristic scalloped giant cells.

The etiology of the condition is not known but there is swelling and proliferation of the lymphatic endothelium in the intestine and lymphonodes causing lymphatic obstruction and œdema. Granulomas containing giant cells are found in the intestinal wall, mesenteric lymph-nodes and liver which slowly hyalinise without necrosis. Fibrosis and muscular hypertrophy of intestine occurs in sub-acute and chronic stages. Warren is of the opinion that cases which were once called hyperplastic tuberculosis should be labelled as Chrone's disease and that the former term is obsolete.

Chronic Diverticulitis is another condition of chronic inflammation of diverticulum of the descending colon which gives rise to intense fibrosis causing chronic and acute on chronic obstruction.

There was a middleaged man admitted with symptoms of acute obstruction the cause of which was stricture in the region of the lower third of sigmoid colon. Transverse colostomy was done. After the obstruction was relieved, sigmoidoscopy showed the presence of stricture at the recto-sigmoid junction. Barium enema also showed stenosis in the region of lower portion of sigmoid colon.

On exploration of abdomen the sigmoid colon was found to be covered with a lot of subserous fat. There were adhesions to the small bowel and appendix. On separation of coils of small intestine there were perforations in them which had to be sutured at two places.

Appendicectomy was done along with resection of the affected stenosed sigmoid colon above the normal portion of rectum. The open end of the rectum was sutured and a terminal colostomy was done in the descending colon.

The patient made an uneventful recovery. The biopsy report of the strictured portion showed chronic inflammation and fibrosis with no evidence of malignancy. Most probably attacks of diverticulitis gave rise to perforation of one of the diverticulæ which was closed by adhesions of the small bowel and appendix.

The cause of the stenosis was chronic diverticulitis which gave rise to intense fibrosis. The bowel affected was about 3" long while the rest of the colon was full of fat in the mesentery and subserous regions.

The operation of excision of the sigmoid colon and rectum was aimed at in the beginning due to the suspicion of malignancy as the cause of the lesion. The operation ultimately was that of Hartman's procedure with the blind stump of the rectum left after excising the affected sigmoid colon and a terminal colostomy. The whole of rectum could not be removed as the patients general condition did not allow it to be done.

Luckily the lesion turned out to be chronic diverticulitis instead of carcinoma in biopsy.

TREATMENT OF STRICTURE OF RECTUM

The rectal stricture met with were mostly due to lymphogranuloma where colostomy was the only treatment possible. Out of four cases it was done only in one case while the rest refused the idea of a colostomy. The treatment should be radical excision of the stricture abdomino-perineal or perineal excision with a terminal or loop colostomy respectively. Colostomy relieves cases of lymphogranuloma of rectum to a great degree. The diversion of fæcal stream through the colostomy opening allows perfect rest to the affected area, thus diminishing the infection and discharge through the sinuses or fistulæ.

In advanced cases with immense fibrosis colostomy is the treatment of choice. The patient is free from symptoms of pain, discomfort, toxæmia, and obstruction of the passage of fæces etc.

Chloramphenicol and tetracyn are useful drugs to combat the virus infection and prevent toxæmia. Streptomycin injections have been tried with little benefit. Frie's antigen injection of 3 C. C. has been given as a curative measure.

Dilatation of stricture may be done but is not successful due to the dangers of hæmorrhage, reaction and even perforation and pelvic cellulitis or peritonitis. Dilatation should never be attempted in a stricture in the upper third of rectum which is tubular in type. Internal proctotomy has not been practised by me and personally I think it is a dangerous procedure. There is a risk of hæmorrhage and recurrence of the stricture unless dilatation for at least two years is persisted.

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Superficial External proctotomy i. e. division of the stricture at the anal margin has been done in several cases when there has been fibrous stenosis following the operation for imperforate anus. Recurrence was avoided by suturing the anal mucous membrane to the skin. Enlargement of stenosed terminal colostomies is done by suturing the colonic mucous membrane to the skin margin after the fashion of V—Y plasty thus enlarging the opening. A dilator is subsequently passed twice daily first and then at gradually increasing intervals until the scar tissue has become firm, and not likely to contract.

THE 1957 INFLUENZA EPIDEMIC

BY A WORLD HEALTH ORGANIZATION'S WRITER

In the space of a few months, the influenza virus can spread throughout the world and, even though causing but a mild infection, it can disorganize for weeks at a time the social and economic life of the countries through which it passes. The highly infectious nature of the disease and the speed with which it spreads have caused it to be said that: "When influenza is epidemic one tends to think — not *whether* one will get it, but *when* will one get it?". What of the current epidemic?

THE influenza epidemic that started in Asia this spring and has since spread to both hemispheres has, for several reasons, put epidemiologists and health authorities on their mettle, according to the forthcoming issue of the Chronicle of the World Health Organization (WHO).

While remaining mild, it has a tendency to spread that is accounted for by the characteristics of the virus concerned, which differs considerably from those responsible for the epidemics of the last 25 years. Although it belongs to the A virus group, it is the most aberrant type reported since the discovery of the influenza virus in 1933. Antigenic variants of the A virus are known to have appeared during previous epidemics, but in recent years these variations have been fairly slight. Nevertheless, wide differences in antigenic constitution have occasionally been observed as, for instance, in 1946—47, with the appearance of strains first isolated in Australia.

The deviations observed in the "new" virus—designated for the time being A/Asia/57—are more pronounced than any so far observed, even including these marked ones of 1946—47. Since most population groups have never been in contact with the virus, and consequently have not acquired immunity to it, the advance of the epidemic is meeting with little resistance.

EPIDEMIOLOGY

The first notifications, reporting the presence of numerous influenza cases, were sent to WHO from Singapore on 4 May 1957. However, as was afterwards discovered, the epidemic had already been spreading for several weeks. It started in the north of China at the beginning of the spring and penetrated into the interior of the country, where the virus was isolated for the first time at Peking, in March. Cases next appeared at Hong Kong in the middle of April. The gaps existing in what should be a world-wide system of epidemiological notification have become painfully apparent on this occasion.

During May, June and July, the epidemic spread very rapidly to the Philippines and Japan, South-East Asia, and the Western Pacific; then on to India, the Persian Gulf, Iran, Yemen, Aden, the Sudan, Egypt, Syria and Jordan. A few foci—for the moment still localized—have appeared as a result of imported infection in the USA, South America, Europe and Australia, but the situation is changing rapidly in some countries.

The epidemic spreads most of all in very dense communities, where contact between individuals is easy and frequent. Thus, in Japan and the Netherlands, for example, schools and camps have been particularly affected, the number of cases sometimes being as high as 60% of the total number of pupils. On board ship, too, series of cases have developed and have spread subsequently to ports and their hinterland. It would seem that these massive influxes of infected persons have played a bigger part in the

(Continued from page 42)

spread of the infection than isolated cases transported by air.

In the southern hemisphere the influenza season begins as a rule in June, the highest incidence being reached during the following two or three (winter) months. This year, the virus has been carried south of the equator during the most favourable season but the epidemic has not spread as rapidly as might have been expected and the proportion of people affected appears to be lower than in some tropical areas.

The disease appeared in Australia in May and was still spreading in June. Early in July it reached the Union of South Africa and Chile, and during August it was spreading in Argentina, Southern Brazil and New Zealand.

CLINICAL CHARACTERISTICS

This epidemic, which has remained mild, has caused very few deaths, and these have been due for the most part to bacterial pulmonary complications. In a few areas, the Philippines for example, a fairly high death rate has been reported. It is difficult, however, in the absence of laboratory diagnoses for the majority of the cases, to distinguish between deaths due specifically to influenza and those caused by other diseases resembling influenza in certain symptoms.

THE VIRUS

The virus responsible for the epidemic is shown by the complement-fixation test to belong to the A virus group. It is quite distinct from any of the viruses which have caused epidemics in the last 25 years, and shows the most important deviation in antigenic composition observed among viruses since 1933. Recently, Professor Mulder found in the Netherlands—and other workers in the United States of America and Australia have confirmed this—that some persons over 70 years of age possess antibodies against the "new virus". It is not inconceivable that virus A/Asia/57 is related to the one which caused the 1889 pandemic. If this is confirmed, it may prove to be a fundamental advance in our understanding of the epidemiology of influenza.

VACCINATION

Experiments in influenza vaccination have been carried out in certain communities for some twenty years past, using the allantoic fluid from the hen's egg infected with influenza virus and then inactivated with formol. While duly recognizing the variability in the results observed in certain cases, Dr. Thomas Francis, jr, of the University of Michigan, still felt able to affirm that "vaccination against influenza has been shown to be uniformly effective under a variety of conditions, when vaccines of proper constitution and potency are employed".

There can be no question of claiming to stop an epidemic by vaccinating against influenza. What is aimed at is the limitation of its effects by preventing high death rates and excessive absenteeism, such as would disorganize the public services and bring society to a standstill. Certain groups should be given priority. First, the medical services must be fit so that they may tend the sick. While there is no specific treatment for influenza itself, most deaths are caused by the bacterial complications of influenza—principally pneumonia—and the antibiotic treatment available today makes it possible, when it is given in time, to keep mortality down to a minimum. Next, the personnel essential for the proper running of the public services and basic industries must also be protected.

The first strains of virus A/Asia/57, as soon as isolation was achieved, were sent by the World Influenza Centre and the International Influenza Centre for the Americas to firms and laboratories preparing vaccines. Their task is to study the possibility of preparing a specific vaccine against this epidemic, so as to be able to meet possible requirements in the near future. Information reaching WHO regarding the suitability of the "new" virus for use as a vaccine is so far not very encouraging. According to the initial analyses carried out in manufacturing laboratories, national centres, and the World Influenza Centre, the virus has very little antigenic potency. Even a strain which appears to grow to a satisfactory concentration in eggs stimulates the formation of very little antibody in man. This may be due in part to the fact that most people have had no previous experience of this virus and that the vaccine is therefore acting as a primary stimulus. If this is so, it seems unlikely that a single dose would be sufficient to produce satisfactory immunization in man.

Vaccination by inactivated vaccines, such as those employed in recent years, has the drawback of

requiring a considerable amount of culture material (up to one egg per vaccine dose or even more in the case of strains with little antigenic potency). An attempt is therefore being made to develop an attenuated live vaccine. The doses required would then be smaller, since the vaccine multiplies in the body.

At an unofficial meeting of some eminent virologists, held at the suggestion of WHO following the recent International Poliomyelitis Conference at Geneva, a new vaccination procedure described by Soviet workers was discussed. With this procedure, the virus strain, after an initial egg passage, is cultured on human embryo tissue (where it undergoes a change in virulence), and then again cultured in the egg. The fluid, either liquid or dried, is sprayed into the nasal passages. In children this may give rise to a mild attack of influenza. The effectiveness of this method is still a matter of controversy.

The low antigenicity of the virus has also led to the failure so far of experiments in prophylaxis with hyperimmune serum. This is prepared by immunizing horses, and the serum is then sprayed into the nasal passages, as in the technique mentioned above. Injection of the Asian virus into the horse has brought about the formation of little or no antibody, certainly insufficient for effective protection.

POSSIBLE RELATIONSHIP BETWEEN HUMAN INFLUENZA AND SWINE INFLUENZA

Shortly after the influenza pandemic of 1918 a similar disease, called "swine influenza", broke out among pigs in the Middle West of the United States of America. It now takes the form in a few States of winter epidemics of a mixed infection of virus and Hæmophilus suis. In the inter-epidemic periods, the virus is not found in the tissues of the pigs. However, earthworms taken from infected pig farms seem to carry inapparent viruses, and these can develop, in pigs eating the worms, into normal viruses capable of being isolated from the respiratory system. The question therefore arises whether the pigs are in fact the virus reservoirs, rather than being secondarily infected by the human virus, as some have maintained.

The occasion of the present epidemic is to be used to attempt to find out whether animals actually play a part in influenza epidemiology. Sera taken from pigs, horses and other animals in regions so far unaffected by the epidemic are to be submitted to serodiagnostic tests, so that later on sera from the same animals can be studied and the antibodies compared, using the same tests, if the epidemic breaks out in these areas. In this connection, WHO has appealed to the veterinary and public health services of a number of countries in different parts of the world to undertake this research in collaboration with the WHO influenza centres.

Oral treatment of pernicious anemia with intrinsic factor concentrate and vitamin B_{12}

Lowther, C. P., Alexander, W. D., and Hendry, E. B., *Lancet*, Great Britain, 1: 495–497, March 6, 1954

Twenty patients, 12 women and 8 men, with pernicious anemia were given an oral preparation containing Vitamin B_{12} and intrinsic factor. Their anemia had already been brought to a state of remission and satisfactory control by the use of either parenteral B_{12} or a refined liver extract for varying periods of time before the oral product was employed. After a six months' regimen of treatment the oral preparation containing B_{12} and intrinsic factor had proven its worth by the fact that no evidence of relapse, either in the blood or the neurological picture, had appeared. No patient indicated that his sense of well-being had either improved or worsened under the B_{12}-intrinsic treatment, and none noted any new neurological symptoms or increasing disturbance associated with any already existing manifestation of the central nervous system. In favour of the use of an oral treatment like this is the fact that all the patients in this series considered the tablets to be much more pleasant and convenient than the parenteral treatment previously received. On the other hand, there are patients who will simply neglect or refuse to take an oral preparation when left to their own devices and in such cases parenteral treatment affords the advantage of compelling the patient to visit his doctor at set times and of permitting the doctor to observe and study his patient more closely.

Quarantinable Diseases on the Decline

A W.H.O. FEATURE

THE years since the Second World War have seen a dramatic decline in the extent and severity of the so-called 'quarantinable' diseases—cholera, plague, typhus, relapsing fever, smallpox and yellow fever. These diseases are now mere shadows of their former menace.

It is against these diseases—the great 'plagues' of history—that quarantine measures have been chiefly applied, both in the past and under the present International Sanitary Regulations of WHO. These Regulations, which took effect just over four years ago, replaced thirteen earlier and often conflicting Sanitary Conventions. They provide measures essential against the quarantinable diseases but which cause the least possible obstruction to international traffic.

Since the Regulations went into effect in October 1952, not a single epidemic of any of these diseases has occurred as a result of international travel. Only 45 ships and one aircraft have been reported as infected (i. e. carrying a person suspected of suffering from one of the quarantinable diseases).

Not only have the Regulations proved satisfactory during the first four years of their existence, but the spirit in which they are being applied bears evidence of a desire for mutual co-operation, understanding and goodwill. International agreement now prevails in a domain which was traditionally one of considerable controversy.

The recent history of each of the quarantinable diseases gives evidence of the dramatic improvement achieved in regard to them all.

CHOLERA IN INDIA

Although cholera has been endemic for centuries in India, and probably also in China, no westward movement of the disease occurred until the 19th century when no fewer than six huge epidemic waves spread to nearly all parts of the world.

Since the 1920s, a striking change has taken place in the world distribution and spread of cholera, and since World War II, the disease has made only brief excursions outside its central Asian stronghold. It appeared in Japan in 1946, in Egypt and Syria in 1947 and Indo-China in 1947—1952. In recent years, cholera has dwindled in importance to the point of being a problem only in its endemic foci in India and Pakistan (in the region of the Ganges and Brahmaputra deltas). Elsewhere, cholera has disappeared.

Even in its traditional home there has been a significant improvement. Cholera deaths have been recorded in India and Pakistan as follows :

1950	:	110,929	
1951	:	62,550	
1952	:	59,156	
1953	:	133,830	
1954	:	18,000	(approximately)
		384,465	

This approximate total of 385,000 deaths compares favourably with the 824,000 reported during the period 1945—1950 and is the lowest on record.

The declining importance of cholera throughout the world may be attributed almost entirely to better sanitary conditions in all countries which make it difficult for the infection to take hold. International transport by its nature is now unlikely to spread the infection.

AN ANCIENT SCOURGE

The first record of a plague pandemic dates from the 6th century A. D., in the time of the Emperor Justinian. It was described as "one of the worst calamities that ever befell mankind". In the 14th century the notorious Black Death killed millions of people in Europe and Asia and brought organized human society almost to an end. This second visitation lasted nearly 200 years.

Still another pandemic started in China in the latter half of the 19th century and was spread by maritime traffic to ports and countries all around the globe. The "plague spots" which continue to exist even today in parts of Asia, Africa and the Americas, are remnants of the epidemics of the last century. The present outlook is bright, however, and the disease in its human form has declined significantly.

General sanitary improvement has contributed to this situation and the new insecticides and rodenticides have helped reduce the threat of infection.

It must be remembered, however, that plague is essentially an animal infection, occasionally "spilling over" to humans. The problem of wild-rodent plague in certain countries remains as important as ever.

COMPANION OF WAR

Epidemic typhus is transmitted by the body-louse, and has a calamitous record throughout the ages as the grim companion of war, famine and catastrophe. It was expected to flare up again during World War II, but actually never got out of hand. Although there were serious outbreaks in North Africa, Yugoslavia and Korea, they did not disorganize whole communities as in the past.

Today typhus is disappearing from Europe and decreasing in Africa (except Ethiopia where a large number of cases was reported in 1951—55). Until 1953, some of the countries of Latin America were still recording significant numbers of cases. In the Pacific area, the only serious outbreak in recent years was in Korea and resulted from war conditions. The position of some countries in Asia and Eastern Europe is not fully known. From the point of view of international travel, typhus retains little importance today.

Relapsing fever, also louse-borne, is the least well known of the quarantinable diseases. Never a serious problem in international travel, it is now on the decline everywhere. Europe has been free from it since 1949, and elsewhere there have been only sporadic cases in recent years. The exceptions are Cambodia (4,261 cases in 1950), Korea (2,738 cases in 1951 but only 25 in 1953) and Ethiopia, where there were significant outbreaks in 1953, 1954 and 1955. To sum up, relapsing fever is today of little significance in international quarantine.

DECLINE OF SMALLPOX

All epochs, regions, climates and peoples have known smallpox. History, even up to very recent times, tells the sad story of its destructive effects. The situation tends to improve, however, as the following estimates show :

	Average number of cases per year	
	1946—50	1951—55
Africa	33,000	25,000
Americas	20,000	9,000
Asia*	139,000	144,000
Europe**	687	119
TOTAL (in round figures)	193,000	178,000

(*excluding China and USSR)

(**excluding USSR, Albania, Bulgaria, Czechoslovakia, Hungary, Poland and Rumania)

For the past five years, 58 per cent of all cases were reported from India and Pakistan, 23 per cent from other countries of Asia, 14 per cent from Africa south of the Sahara, and 5 per cent from Latin America. The fact that the severe type of smallpox is now confined to certain endemic areas of the globe is evidence of the dramatic decrease in this scourge. The persistence of endemic foci requires vigilance to prevent the infection from spreading elsewhere—but smallpox is no longer the threat it used to be even at the beginning of this century.

YELLOW FEVER

A disease of tropical Africa and America, yellow fever has in the past been known to invade Europe and North Africa, but has *never* spread to Asia. This is an epidemiological mystery, and one of the major considerations in present quarantine practice concerning this disease.

After centuries during which outbreaks of "yellow jack" periodically spread panic in two continents, and was a continual hindrance to the development of new areas, the disease has today been restricted to a definable position. Thanks to mosquito eradication campaigns and wide-spread vaccination, control of yellow fever has now been successful over large areas.

There are trends clearly discernible today with regard to the quarantinable diseases which give hope that cholera should be eliminated within the not too distant future; plague is no longer a problem in international traffic, but there must be no lowering of sanitary requirements for ships and ports, no relaxation of efforts to keep ships and warehouses free from rats; relapsing fever and typhus are now of little concern and the regulations which apply to them are almost never used; smallpox continues to be a nuisance in international quarantine practice, but even this highly infectious disease is receding.. and should soon join the other diseases which are passing from the active quarantine scene; yellow fever is the most serious problem in international quarantine; the fears of Asian countries concerning possible importation of this disease are legitimate, but there is cause for optimism in the success obtained in the Americas, which shows that the disease can be suppressed from urban areas.

THE SHADOW OF ANTIBIOTICS

BY K. N. RAMAN, M. B., B. S.
Anaimalai, South India

SIR ALEXANDER FLEMING discovered a valuable and wonderful drug in 1930, and it came to our hands in 1944. This has been hailed as the dawn of the antibiotic era in medicine. Since then a vigorous search has been in progress for antibiotics. Many attempts at synthesis have been made, and samples of soil from practically all corners of the world have been examined. Literally thousands of antibiotics have been isolated, of which about thirty have been found useful in clinical medicine.

By providing very effective control over infections without apparent serious toxic effects, these drugs have gained a great reputation. They have been used in all fields of medicine and surgery, and they have begun to cast their shadow on all aspects of medical practice.

OVERGROWTH PHENOMENA

We are so used to considering bacteria as causing disease, that we tend to forget that the human body normally harbours millions of micro-organisms of various types. Among these may be found the pneumococcus in sputum, the meningococcus and diphtheria bacillus in the throat, the staphylococcus in the skin, and even cholera vibrio in the gut. All these seem to exist in small numbers without producing disease. During the active phase of a disease, we find an enormous overgrowth of the organisms concerned, and they may easily be demonstrated in the lesions and exudates. When recovery occurs, (naturally or as a result of treatment) this excessive growth is controlled, and the original levels are restored.

Normally, many types of bacteria, fungi and viruses co-exist in the human system—nose, mouth, skin, gut and vagina. These areas are miniature factories producing antibiotics—enzymes, metabolites and toxins of the organisms—which inhibit overgrowth of any one constituent, and thus maintain the flora at normal levels.

It might have been better if we had antibiotics available which were specific for particular organisms. But those in use at present have varying degrees of 'bacterial spectra', and act not only on the pathogen but also on the others. But even the broadest spectrum is not a complete one, so that a few species remain uninfluenced by the antibiotic, and produce overgrowth phenomena. A child with enteritis may have its symptoms controlled by antibiotics, but after a week of continuous treatment, may exhibit diarrhoea as an overgrowth phenomenon which is wrongly assumed to be due to relapse. Fungal infections of the mouth and perianal regions may also occur as overgrowth phenomena.

BACTERIAL RESISTANCE

Bacteria exposed to the action of antibiotics are capable of developing resistance to the drug by genetic or mutational change after varying periods of time. With streptomycin, such resistance appears in a few hours or within a few days. A combination of streptomycin and penicillin appears and attractive proposition to the surgeon and practitioner, as it acts on both gram-negative and gram-positive bacteria. In fact the manufacturers have not been slow to exploit this psychological appeal, and such products have been available for a long time now. It would be interesting to find out the extent of increase in the sales of streptomycin and penicillin products in our country during the influenza epidemic in May—June 1957.

Such combinations are commonly used with the aim of preventing secondary infections in common ailments like cold, minor respiratory tract affections, after normal labour, after laparotomy for 'clean cases', after draining an abscess, and so on. Quite possibly, no such prophylactic action is obtained, but a likely result is an overgrowth of streptomycin resistant organisms in the nasopharynx, which may cause disease in the patient himself, or by droplet infection, in a more susceptible contact. A more serious risk is the development of bacterial resistance to streptomycin in a quiescent tubercular focus. If the patient later develops an active lesion, not only will he resist treatment with this drug, but he will pass on infection with resistant bacilli to those who come in contact with him.

Another good reason for withholding antibiotics from minor and self-limiting infections is that these drugs, by acting directly on the organisms, interfere with the immunological processes in the body, which are essential for the future well being of the patient. This is especially important in children.

THE STAPHYLOCOCCUS

Among the pathogenic bacteria, the staphylococcus has almost unique powers of adaptability, and develops resistance to antibiotics quickly. Newer antibiotics are being constantly developed and used, but it is not long before the staphylococcus gets resistant to each one. Bacteriological studies in hospitals have shown that the staff and patients resident for some time carry resistant staphylococci in their nasopharynx and skin. It is a matter for regret that the rigorous standards of asepsis developed in the pre-antibiotic era have been relaxed due to our confidence in the efficacy of the 'wonder drugs'. Hospital staff who go about blowing their noses, and attend to the dressing of wounds in the wards, without properly washing their hands in between, are no doubt responsible for a good deal of cross infection, and for dissemination of resistant bacteria.

THE SHADOW OF THE ANTIBIOTICS

It is in the field of diagnosis and management (most important aspects of good medical practice), that we find the darkest shadow of the antibiotics.

Any patient with fever is promptly treated with penicillin or a streptomycin penicillin combination. If there is no response, the newer 'broad spectrums' are tried singly or in various combinations until the patient develops side effects. By now, the true picture of the disease has probably been masked, and diagnosis and further treatment made more difficult. Fever by itself is no indication for antibiotic therapy, and the causes of fever in our country are legion. Recent studies have disclosed that virus infections are responsible for a large number of diseases. It is possible that improved diagnostic procedures have helped in the recognition of the viruses, or it may be that there is an actual increase in the incidence of virus infections. The antibiotics are ineffective against these, and yet they are used routinely as in the influenza epidemic referred to above.

Before the antibiotic era, it was the practice in our country to treat almost all cases of fever with quinine for three days, but now it is possible to come across malaria patients who have not had any quinine, but have been drenched with antibiotics without benefit. Any enlarged liver in the earlier days indicated emetine therapy, but now, cases are recorded where amœbic infection of liver has been treated with penicillin and tetracyclines, and the condition diagnosed post mortem. The psychological appeal of the wonder drugs is so great that old procedures developed as a result of experience are cast aside without critical examination. In the field of surgery, emphasis on rigorous aseptic technique developed by experience is being shifted to 'antibiotic cover', with the risk of producing and disseminating resistant staphylococci. Good aseptic technique is not confined to the operating theatre alone, but to all activities of those coming in contact with surgical as well as medical cases. It is an attitude of mind which is constantly aware of bacteria, contamination, fomites, and of a 'no touch' technique. A good surgeon is cautious in handling bacteriologically dangerous substances whether he is on or off duty—specimens in the autopsy rooms, articles contaminated with road dust etc. Our confidence in the efficacy of antibiotics need not lead us to discard these precautions evolved by hard work over a period of decades.

VENEREAL DISEASE

Penicillin has been found very effective in gonorrhœa and syphilis. Though it has been used in these conditions since 1945, it is fortunate that there is no evidence of resistance developing in the organisms concerned. But the lack of a critical attitude in using the drug is responsible for casting a shadow in this realm too. "The problem of treating venereal disease has boiled down to treating two diseases with one drug!." Is the problem really so simple? Is it a relapse or a primary infection? Any extramarital contacts? Has the spouse been exposed to the risk? Is treatment necessary for her or for him? How long is surveillence necessary? These are some aspects that have to be considered. Then there is the problem of lymphogranuloma, non-specific urethritis, non-specific balanitis, and other conditions. Treatment of sores and discharges with 'shots of penicillin' without a reasonable attempt at bacteriological diagnosis may lead to bewilderment when there is no clinical response. A venereologist of vast experience and knowledge during the course of a recent talk (Ref. 1.) described how the antibiotics have given rise to a crop of

problems for him in the field of diagnosis and management. Now it is rare for him to see a patient in his original clinical condition before he has been drenched with penicillin, sulphonamides, and tetracyclines.

SURGERY

Antibiotics have undoubtedly saved many lives and prevented much morbidity in severe injuries, burns, difficult labour and trauma, but comment has been made above on the prevalence of unnecessary prophylaxis. Hernia rapair, 'cold' cæsarian section and gunshot wounds heal quite well without antibiotics, provided a good aseptic ritual has been available.

In the presence of necrosis or suppuration, antibiotics cannot reach the avascular areas in sufficient concentration, and surgical measures are necessary to deal with this source of infection. In other words, the old surgical axiom "when there is pus, let it out", is as true today as it ever was. Patients with quinsy, gum boils, carbuncles, ischio-rectal abscess, pelvic abscess, are put on streptomycin penicillin combinations for days or weeks in the hope of controlling pyrexia, whereas a suitable incision when there is evidence of softening and pus formation would have promptly relieved the condition.

The use of antibiotics in puerperal mastitis was evaluated in a recent study (Ref. 2). It was found that patients treated with mechanical support of the breasts and application of local heat recovered on an average in twentyfive days. Penicillin and sulphonamides delayed the formation of abscess, and the illness lasted thirtyone to thirtyfour days. Incision was necessary when abscess formed in both groups of patients. This is one instance emphasising the need for a constant critical attitude on out part.

I have seen a patient with pyometra being treated with penicillin and streptomycin for about one month, while she was gradually going down hill. The uterus was a huge bag of pus, and an incision through the posterior fornix relieved the patient in a matter of hours, and put her on the road to recovery.

It is probably true that the lament of the venereologist about his dilemma is not peculiar to his branch alone, but the difficulty is felt by practitioners of other specialities as well. The otolaryngologist probably sees a number of discharging ears after the sufferers have had the whole array of antibiotics administered locally, orally and parenterally. The good surgical principle of drainage established by experience is ignored. The patients might have had better progress if cleaning the ears had been meticulously performed. I should not wonder if the ophthalmologist has an equally sad story to relate. The phthisiologist commonly sees patients who have had 'courses of streptomycin' off and on, while no attempt has been made to chalk out a therapeutic programme for the individual patient. The old established methods of adequate rest, nutrition fresh air, and the appropriate use of surgical methods are emphasised in lectures, but sorely neglected in practice. The magic of the antibiotics has lulled us into a false sense of security.

SUMMARY AND CONCLUSIONS

Antibiotics provide very effective control over infections, and it is our privilege to have them in our armamentarium. As with all privileges, care has to be exercised not to misuse them.

Precautions and procedures that were well known to the earlier generation need not now be cast aside.

Antibiotics are by no means a sort of ultimate weapon in the fight against disease, and a constant critical attitude is essential to use them safely and effectively. Improper use gives rise to difficulties in diagnosis and management. Development of resistant strains of bacteria can do much harm to the patient himself, and by dissemination, to others coming in contact with him.

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A somewhat tipsy gentleman boareded a two-story bus in Chicago and sat down near the driver. He talked and talked until the driver tactfully suggested that he go up to the top deck to enjoy the fresh air. The drunk amiably went upstairs. In a few minutes he was back.

"What is the matter?" asked the driver "Disn't you like it up there?"

"Yelp. Nice view. Nice air. But it ain't safe. No driver."

Pathologico-Physiological Characteristic and Principles of Treatment of Intracranial Injuries

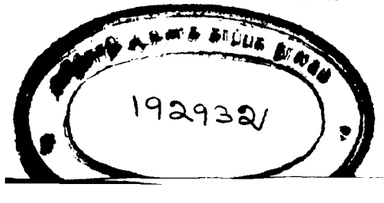
BY N. GRASHCHENKOV, I. IRGER AND G. KASSIL

CLINICAL and anatomical comparisons have shown that, in cases of brain injury, we must distinguish between intracranial hæmorrhages, caused by injury of the blood vessels, and hæmorrhages conditioned by acute dynamic disorders of the cerebral blood circulation and by changes in the permeability of the vascular walls.

It has been established, by means of research with the aid of radioactive isotopes, that in all forms of intracranial injury, beginning with light forms of concussion of the brain, the hemato-encephalic barrier becomes more permeable.

On the strength of this data, slight subarachnoid hæmorrhages, in whose case clinical and physiological examinations fail to establish symptoms of the cortex, may be regarded as consequences of an acute disbalance of cerebral blood circulation. Hæmorrhage into the soft cerebral membranc, caused by the disbalance, can manifest itself through symptoms of the cortex as well. But the slow disappearance of these symptoms and concentration of the pathological electric activity of the brain are symptoms in favour of injury of the cerebral substance and blood vessels.

The development of a massive centre of intracranial hæmorrhage in the closed cranium provides an additional condition for symptoms of acute disorder of the cerebral blood circulation developing in areas lying at a distance from the centre of initial hæmorrhage.



Surgery is applied with the object of removing the centre of initial hæmorrhage, but the success of the operation also depends on the degree to which secondary hæmorrhages have developed and the reversibility of the cerebral lesions.

In cases of slight and medium intracranial injuries, a decided effort should be made to increase the resistence of the hæmo-encephalic barrier. In grave cases of intracranial injury the problem of diminishing the irritability of the cerebral nerve centres acquires major importance.

DIAGNOSIS OF BRAIN TUMOURS WITH THE HELP OF TRACER ATOMS

The tracer atoms method is of great importance for the solution of the problems of topical diagnosis of brain tumours. The utilization of tracer atoms increases the accuracy of topical diagnosis to 96—98 per cent, eliminates the necessity of subjecting the patient to pneumo-encephalography, and arms the neurosurgical clinic with a new technically simple method of diagnosis which is harmless both to the patient and to the staff. The best results are gained by applying the radioactive isotope of iodine—131. Iodine is selectively taken up by the tumour tissue and creates a centre of gamma-radiation in the brain which is caught by a sensitive scintillation counter through the integuments of the skull. The site of the tumour in the brain is determined by maximum gamma-radiation.

The methods of applying radioactive iodine in the diagnosis of brain tumours are as follows: The patient is given 200 microcuries of radioactive iodine internally (after preliminary saturation of the thyroid with Lugol's solution in the course of 4 days). An hour after the introduction of iodine—131 the scintillation counter assesses its spreading through the brain tissues.

The surface of the patient's skull is studied at 30 different points, symmetrically at 15 points on each side according to a craniometric grid. The study of each field continues for 30 seconds and the entire examination takes half an hour. The data of radiometric examinations are registered in the form of an asymmetrogram on a ribbon of a self-recording potentiometer and then plotted on a diagram of the skull.

The results of the examination show that gamma-radiation coming from the brain is highest from one to two hours after internal administration of iodine. The intensity of the counts varies from 3000 to 6000 impulses a minute. The zone of the suspected tumour shows a frequency of 1000—3000 impulses above normal. Oscillations of over 10—15 per cent are indicative for the presence of a tumour.

The scientific elaboration of a method of diagnosing brain tumours with the help of labelled iodine has been conducted in the Leningrad Neurosurgical Institute since January 1954. A highly sensitive experiment scintillation counter was built. It has been tested on patients with brain tumours of various location and genesis. More than 100 patients were examined. In the majority of cases a correct topical and differential diagnosis of brain diseases was made with the help of iodine—131.

The method of isotope diagnosis of brain tumours should be widely introduced into practice. An important condition for the further development of this method is the application of a two-channel system of detection and the development of the scanning method.

A movie usher, noticing a woman groping over the floor in front of her seat, waved his flashlight around. "What are you looking for?" he whispered

"A caramel," she said.

"All this fuss over a piece of candy!" exclaimed the disgusted usher.

"Well, yes" said the woman "My teeth are in it!"

* * * *

The haughty society woman called at the hospital to see her injured chauffeur.

"He's a very sick man" said the nurse "Are you his wife?"

"Certainly not. I'm his mistress" the good woman blurted.

Some Common Diseases in Children and Advances in their Treatment

BY CH. KRISHNAMURTY
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THE discovery of Chemotherapeutics and antibiotics like Sulphanilamides, Penicillin, Streptomyecin, Chloromyecetin and aureomyecin has changed the treatment of diseases in children as much as in adults. Injudicious use of broad spectrum antibiotics has also brought in new complications like monilial infection, agranulocytosis or aplastic anæmia. These changes are more marked with aureomyecin or chloromyecetin. The whole ailmentary canal from the mouth to the anus is inflamed severe stomatitis, exfoliation of the mucus membrane in whitish patches, vomiting, diahrrhœa with greenish mucoid stools, ulceration round the anus and malena occur. Monilial infection of the lungs after treatment for pneumonia in children with broad spectrum antibiotics was reported. The cause appears to be fall in the normal vitamin B complex level and super added infection by the fungus, Candida albicans. The child will be unable to suck or take its feeds and what with the vomiting and diahrrhœa, becomes emaciated. The first principle in treatment therefore, is to stop the antibiotic that caused it and put the child on curds, butter-milk or Eledon for its diet. Pentamidine 200 mg. intramuscularly every 12 hours rapidly improves the condition in 4 days. Other drugs useful are Nystatin, Mysteclin, Erythromyecin, or Entero-vioform. A 1% solution of gentian violet can be painted locally. Children however prefer glycerinum boracis as the former is rather bitter. I have seen a few cases and found the above treatment satisfactory.

The common infections of childhood met with are (1) Upper respiratory infections, usually due to Streptococus, namely sore throat, Coryza and inflamed tonsils, (2) Otitis media, (3) ailmentary disorders of the gastro intestinal system, namely Colic, Constipation, indigestion, vomiting and diahrrhœa particularly in summer, and dysentries, (4) Exanthematious fevers like measles or chicken pox, (5) Urinary tract infections namely pyelitis from B. coli usually.

Bronchitis, Bronchopheumonia, Whooping Cough, are also common in certain seasons, as also influenza, Malaria, Polio or meningitis. Enlarged tonsils or adenoids are common but they run a chronic course and Scarcely attract the attention of the parents. They are more often pointed out by the school medical officer or the family physician. If the Child is crying incessantly, usually there is an acute sore throat or a middle ear infection or intestinal colic from constipation. The standard treatment for inflammation of the throat or the ear is with sulphanilamides with or without Penicillin. An alkaline diaphortic mixture with sodium salicylate can be usually given in addition. For a child of one year 1/2 a tablet of Sulphadimidine or sulphadiazine every four hours with two teaspoons of the mixture is good. Penicillin can be added on to the treatment if the infection is resistant to sulphas, or when it is vomitted. 2 lacs of procain penicillin intramascularly once or twice a day according to necessity can be given. Children are very fretful and nervous and more so when temperature is high, and the parents are more worried. A sedative like phenobarbitone or largactil quietens the child, gives it the much needed rest and helps to bring down the temperature. Local applications to the throat like mandell's pigment and fomentations externally greatly help. If an upper respiratory infection has crept to the bronchi or the lungs, more drastic treatment becomes necessary. If there is cyanosis or dyspnœa, oxygen inhalations become necessary. If sulphas or penicillin are not effective, chloromyecitin, aureomyecin or Tetracycline have to be used. Colic from constipation is relieved by glycerin enema and if due to indigestion, carminatives with bromide and belladona and attention to proper dieting is needed. Gastro intestinal troubles, particularly summer diarrhœas are due to (a) Food irritation through faulty feeding, (b) infection carried through hands, feeding bottles or flies, (c) specific causes like dysentry or enteric group of infections, (d) nervous causes. The old treatment with Castor oil emulsion, Hyd. c. creta, pulvis. rheii co, fractional calomel doses, combined alkaline saline treatment and apple jelly treatment have all gone out of use. Fear of dehydration, disturbance of water and salt metabolism mostly

account for it. Sulphaguanadine, Thalazole, kaolin and in severe cases Streptomyecin, Aureomyecin or Chlorostrept have taken their place. Many proprietary brands like cremosuxidine, streptomagna, Guanomyecin zinalka, are now put up. Elkosin is another sulpha compound used extensively for all streptococal infections of children. If a specific cause can be found on examination of the stool, as Entamœba histolytica, appropriate treatment is given. If a child is nervous, a sedative like phenobarbitone with kaolin mixture or cremosuxidine answers well.

Exanthematous fevers like measles or chicken-pox are common in children. In fact a child rarely escapes measles. There is no specific treatment for measles or chicken-pox nor can it be protected against with vaccination as in smallpox. Convalescent serum is reported to be effective against measles as a phophylactic. Although the parents have sentimental objections to continue medication after the rash has appeared on the fourth day of the fever in measles, continuance of treatment is desirable as sulphas and pencillin prevent complications.

Urinary tract infections are often a cause of illness as a result of pyelitis from B. coli infection. Treatment with sulphas and streptomyecin cures it.

Infantile convulsions as an emergency is commonly a result of constipations, round worms, onset of acute infectious diseases, teething rickets, meningitis or epilepsy. The parents are frightened and all sorts of home remedies are tried, most often branding on the fore head or the temples. The child should be put in a hot bath and cold applied to the head, an enema of glycerin, a dose of calomel, santonin and soda bicarb and paraldehyde intramascularly or per rectum control the convulsions. If convulsions are frequent, luminal 1/4 grain or phenobarbitone can be given to the child of one year and repeated if necessary. In bad cases, inhalations of chloroform or even morphine may be necessary when all this fails. When the child comes round chloral hydras with bromides can be given. The cause of convulsions must be investigated and appropriately treated.

Infantile beri-beri is more common than is supposed. A number of children die successively even in the same mother. The essential cause is a deficiency of vitamin B1 in the mother inherited by the infant. The diet of the mother during the antenatal period is improper or in adequate or both. Thanks to the economic stress in the average poor and middle class families, milled rice, milled dhall, lacking in vitamin B1 content, insufficient proteins, minerals, fresh vegetables, milk and fats are responsible. Most of the families cannot afford milk in their dietary. The middle class have some watery coffee or tea with an ounce or so of so called milk diluted both at home and by the unscrupulous vendor outside. The mothers usually show signs and symptoms of vitamin B1 deficiency in the antenatal period, in the form of tingling and numbness of legs, and hands, pricking sensations and chelosis. These become worse as pregnancy advances, œdema and general anasarcd with dyspnœa on exertion and anæmia follow. The prevention of infantile beri-beri is therefore proper antenatal care of the mother and adequate feeding. The signs and symptoms of infantile beri-beri vary from intermittent crying as if having an abdominal colic, greenish mucoid stools, hoarseness of the voice and ptosis, to dyspnœa, sighing and gasping for breath and immediate death. Many diseases like bronchitis, brochpneumonia, diarrhœa or dysentery may be associated with it. Prompt use of Vitamin B1 saves the life of the infant. I have studied this for over 15 years and published my experiences in the Antiseptic and Medical and Surgical News.

Diseases of infants due to deficiency of Vitamins A and D. The triad laryngismus stridulus, infantile tetani and rickets come under this head. The first two present an alarming picture. In laryngismus stridulus the child is breathless, cyanosed and has a stridor. The child appears moribund. The room should immediately be set up with a steaming kettle, with tincture benzoin co added to it. A small dose of liquor adrenalin hydrochloride, m 2, to a child of one year hypodermically or a dose of syrup ephedrine by mouth followed by aureomyecin or chloromyecetin every six hours relieve this acute phase. Vitamin A and D should next be given in the form of Adexolin or Haliverol, Ostelin and calciferol. Calcio-ostellin, parenterally is valuable.

Infantile tetani shows in the form of convulsions and carpos pedul spasms particularly. Injections of Calcium gluconate or chloride ward off the convulsions. Vitamins A and C to retain the blood calcium level later, should be continued for a long time to prevent further seizures. Rickets due to lack of Vitamins A and D in the diet of the child is seen more often in those brought up on artificial foods. The child is irritable fretful, kicks off its bed clothes, has sweating

of the head easily observed while the child is asleep and is a very early sign, frequent gastrointestinal upsets like vomiting, diarrhœa, tumid abdomen and an enlarged liver and later cartilagenous or bony changes set in, tenderness of epiphyseal ends, ricketty rosary, curvatures of bones like genuvalgum, or varum etc. Cows milk, cod liver oil, fruit juice and sun's light after injunction of the body with shark liver oil or any other in the morning are the remedies. Liver extract is also helpful in the cure of rickets. There is an ancient practice in some of the districts of Andhra Pradesh of smearing gingelli oil a numer of times every day on the infant's body and fomentation with oily hands to the abdomen, chest and back on alternate days. This has much to commended it though it looks brutal to day. This regime manufacturers vitamins A and D and stores it in the body of the infant, and thus raises its resistance. Children brought up this way resist infection and rarely suffer from the common ailments as others do.

Whooping Cough, runs in epidemic proportions and has a protracted course. Chloromyecetin and aureomyecin have of late been used in its treatment. They are effective only if the case is seen within ten days. The older remedies like bromides, Belladona, Ipecac, camphor co, Ephedrine, Vitamins C and K are still the main stay, as the broad spectrum antibiotics are costly and fraught with dangerous complications. Sometimes, and have a limited application. Aerial rides are also helpful. Pertussin, containing thymus extract is also helpful. Immunisation with triple vaccine against Diphtheria, Tetanus and Whooping cough is used nowadays for prophylaxis. There is great affinity between measles and whooping cough and the latter is a frequent complication of the former. The temperature in children is more unstable than in adults and abnormal heat is more liable to escape notice. It means it causes less definite symptoms of illness. Temperatures of over 102°F. even, are often overlooked. Some children of even six or upto—eight years get a sharp rise with a fit of indigestion or cough with a foul tongue. A mild aperient sets it right. Others have sharp fever with sore throat. A number of children have simple continuous hectic fever like tuberculosis. Epidemics of gradual onset rising to a peek and then slowly declining are common with infections fevers of childhood. Such epidemics are usually air borne, that is droplet or dust infection, many such show a seasonal incidence as polio, in late summer months, others show a rhythm over a period of years as measles, which may be endemic at all times and in all probability assume epidemic proportions when susceptible children accumulate. Infections due to malaria influenza, septicæmia or pneumonia are not uncommon in children and are treated as in adults.

Enlarged tonsils and adenoids: are frequently seen in children and are usually pointed out by the school medical officer or the family physician. Many parents believe they should be removed and there was a time when their removal was the rule. Statistics proved that those who had their tonsils removed were more prone to infection. They should not be removed unless they cause obvious discomfort such as difficulty for swallowing; nasal obstruction, frequent infection or predisposition to status lymphaticus. Mild treatment on general principles and local application of mandell's solution with ether answers well. The tendency of lymphoid tissue towards involution about the time of puberty should not be forgotten. If their removal becomes imperative, preliminary treatment with pencillin and sulphas before operation and there after should be given. No operation should be undertaken when polio is round about. Keratomalacia is another fell disease which accounts for a good number of cases of previtable blindness in children and is due to deficiency of Vitamin A. Xerosis, night blindness, loss of lustre of the cornea and ulceration leading to a loss of the eye occur. The child has photophobia, Lacrymation and blepharospasm and sun's light. The skin is dry, there is diarrhœa, the liver is enlarged and the abdomen tumid. Treatment on the same lines as for rickets with cow's milk, cod-liver oil, oil injunctions with sun's rays and fruit juice are necessary. Small doses of Thyroid improve the skin condition. If the child is having diarrhœa, it should be started on whey and slowly replaced with milk. Treatment for the eye condition should be carried out symptomatically with mild remedies. Atropine in oil, argyrol, pencillin drops etc.

Another disease I would like to refer to is rheumatic fever in children, a child generally over five years of age has slight fever about 101°F. for a couple of days and complains of vague pains in the limbs, more often the lower, occasionally, pain and swelling of the Joints but not as markedly as in adults. Examination of the throat shows enlarged tonsils, the attack passes off and similar attacks may come on three or four times once in two or three months and leave the child with a damaged heart. In its insidiousness lies the danger, as it does not attract

attention. The saying that rheumatic fever licks the joint, Kicks the brain and bites and heart is perhaps more true in children. There has not been any great change in its treatment and the salicylates are still the specific while sulphas have come in as additional remedies. The latter are used as prophylactics to prevent relapsis in winter and have been found useful.

Tuberculosis meningitis though not common, is a dangerous disease in children and they are more suspectable. The infection is conveyed by the blood stream to the brain from some focus in the body like the lungs or mesenteric or the mediastinal glands. Its onset is insidious and signs and symptoms are slow in development. Lumbar puncture and examination of C. S. F. clinch the diagnosis. Daily injections of Streptomyecin intramuscularly and intrathecally with P. A. S. and I. N. H. by month is the best treatment. Before the discovery of Streptomyecin in 1944, there was no treatment for T. B. meningitis and mortality was very high.

Anæmia in children from helminthic infections as hook worm or round-worms, after acute infectious diseases, and improper nutrition is common in the poorer classes. Treatment with iron after eliminating the cause and adequate intake of proteins and vitamins cures the condition. Many piperzine derivatives like Helmacid, Crystoids and various others safer than the old santonine, Carbon tetra chloride or oil of chenopodium, have come in and are less toxic and more agreable for children as anthelmantics.

Any disease may affect children. I have tried to present some common ones in my experience of over 43 years. I do not claim anything original and I have avoided details lest it should make the paper lengthy.

Pharmacological treatment of aged patients in a state mental hospital

Levy, S., *Journal of the American Medical Association*, U. S. A., 153 : 1260-1265, December 5, 1953.

The value of various stimulatory, vasodilatory, and enzymatic drugs in the treatment of aged persons hospitalized in a state hospital for the mentally ill was studied. It was found that the greatest improvement for this type of patient was obtained with a combination of pentylenetetrazol (Metrazol) and nicotinic acid. These drugs were combined in an elixir containing per drachm 3 grains (0.2 gm.) of pentylenetetrazol and 100 mg. of nicotinic acid with compound pepsin elixir as the vehicle. It was given in doses of 1 drachm three times a day. This elixir produced physical improvement in the patients both objectively and subjectively, produced a marked improvement in their behavior and a better performance on psychological testing with an increase in the intelligence quotient, restored to normal previously abnormal blood lactic acid values, and restored to normal some of the previously abnormal electroencephalographic tracings. Cytochrome C on the other hand, which previously has been said to be of value for this type of patient, has not shown beneficial effects, at least in the doses administered in this study. In fact, it was found that, after administration of cytochrome C, there was not only a slight deterioration in the patients' behavior but also a tendency toward secondary microcytic anemia.

On the basis of this study it is, therefore, felt that the combination of pentylenetetrazol (an analeptic) and nicotinic acid (a vasodilator) is of value in the treatment of aged patients hospitalized in an institution for the mentally ill. It is particularly helpful for those with only mild memory defects, confusion, and deterioration in the absence of more serious emotional and psychiatric disturbances. It seems especially helpful in combating symptoms of abnormal behavior, and those are the symptoms that are most objectionable to the family members and relatives. On the other hand, symptoms pertaining to intellectual impairment are not combated so effectively with this combination of drugs. This might be due to the fact that intellect and memory are first to suffer, while personality and behavior changes occur later. Thus it may be assumed that the former phenomena depend on more definite organic changes that may be irreversible, while the latter symptoms, those dealing with impaired behavior, to some extent may still be reversible.

This combination has proved safe and simple as well as practical and inexpensive, and thus can be used without hesitation on an ambulatory basis. With its use it should be possible to ease the burden of caring for the mildly confused and mildly deteriorated aged patients in public and private psychiatric institutions. Thus a smaller proportion of hospital personnel and budget would be needed for what previously amounted only to custodial care of this group of patients. This saving would eventually enable the mental hospital to return to its primary function, namely, the treatment and rehabilitation of younger mentally ill patients, instead of becoming a purely custodial organization for the aged. Since many of the aged persons studied showed only the commoner evidences of simple deterioration, only modification of the conditions for which this elixir has proved successful was required. Many of these patients, with the aid of this elixir, or possibly similar acting drugs would therefore not inevitably have to be committed to psychiatric institutions and could be permitted to live in the community with safety and without harm to others.

Some Observations on the Epidemic Influenza

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AFTER about forty years we are having our national share of epidemic influenza. As compared to the previous epidemics this seems to be a little less severe. In the modern era with the speed of human travel, space and rapidity of spread of the disease is not limited. Sometimes the origin of the disease appears to be simultaneous in many countries. This disease is still evasive to preventive medicine and all public health measures. This disease has been known for over five centuries, occurring in pandemics and epidemics at irregular intervals. During such times the disease assumes a more virulent form and is highly infectious. One attack does not confer an immunity and in fact it is observed that it produces susceptibility.

Certain observations of a general nature about this epidemic are made. These are more or less disjointed ; so they are divided into certain convenient headings.

PYREXIA

Abrupt onset of the fever with the invasion of symptoms is a marked feature. The onset is so abrupt that the patient can even tell the exact time of getting the fever. This is well illustrated in the following case. An attendant who accompanied a patient to my office returned back in less than an hour with a temperature of 102°. The temperature may go upto 105° or more and in some cases goes to hyper-pyrexia. The cases coming up at the beginning of the epidemic do not show as high a temperature as those coming up later on when the epidemic is at its peak. The temperature is remittent or intermittent and in uncomplicated cases lasts about 3 to 5 days and falls to normal, mostly by lysis. Only in a very few cases it comes down by crisis. Very often after the temperature touches normal it tends to remain at sub-normal level for a few days before gradually coming back to normal.

Response to various anti-pyretic drugs is a good sign. At an early stage with anti-pyretics the temperature comes down with a sweat and rises again. Intensely toxic cases do not show response to such drugs and they should be taken as serious ones and repetition of such drugs is unwise. It is also unwise to give such drugs to cases of hyperpyrexia.

Rise of temperature to a higher level without remission indicates that the case is a severe, toxic one. Sudden rise in temperature after it is once normal at a lower level indicates some pulmonary complication. Sometimes with the onset of complication the temperature goes up to hyperpyrexia with shallow respiration, dry tongue and lips and proportionately low pulse rate. The subsequent course of temperature depends upon the type of complication.

True relapse of the disease is not uncommon but preventible. Too soon a resumption of activity and dietetic factors both quantity and quality, are the commonest causes of relapse.

The invasive symptoms are pain in the body, limbs and back, headache, pain in the eye balls. These symptoms, particularly headache and backache continue for varying periods even after the temperature drops down to normal.

RESPIRATORY SYSTEM

This system is affected in very many ways. Catarrhal process of the lower respiratory tract is more often met with than upper respiratory tract. These manifestations extend from laryngitis tracheitis, bronchitis to lobar and lobular pneumonia, and pleurisy. Laryngitis is not much in evidence in this epidemic excepting in a small percentage of cases.

The characteristic feature is pulmonary congestion of varying degree, being very intense in severe cases. It may be unilateral or bi-lateral, and more common in the bases than in the apices. Sometimes signs are heard all over the lung fields. Copious fine rales and impaired breathing are the main physical signs in all cases. These physical signs vary from day to day depending upon the development of the case. In all severe cases there is an intense pulmonary congestion which is the cause of bloody sputum and cynosis. The severity of the case is directly proportionate to

the degree of pulmonary congestion. The more intense the pulmonary congestion is, the more severe the case is and the cardiac embarrassment is also proportionately more. These cases are more prone to get consolidation. The outcome of the severe cases depends upon the extent of the pulmonary congestion and the effect of toxæmia on the heart and central nervous system. The prognosis of the case also depends on the general condition of the patient. The extent of consolidation is not a criterion.

Cough varies from the dry, distressing type to that of throwing out a large amount of frothy sputum. Dry cough is often found in mild involvement of the respiratory passages. Sometimes the sputum may also be absent during the whole course of illness, even though the case is severe with intense pulmonary congestion. The amount and quantity of sputum vary considerably. There are two kinds of sputa characteristic of influenza.

1. Large quantities of bright, pink, mucoid type. The reddish colour in this kind is due to the pulmonary œdema. The quantity may be very large and thrown out both by cough and involuntarily through the nostril.

2. Tenacious mucous of different colours, red, brown saffron and green, all at the same time. This kind of sputum is diagnostic of influenza.

Less characteristic sputa like tenacious mucous, muco-pus and rusty colour also occur.

GASTRO-INTESTINAL SYSTEM

Vomiting is a common feature both in mild and in severe cases. In some cases it simulates food poisoning. Nausea without vomiting is much more commonly present in many cases. This is particularly severe in the gastro-intestinal type of cases. Sometimes the onset of illness is with incessent vomiting, high fever and prostration. There may be pain in the addomen and tenderness in the epigastric region. When it is attended with diarrhœa it is likely to cause confusion in the diagnosis. Rashes like those seen in measles are met with occasionally, particularlly in children.

POST-FEBRILE PERIOD

The fever having subsided and the acute symptoms passed, then comes a state of extreme cardiac and nervous fatigue which is quite disproportionate to the severity and duration of the illness. This period is most annoying to the patient and the practitioner. Most patients seem to think the pyrexial period itself was less trying. It is this period that is the important phase of the disease. Great caution is required now in handling the case. Most patients sweat profusely at this stage.

Relapse is a preventable complication. Too soon a resumption of work, indiscretion in diet, both quality and quantity are the contributary factors. Careful enforced rest in bed is necessary.

CIRCULATORY

Toxic myocarditis sometimes occurs, but this passes off after a few days of continued recumbency. There is a certain amount of dilatation of the heart during an attack of severe type. Perhaps, much more common affection of the heart is what may be termed cardiac neurosis. Patient complains of palpitation and discomfort or pain on the chest. This arises some days after the fever subsides. No defects can be discovered on examination. This is associated with mental depression that often follows an attack of influenza. These are more often seen in women.

NERVOUS SYSTEM

Higher centres are affected mainly. Intense depression is common and sometimes emotional instability follows. The depression manifests itself in the acute phase of the fever and continues for a considerable time.

The headache of the acute illness sometimes continues for some days after the acute phase settles down.

RESPIRATORY SYSTEM

Pulmonary system is another site that bears the brunt of the disease.

1. Persistence of a state of chronic congestion of the lung or bronchiolitis. Sometimes this may involve the pluræ. This state may persist for weeks or even for some months. The main symptom is the brassy cough.

2. Persistence of pneumonic patches. This may be the patch of consolidation that occurred during the fever continuing to persist or it may arise after the temperature comes down to normal. These patches clear up with antibiotics, though in some cases of low general condition it may take a few days more than those with better tone of strength.

3. Bronchiectasis is rather a late complication and not very common. I have had one case so far, who developed bronchiectasis changes in the right lower zone.

4. Asthma is rare. But all patients who are already subjects of asthma have flare up and bronchespasm is noticed both in children and in adults.

DIAGNOSIS

The clinical diagnosis of influenza during an epidemic is not difficult, mainly because most of them present common symptoms which are similar. Also there is no time for bacteriological examination. In these circumstances, when the practitioner is in doubt, it is best to treat the case for influenza. Mild cases do not cause any problem and in all severe cases it is worth treating them for influenza, unless there are definite clinical signs indicative of some other disease, because most of these cases do need some antibiotic. This is particularly applicable to the respiratory type of cases. Cases that do not have pulmonary signs and those of the gastro-intestinal types need a careful examination. In cases where the temperature touches normal for a few days but again shoots up a relapse or a complication should be suspected.

PROGNOSIS

In spite of the various manifestations and various grades of severity, it is not very difficult to assess the prognosis. The rapidity of onset, the severity of the initial symptoms, initial high temperature, and the patient's discomfort are really the signs to be relied on.

Prognosis depends on 1. Earliest medical attention. Cases that get early medical attention show good prognosis, unless they are fulminating cases. Most of the cases that come late for treatment are severe and probably have complications. Prognosis is bad in these cases.

2. Prognosis is bad in fulminating cases.

3. Cases with continued high fever and severe pulmonar congestion have poor prognosis.

Prognosis is good in mild cases and in those who have had pulmonary complications but had early treatment.

TREATMENT

In influenza treatment should be instituted promptly and carried out thoroughly. This is important both from the point of the individual case and from the point of public health. Every promptly treated individual prevents further spread of the disease. Also the prompt attention gives the patient the confidence that he will recover soon and prevents the anxiety about the dreaded complications.

The treatment is directed to cut short the course of the illness, and is regarded mainly as expectant. In as much as one cannot foretell in the beginning as which case is mild and which one is severe it is best to treat all cases as severe ones at the time of the onset of illness.

Patients should be put to bed as soon as the first symptoms are noticed, and kept in bed for a period of 48 hours after the temperature is normal in mild cases and even longer in more severe and complicated cases. The room should be well ventilated as far as possible. Premature resumption of work is liable to cause relapse, which is likely to be more severe.

DIET

Hot drinks can be given frequently. As the illness clears up it can be gradually stepped up.

Constipation should be corrected. Milk of magnesia is useful for this. Diarrhœa should be treated with koalin and pthalylsulphathiazol.

Vomiting, if mild, passes off with a little correction in diet. If severe, Chlorpromezine can be given in small doses which arrests it.

Control of pyrexia is very important and for that it is still the time-honoured aspirin and Dover's powder that hold the field Aspirin in 5—10 grs. doses can be given and repeated every six hours or aspirin and Dover's powder each in 5 grs. doses can be mixed and given. This makes the patient comfortable, as

the temperature is controlled and pain relieved. Together with this some simple diaphoretic can be given.

Cases of hyper-pyrexia should be handled carefully. Here febrifuges must be avoided. Tepid sponging should be resorted to, till the temperature settles down a little. Stimulants should be given to counteract the circulatory failure.

Cases showing pulmonary signs need the greatest attention of the practitioner; and probably most of his cases are of this type. The treatment of the respiratory catarrh is the same as those that occur independent of influenza. But the problem that confronts the general practitioner in the treatment of influenza is in deciding when to give the anti-bacterial therapy and if so what to give. It is certainly not wise to put all cases on anti-bacterial therapy, because minor catarrhal infection of the upper respiratory tract will recover without anti-bacterial agents. During the epidemic the practitioner will not wish to prejudice the recovery of his patient by with-holding such drugs. It is therefore probable that he will err on the side of overprescribing than underprescribing, but it should be remembered that an excess of prescribing is not overdone. One of the reputed physicians of this city in a report to the lay press, advised people to take a particular brand of supha drug as a preventive of influenza. It is a deplorable kind of propaganda. No sulpha drug has any place as a preventive of influenza.

Once it is decided to use anti-bacterial therapy then comes the problem of what to use. It is certainly wise to put all cases needing such treatment, either on Pennicillin or on Sulpha or both, if necessary. There are certain exceptions to this.

1. Those patients who are known to be sensitive to any one of these drugs.

2. Those patients who are severely ill when first seen and the necessity of a Tetracycline drug is felt.

It is difficult to give an indication for use of anti-bacterial therapy or for any particular type of drug. But it is wise for any practitioner to put the patient on this therapy, when in doubt, rather than with-hold it. All this he has to do on clinical evidence. And the clinical evidence one depends on are the severity of the illness on first examination, the physical signs, and the nature of the sputum. It must be remembered that sufficient dosage of the drug is necessary, be it Sulpha, Pennicillin or Tetracycline group of drugs. Side by side symptomatic treatment can be carried out.

CONVALESCENCE

During convalescence adequate rest should be given. Early resumption of work should be forbidden. Diet should be gradually increased, both in quality and in quantity to ensure complete recovery. Adequate amount of vitamins may be added to the diet.

During the epidemic instances of people coming to the practitioner, complaining of pain in the body and respiratory catarrh, but without any raised temperature, are not rare. This brings the question of apyrexial type of influenza. Making a definite diagnosis, in the absence of fever is rather difficult, but one can with a certain amount of confidence treat them for influenza, particularly during an epidemic. One should remember that Typhoid fever may be apyrexial at times.

A second wave of epidemic is anticipated, and this is not unusual. It has been in record that all most every pandemic has been followed by a secondary wave, which appear to be more severe. The second wave that may come will probably a different strain of virus and all machinery in public health must be put to gear to prevent it.

HARMFUL EFFECTS OF DIETS DEFICIENT IN PROTEINS

Arends, A. and Nieweg, H.O., *Nederlandsch Tijdschrift v. Geneeskunde*, Netherlands, 97 : 2123 - 2130, August 15, 1953; through: *Journal of the American Medical Association*, 153 : 1589, December 26, 1953.

The histories of five patients in whom various pathological conditions developed as the result of low protein diets are presented. A woman, aged 52, had eaten a low protein diet for about 18 months because of disturbance in renal function, and for about six weeks her diet had been practically free of protein. After this megaloblastic anemia developed. Liver function tests revealed megaloblastic anemia in a 42-year-old woman whose diet over a period of six years had contained no animal proteins because she had renal disease with hypertension. An 18-year-old boy who had received a diet very low in protein because uremia was always impending, had a blood picture characteristic of erythroblastic anemia. He died and necropsy revealed severe atrophy of the spleen. The fourth patient, a 53-year-old woman, had been given a low protein diet for six months. This woman and the fifth patient, a man aged 45, showed severe liver damage at autopsy. Protein deficiency may have a harmful effect on the liver.

POST PARTUM HEMORRHAGE

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THE chief cause of maternal mortality is obstetric hæmorrhage (Lund). The hæmorrhage which kills in child-birth occurs chiefly during and after the third stage of labour (Randall). According to Miller, a large proportion of deaths due to it is preventable—possibly as much as 60%.

The birth of a baby evokes considerable excitement all round. Yet, as soon as baby is born, enthusiasm tends to flag. It is very often during this stage that post partum hæmorrhage strikes. The wise obstetrician devotes the same vigilance to his patient after delivery as he would to a patient who has just had a major abdominal operation. Prevention is always better than cure. There are certain conditions in obstetrics in which the incidence of post-partum hæmorrhage is high and it is possible to be prepared to deal with such an emergency. Some of these conditions should be borne in mind.

A uterus bleeds because it is tired, or has been insulted. The insults may be inflicted by nature as in over-distention by multiple pregnancy, a very large or awkwardly placed baby and poly-hydramnios, or by the obstetrician. Obstetric insults take the form of a violent internal manœuvres such as versions, extractions, the oversight of a mild degree of cephalo-pelvic disproportion and the untimely application of forceps or even by an operation like Cæsarian section.

Once the child has been delivered, the uterus may be violated by meddlesome third stage management. A tired patient usually means a lax uterus. The tone of the uterus is greatly diminished.

The uterus works hard during labour. To work efficiently it needs oxygen. Anæmia during pregnancy, left untreated impairs oxygen supply to the uterus. Heavy sedation and deep anæsthesia both subject the patient and hence the uterus to profound anoxia. A protracted labour tires the patient, for a tired uterus is atonic. An atonic uterus bleeds. An uterus, the tone of which is disturbed or reduced, does not function properly. This is " inertia ". Fibroids and other local organic diseases which affect the uterus, as well as fear which exerts a powerful effect on the lower segment and inhibits cervical dilatation–all interfere with uterine tone.

When a placenta is attached to the relatively passive lower uterine segment, the large open venous sinuses of the placental site may be the source of profuse hæmorrhage. A partially detached placenta interferes with the ability of the uterus to contract and hæmorrhage may go on until the cavity of the uterus is emptied by manual removal of the placenta. Apart from insults to the uterus, severe injury can be inflicted on the genital tract. The use of strength rather than skill in extracting the reluctant child by the use of forceps applied through an incompletely dilated cervix can cause extensive lacerations. Even a timely episiotomy may not prevent further tears resulting as an unrecognized occipito-posterior head is delivered by powerful traction with forceps. Precipitate labour can injure the genital tract. The sudden emptying of the uterus may cause postpartum hæmorrhage (Fig. 1.).

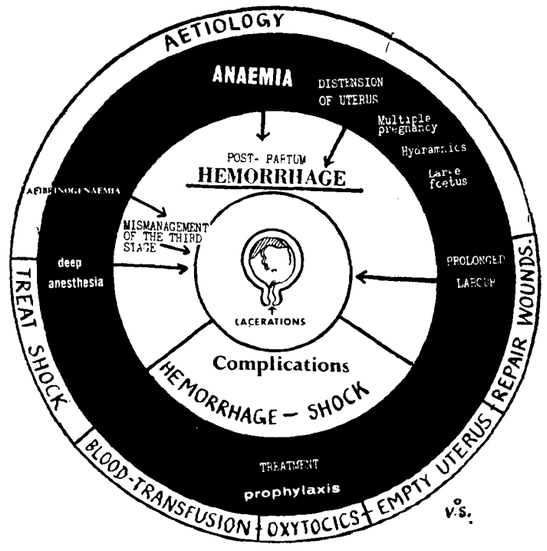

Fig. 1. This diagram devised by the author illustrates the ætiology, complications and principles of treatment of post-partum hæmorrhage.

For all practical purposes, postpartum hæmorrhage may be defined as that degree of hæmorrhage which occurs in that volume to cause a hazard to the well being of the mother (Howkins). It stands to reason that the same quantity of blood loss which may be tolerated by a well-built, well-nourished patient might prove sufficient to kill one who is very anæmic, tired and ill-nourished. Most obstetricians accept a blood loss of more than 20 ozs. in volume as post-partum hæmorrhage.

Post-partum hæmorrhage is a very important complication of the third stage which begins as soon as the child is born and ends with the delivery of the placenta. Post-partum hæmorrhage may occur in the immediate puerperium (within 24 hours after birth) or later. Hæmorrhage which occurs in the late puerperium is termed secondary post-partum hæmorrhage.

What can be done to reduce the risk of post-partum hæmorrhage and prevent it from becoming a killer? In conditions in which the incidence of the post-partum hæmorrhage is high, we can "be prepared". When labour is delayed good obstetric practice enables us to discover the cause. In prolonged labour, we can by re-assurance and the timely prescription of adequate and suitable sedation, allay fear and mental apprehension. Under no account should a patient be allowed to pass into a state of extreme exhaustion. De-hydration and de-chloridation can be prevented, if necessary, by giving glucose-saline intravenously.

We have some very important drugs to control hæmorrhage. Blair Bell, first President of the Royal College of Obstetricians and Gynæcologists in England discovered the oxytocic property of pituitary extract. Prof. Chassar Moir, Obstetrician and Gynæcologist at Oxford University isolated ergometrine. An account of the discovery of ergometrine is described very vividly by him in the latest edition of his excellent book (Munro Kerr's Operative Obstetrics, 6th edition by Prof. Chassar Moir, Bailliere Tindall and Cox, London, 1956.) "In 1932, while experimenting with graphic recording of uterine contractions, I discovered that there was in ergot a highly active substance which had hitherto eluded pharmacological detection. To it can be attributed the traditional clinical effect of the drug "the Dr. John Stearn's effect" – as it may be called, after a classical description (1808) of the action of crude extract on the labouring woman. At once an intensive search was begun. The late Dr. H.W. Dudley devoted himself to the chemistry of the problem and, over a period of nearly three years prepared many scores of ergot fractions each of which, I, in collaboration tested by the only method available to us – graphic recording of the uterine action of the puerperal woman. Early in 1935, after many disappointments, the work bore fruit: a new alkaloid with unusual solubilities was isolated. It was crystalline; it was chemically pure; it was non-toxic; it had the "Dr. John, Stearn's effect". We named it Ergometrine.

Meanwhile, search had also been in progress elsewhere, and from Baltimore, Chicago and Basle came the news of almost simultaneous success. But Ergometrine, now isolated by Dudley in a highly purified form, was unique in having its chemical characteristics accurately described and its method of preparation fully explained for others to follow. Moreover, it was, and continues to be, free from all patent rights and all danger of commercial exploitation.

A later and most interesting development has been the elaboration by Stoll and Hoffman of a new alkoloid methyl ergobasine (methyl ergometrine) or Methergine. This is a semi-synthetic product derived from lysergic acid which is the essential nucleus of all the ergot alkaloids. Gill, working in my department, has shown that the clinical properties of Methergine are very similar to those of ergometrine. It is somewhat slower in producing a uterine response, taking an average of 96 seconds after intravenous injection, as compared with ergometrine's 55 seconds; but weight for weight, it is rather more powerful and slightly more prolonged in its oxytocic effect than is ergometrine."

In cases where there is the remotest possibility of hæmorrhage or perhaps even in the normal course of labour it is customary to inject ergometrine intravenously after the birth of the head or the anterior shoulder of the child. If bleeding occurs, it may be repeated, and pituitrin may also be given but always by the intramuscular route. Pituitrin is the oxytocic fraction of pituitary extract. Within two minutes of intramuscular injection of 5 to 10 units, the uterus goes into a powerful spasm. This is maintained for about eight minutes. Strong contractions at frequent intervals follow. The effect wears off in half an hour. It should always be given intramuscularly because if injected into the vein alarming and serious effects may result. Very occasionally the drug gives rise to shock and collapse, probably due to constriction of the coronary vessels of the heart. It should never be given in doses of more than 10 or preferably 5 units. It

should never be repeated within half an hour of a previous injection. As a general rule it is always safer to relay on ergometrine rather than on pituitary extracts.

One of the great misdeeds which precipitates post-partum hæmorrhage is the mismanagement of the third stage. Who can fail to be impressed with the dangers of third stage mismanagement having once listened to this vivid but deliberately exaggerated account of middlesome midwifery by a renowned lecturer at St. Bartholomew's hospital? "The misguided massive midwife leaps on the patient like a tigress on her prey and performs a ferocious Crede – so violent that the abdominal compression results in evisceration of her abdominal contents through the vagina." Is it only midwives that are to blame? Are we not also prone to act likewise when we become impatient at the length of time the placenta takes to separate? Yet it is this very act which may lead to a catastrophic and torrential hæmorrhage.

When the mother is lying on her back and the child has been delivered and taken away to be cared for, there should be no interferance whatever with the fundus of the uterus. The terminal end of the umbilical cord to which an artery forceps had already been attached should be put in a dish placed between the mother's thighs. Usually the height of the fundus can be seen at a level about two finger breadths below the umbilicus. While the attendant should watch the fundus like a hawk he should restrain himself from unnecessarily prodding it about or squeezing it just to find out if the placenta has separated. There are certain characteristic signs of placental separation. The uterus which was hitherto antero-posteriorly flattened and not mobile becomes globular in shape and freely mobile from side to side. The fundus rises above the level of the umbilicus. There often is a slight discharge of blood and the extra-vaginal cord may lengthen. When these signs are present and an attempt is made to draw the uterus upwards, the extra vaginal cord does not shorten. The presence of all these signs in an almost certain indication that the placenta has separated and partially descended. When once it is certain that separation has occurred it is quite permissible to use the contracted uterine fundus as a piston and press it downwards and backwards so that it pushes the placenta from the vagina. As soon as the placenta is delivered, it should be supported with the right hand. The fundus should be drawn upwards, so pulling the uterus away from the membranes rather tearing the membranes out of the uterus. The uterus should then be massaged. The patient should be watched with great vigilance lest any subsequent bleeding occur (Fig. 2, 3, 4).

Fig. 2. This Photograph taken within a few seconds of the birth of a child shows the contour of the abdomen. The placenta has not yet separated or descended in the birth canal.

Fig. 3. This photograph taken by the author a few minutes later shows how the contour of the abdomen changes as the result of the fundus of the uterus drawing itself away from the placenta. The height of the swelling is more obvious. Palpation would reveal its globular shape and its free mobility from side to side.

When confronted with alarming and severe post-

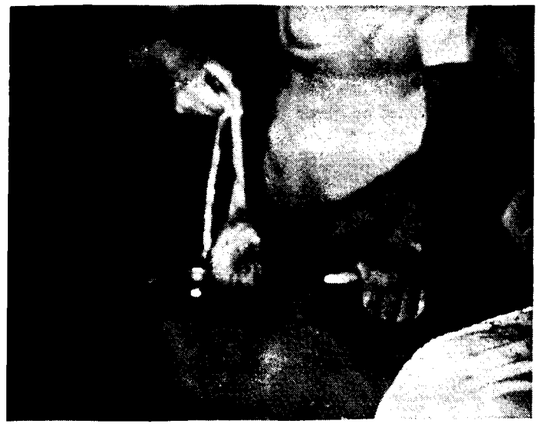

Fig. 4. Once it is certain that placental separation and descent has occurred it is permissible to use the contracted fundus as a piston and push out the placenta which lies in the lower part of the birth canal, simultaneously exerting slight traction on the cord with the right hand. Traction on the cord would be ill advised unless the accoucheur is certain that signs of placental separation and descent are present.

partum hæmorrhage what should the obstetrician do?

There is no time to find out why the patient is bleeding and the immediate thing is to stop it. Massaging a relaxed uterus merely adds further injury to insult. Use one closed fist as a uterine tampon, put the other hand over the abdomen and grasp the uterine fundus (bimanual compression of the uterus) to staunch the hæmorrhage. Then investigate. Give ergometrine intravenously and repeat soon after, if required. Inject oxytocic principle of the posterior pituitary lobe intramuscularly. On some occasions a very dilute solution of pitocin may be added to the glucose saline drip. Start plasma (dry or wet should be available) or synthetic plasma substitute (plasma expander) such as Plasmosan or Dextran. Nothing has to this day displaced blood as an ideal medium for the replacement of fluid volume in hæmorrhage. Beware of giving Rhesus positive (imcompatible) blood to a Rhesus negative woman. Put the patient in a Trendelenberg position. Reassure the patient. Inject morphia. Keep the patient warm but not hot. Early attention will prevent the establishment of irreversible shock. Vasopressor drugs have a useful role in that they raise and maintain blood pressure even temporarily until the blood volume has been restored. Give oxygen straightaway. Do not wait till the patient is almost moribund and then satisfy your conscience by giving it through a nasal catheter. Oxygen should always be given through a B.L.B. face mask, at 6 to 8 litres per minute as indicated by a flow meter attached to the cylinder, to be effective and useful.

Although blood in post-partum hæmorrhage usually comes from the placental site it should be remembered that severe lacerations of the birth canal may also give rise to profuse bleeding. The difference is this. In one case the uterus is generally atonic. In the latter, the uterus is well contracted and the patient still bleeds. In all circumstances, the birth canal should be carefully inspected with the aid of good illumination as well as the use of wide retractors to locate the site of the injury. Although cervical lacerations may bleed it is generally seen that vaginal lacerations, especially in the vascular area close to the clitoris and urethra bleed most. When the cervix is pulled downwards for inspection this act may in itself temporarily arrest hæmorrhage. Careful and accurate suture of the lacerations and/or packing of the vagina generally controls blood loss. In recent years, disturbances in the blood clotting mechanism has come into prominence. In this rare condition where hypo-fibrinogenemia is present, bleeding is profuse and almost nothing which the obstetrician does controls it. This condition is generally met with in severe cases of concealed accidental hæmorrhage. The obstetrician should know if he is dealing with such a condition. A simple test is to withdraw 5 c. c. of blood in a clean dry test tube; normally the clot should form within five minutes. Within ten minutes a formed clot should be present. In hypo-fibrinogenemia the blood does not clot at all. In such circumstances treatment consists of giving fresh blood. Ideally plasma fibrinogen should be given but this substance is virtually impossible to get.

If post-partum hæmorrhage occurs when the placenta has not been delivered it is important as soon as the patient has been treated for shock and her general condition has improved to empty the uterus. Occasionally post-partum hæmorrhage results from a part of the placenta (succenturiate lobe) being left behind. The obstetrician should always examine the placenta and the membranes and make sure that everything has been extruded.

Post-partum hæmorrhage is an important cause for maternal death. The practice of preventive obstetrics and wise obstetrical care can do a great deal to prevent this serious complication of labour. The advance which modern medicine has made in resuscitation (blood, plasma-expanders, vasopressor and oxytocic drugs) have all enabled post-partum hæmorrhage to be treated effectively when it occurs. On no account should the obstetrician be complacent after a child has been born because this is a most critical time. With constant vigilance and good obstetrics, we should strive to reduce maternal mortality from this cause.

ACKNOWLEDGEMENT

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"A Probe into Certain Common Neurological Problems of Interest"

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(1) Corpus Striatum, its physiological importance and its Pathology in Paralysis Agitans and the therapeutic efficacy of drugs used in its treatment and their mode of action.

Corpus Striatum, made up of the Lenticular nucleus and the Caudate nucleus, is an important area of the grey matter of the Brain, lying at the base of the cerebral hemisphere, in close relation to the Thalamus. The two nuclei are incompletely divided from each other by the anterior limb of the Internal Capsule, the caudate nucleus lying on the medial side of the anterior limb of the internal capsule, its head bulging medially into the anterior horn of the lateral ventricle, and the tail ending in the amygdaloid nucleus, a small globular mass of the grey matter, which constitutes a part of the olfactory pathway and the lenticular nucleus, occupying a corresponding position on the outerside of the internal Capsule. The lenticular nucleus is wedge-shaped and is divided into an outer and inner part, the Putamen and the Globus pallidus respectively, and becomes continuous with the head of the caudate nucleus beneath the anterior limb of the internal capsule. On the outerside of the lenticular nucleus, there is a narrow band of white matter, —the External Capsule, and lateral to it is an elongated island of grey matter—the Claustrum. The corpus Striatum, the amygdaloid nucleus and claustrum are together known as Basal Ganglia or nuclei.

The fibre and tract connections of the Corpus Striatum may be divided into the following groups :—

(1) *Internuncial fibres,* arising and ending within the Corpus Striatum passing mainly from (a) Putamen to globus pallidus. (b) from the caudate nucleus to the Putamen and globus pallidus and (c) between the lateral and medial zones of the globus pallidus itself.

(2) *Striofugal fibres,* which arise in the Corpus Striatum and end elsewhere, the great bulk of these arising from the globus pallidus. These are mainly (a) Strio-thalamic, from the globus pallidus to the lateral nucleus of the thalamus, through which and the Thalamo-olivary and Olivo-spinal tracts, a possible pathway exists for striatal

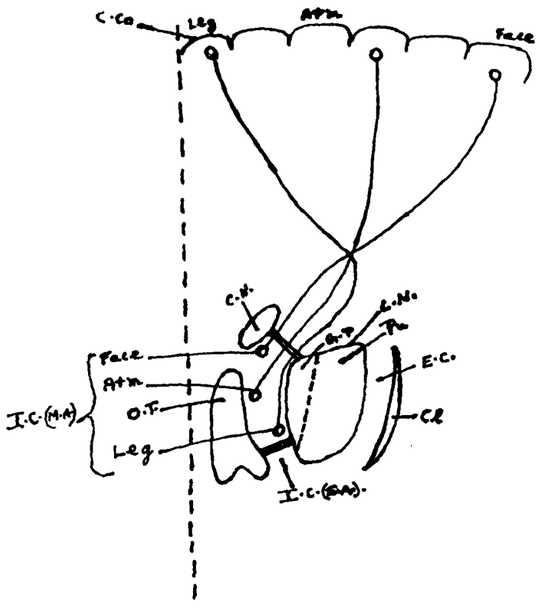

Fig. 1

Diagram of Internal Capsule and Corpus striatum.

Pu	-	Putamen
G. P.	-	Globus Pallidus
Cl.	-	Claustrum
I. C.	-	Internal Capsule
E. C.	-	External Capsule
Py	-	Pyramidal fibres
C. C.	-	Cerebral Cortex
L. N.	-	Lenticular Nucleus
O. T.	-	Optic thalamus
C. N.	-	Caudate Nucleus

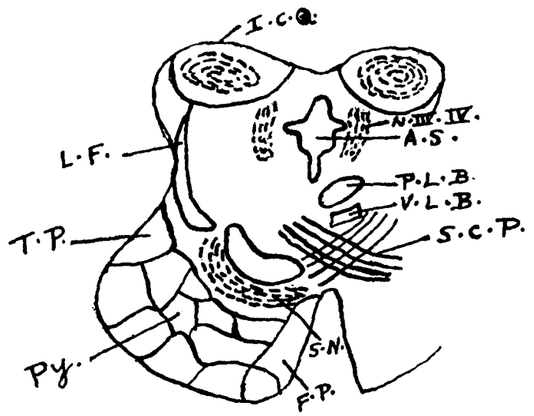

Fig. 2

Diagram of Section through midbrain at the level of inferior corpora quadrigemina.

I. C. Q.	-	Inferior Corpora quadrigemina
L. F.	-	Lateral Fillet
M. F.	-	Mesial Fillet
A. S.	-	Aqueductus Sylvius
P. L. B.	-	Posterior Longitudinal bundle
V. L. B.	-	Ventral Longitudinal bundle
S. C. P.	-	Superior Cerebellar Peduncle
N. III. IV	-	Nuclei of III and IV nerves
S. N.	-	Substantia Nigra
T. P.	-	Temporo-pontine fibres
F. P.	-	Fronto-pontine fibres
P. Y.	-	Pyramidal Tract

impulses to reach the spinal cord. (b) Strio-subthalamic (Ansa Lenticularis) :— These arise from the globus pallidus and pass to the Red nucleus, Substantia Nigra and the Body of Luys or Subthalamic nucleus. (c) According to Morgan, there is also a direct path from the globus pallidus of the Corpus Striatum to the Bulbar nuclei of the Medulla. They terminate around cells in the *Reticular formation* of the pons and Medulla and the Trochlear, Abducent, Trigeminal (motor), Glosso-Pharyngeal and Hypoglossal nuclei of the same and the opposite side. *The Reticulo-Spinal and Rubro-Spinal* tracts are pathways, whereby striatal impulses, reach the spinal centres. (d) Pallido-Hypothalamic, fibres pass from the globus pallidus to the Hypothalamus. It is also possible that direct fibre connections passing from Corpus Striatum to the cerebral cortex exist.

(3) *Strio-Petal fibres,* arising elsewhere and ending in the Corpus Striatum are (a) thalamus to caudate nucleus, putamen and globus pallidus. (b) Body of Luys to globus pallidus. (c) Red nucleus to globus pallidus. (d) Cerebral cortex to caudate nucleus. Area 6 (Premotor) sends fibres to this part of the corpus Striatum, possibly also to the putamen and globus pallidus.

(4) *Commissural fibres,* fibres joining the corpora striata of the two sides pass from the globus pallidus of one side to the corresponding nucleus of the opposite side.

(5) *Fibres of passage* (i. e.) fibres passing through the Corpus Striatum, are ascending and descending fibres of the internal capsule :—cortico-spinal and thalamo-cortical etc. The corpus Striatum is also most certainly in communication with the Cerebellum through relay stations (e. g.) Red nucleus.

THE EFFECTS OF EXPERIMENTAL STIMULATION AND INJURY OF THE CORPUS STRIATUM

Physic movements in anyway resembling those, which can be elicited by excitation of the Motor Cortex, cannot be induced by stimulation of the basal ganglia or the subthalamic region. The outstanding result of the excitation of the corpus striatum is observed during muscular movements initiated from the cortex or when the limbs are held by tonic postural contractions, when inhibition promptly occurs. The most definite experimental results are those of Mettler and his associates. They observed the following effects of electrical stimulation of the corpus Striatum in monkeys. (a) movements induced by excitation of the motor cortex were inhibited by concurrent stimulation of the caudate nucleus, putamen or claustrum. (b) stimulation of the globus pallidus added to movements initiated from the cortex, an element of "plastic tonus," which exerted a "holding" action upon the movements and prolonged their reaction time. Experimental lesions of the striatal region in dogs or cats results in no noticeable motor defects nor is any pronounced effect observed in monkeys. Kinnier Wilson found that when extensive unilateral lesions were made, the animals used by preference, the arm and hand of the ipsilateral side and showed clumsiness of movements on the opposite side. There was no paralysis or paresis. In chimpanzees, striatal injury is followed by athetoid movements, closely simular to those seen

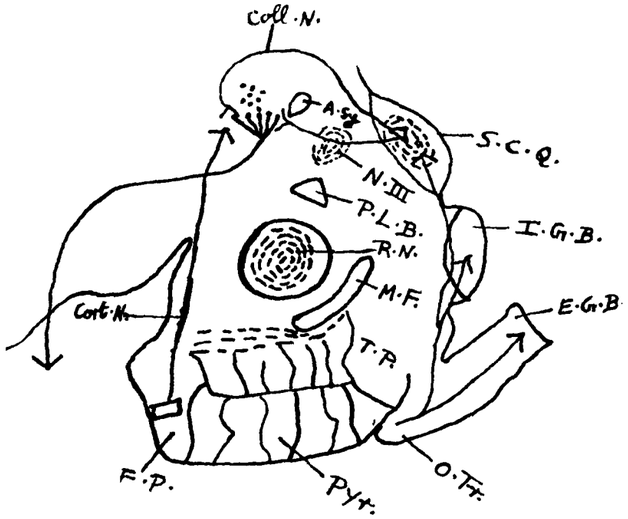

Fig. 3

Diagram of Section through midbrain at the level of the superior corpora quadrigemina.

S. C. Q.	–	Superior Corpora quadrigemina
Coll. N.	–	Colliculo-nuclear fibres
A. Sy.	–	Aqueductus Sylvius
I. G. B.	–	Internal Geniculate Body
E. G. B.	–	External Geniculate Body
N. III	–	Nucleus of the III nerve
O. Tr.	–	Optic Tract
P. L. B.	–	Posterior Longitudinal Bundle
R. N.	–	Red nucleus
M. F.	–	Mesial Fillet
Pyr.	–	Pyramidal tract fibres
F. P.	–	Fronto-pontine fibres
Cort. N.	–	Cortico-nuclear fibres
T. P.	–	Temporo-Pontine fibres

in persons suffering from disease of this region. Tremors are observed in monkevs following large bilateral lesions in the putamen or smaller bilateral lesions of the globus pallidus. Electrolytic lesions in the corpus striatum are found to produce slight but persistent hypertonus in the extensor muscles of the opposite side and flexor hypertonus on the same side. Placing reactions are imperfect and closure of contra-lateral eyelid is defective. The highest integrative level of the cortico-Strio-Nigral system consists of cells situated chiefly in the premotor area (Area 6).

FUNCTIONS OF THE CORPUS STRIATUM AND THE EXTRA PYRAMIDAL SYSTEM

The Corpus Striatum is one of the oldest parts of the cerebrum and globus pallidus, otherwise known as *Paleostriatum* is older phylogenetically than the putamen caudate portion, which is known as *Neostriatum*. The connections of the Paleo-Striatum are chiefly efferent; the neostriatum is mainly receptive. In lower vertebrates in which cerebral cortex is absent or rudimentary and the pyramidal system has not yet come into being, the corpus striatum is looked upon as homologous with the motor cortex of the higher forms (e. g.) fishes, amphibia, reptiles and birds. Upon this old motor centre and its connections with lower levels, the motor activities of the submammalian forms very largely depend. As the phylogenetic development of the cerebral cortex and the pyramidal system progresses, corticalisation of functions also takes place. But the functions of the Extra-Pyramidal system, though in some ways subordinate to those of the motor cortex, are by no means lost. The phylogenetically older system continues to carry out those more or less automatic or semi-reflex movements, concerned in maintenance of posture, defence, feeding etc. In the cat or dog, decortication is not followed by any significant alteration in motor functions, as compared with the effects of this operation in primates. The motor disability of the decorticated monkey is profound. In Man, the cortical representation of the extra pyramidal system, is placed in the premotor area. From the results of ablation experiments, involving the premotor cortex, this frontal region in primates appears to have become intimately associated through intracortical connections with the motor area, serving to synthesise larger complex actions from the smaller, more discrete movements governed by the latter area. Through the convergence of its paths on the spinal motor nourons, the extra pyramidal striatal system in the human subject maintains a postural background or substructure, against or upon which voluntary movements are executed. Impulses travelling along these paths, exert á steadying effect upon such movements, but do not themselves initiate them. Kappers considers however that the habitual or automatic acts in daily life, are mediated through this extra pyramidal system and it is such movements that suffer the greatest impairment in any disease involving the corpus striatum.

Parkinson's Disease or Paralysis Agitans :–is a disease characterised by muscular rigidity and tremors.

Aetiology :—due probably to degenerative changes occurring in the nuclei of the corpus striatum, with

old age. The exact cause is not known. It usually occurs in persons over the age of 50, and males predominate.

Pathology :—The lesion involves all the nuclei of the corpus Striatum, especially the putamen and caudate nucleus and results from arteriocapillary fibrosis. The pathogenesis of this condition is illunderstood. The mode of production of the principal symptoms, tremor and rigidity, in this condition, is most probably due to interruption of the suppressor tract pathway passing from the motor suppressor area (Area 4S of the cerebral cortex), lying just anterior to the primary motor area (area 4), to the thalamus through the caudate nucleus of the corpus striatum, due to degenerative changes occurring in the caudate nucleus and consequent effect of defective functioning of the suppressor tract pathway, resulting in the loss of inhibitory control over the thalamus and through it, the spinal motor neurons and the electrical activity of the cerebral cortex, with resulting rigidity and involuntary tremors, due to release of the lower centres from higher control.

Area 4 S of the cerebral cortex is an important area, as it controls the activity of the primary motor area (Area 4). This is a narrow band of cortex, also known as the strip area of Hines, lying between the upper parts of areas 4 and 6. Its cytoarchitecture is of the granular type, resumbling that of area 4 except that the giant pyramidal cells are absent or scarce. Electrical stimulation or strychninisation of this area inhibits muscular contractions elicited from stimulation of area 4 and raises the threshold of excitation of the latter. Its ablation results in spasticity and an exaggeration of the Myotatic reflexes. Area 4 S projects to the caudate nucleus of the corpus striatum and through it to thalamus, which again connects with area 4. Its also sends fibres to the subthalamus and substantia nigra and to the pontine nuclei. It contributes to the pyramidal tracts also. Through the reticular formation of the brain stem extending from the thalamus, subthalamus, substantia nigra and red nucleus to pons and mudulla by means of *reticulo-bulbar tracts* and the reticulo spinal or extra-pyramidal tracts which are mainly vestibulo-spinal which arises form Deiter's nucleus in the pons and extends to spinal motor neurons and rubro-spinal tracts, the fibres of which end around the anterior horn cells of the spinal cord in the lateral horn cells, the activity of the pyramidal (cortico-spinal) tracts and the medullary and pontine cranial nerve motor centres is controlled and stabilised. The main signs and symptoms of rigidity of muscles, tremors of fingers especially and ankles at times, the attitude of flexion of the neck and trunk, the festinant, propulsive gait, the flexion of metaacarpo-phalangeal joints with extension of the inter phalangeal joints and opposing of the thumb with the index finger, abduction of shoulders with flexion of elbows and holding of the arms away from the sides, with the hands infront of the body suggest that the lesion most be in the extra-pyramidal system, involving the suppressor tract pathway, passing through the caudate nucleus, which is found to be degenerated in these cases. The pyramidal tracts are not involved, as is shown by the plantar reflex being flexor, and there being no paresis or paralysis of muscles, but only rigidity resulting in extreme stiffness and slowness in the action of voluntary muscles with consequent mask like expression of face, and tremors, which are due to rhythmical contractions of muscles and their antagonists resulting from extra pyramidal involvement.

Post-Encephalitic parkinsonism, (i.e.) the symptoms of paralysis agitans following Encephalites Lethargica, mainly affects persons of an younger age group (10—40 years), the rigidity of muscles is much more prominent than tremors, and there is in most cases, a history of a preceding febrile attack with disturbances in sleep rhythm and duration. Purely senile tremors are differentiated by their not being of the rhythmical variety as found in parkinsonism, the absence of rigidity of the muscles and the normal expression of the face, instead of the mask like face. Cerebral arterio-selerosis may also produce symptoms akin to parkinsonism, but is differentiated by the normal expression, the affection of trunk and legs mainly and the tremors, being slight. Salivation, oculo-gyric crises, tics and disturbances of sleep also commonly occur in this condition.

Treatment and its therapeutic basis :—The rigidity and tremor of paralysis agitans, especially that following encephalites Lethargica usually respond well and some times dramatically to treatment with Belladona or its derivative hyoscine hydrobromide. Tincture belladona (15 m) is given thrice daily for long periods with short intervals of not more than a week, as slight tolerance is developed towards it, unless such intermissions are made. As an alternative, hyoscine hydrobromide ($\frac{1}{100}$ gr.) tablet twice or thrice daily for long time, has also a good effect in relieving the symptoms to some extent or bellafoline or belladenal

tablets may be given continuously for some time for good results to follow. Light massage to the muscles and daily exercise to the muscles by passive movements helps to reduce rigidity of muscles and stiffness of movements to some extent.

The probable mode of action of belladona and its derivatives is through its suppressor action on the anterior hypothalamic nuclei, with resulting over activity of the posterior hypothalamic nuclei, with its connections to the lateral horn cells of grey matter adjoining the anterior horn cells of the spinal cord in the thoracic and Lumbar regions, which exert an inhibitory effect over the activity of the lower motor neurons, released from higher control by a defective functioning of the suppressor tract pathway passing from the motor suppressor area (Area 4 S of the cerebral cortex), to the thalamus through the caudate nucleus of the corpus striatum which is degenerated in parkinson's disease, either occurring primarily due to changes occurring with senility or following encephalites lethargica in younger persons resulting in rigidity and tremor. The undue drowsiness and a tendency to sleep for long duration, which is present in the post-encephalitic parkinson's disease and in the severe forms of primary parkinson's disease of senility is prevented by the suppressive actions on the anterior Hypothalamic nuclei including those of the Tuber Cinereum, by the Belladona group of drugs, resulting in lessening of para sympathetic activity which normally maintains sleep and the consequent increased activity of the posterior hypothalamic nuclei, in which the waking centre, controlling the sleep-wakefulness rhythm, is present.

The new drugs which could be given with benefit to patients suffering form this ailment are (a) Parpanit (Geigy's) or (b) Artane (Lederle) both drugs having a para sympatholytic action. *Artane* may be combined with hyoscine hydromide in doses of 2 mgm, 3 or 4 times a day, under good supervision. The usual daily dose of *Artane* is one to ten mgm.

(2) Narcolepsy, Cataplexy and their Pathological Basis and Inter-relationship.

It is a problem of great interest to enquire into the reason as to why Narcolepsy, though it may occur alone without Cataplexy, the converse is extremely rare. Narcolepsy is a condition characterised by frequent Paroxysmal occurrence of attacks of an irresistible desire for sleep during daytime, lasting from a few seconds to about twenty minutes, closely resembling normal sleep. Nocturnal sleep may be normal, but, is often disturbed or there may be insomnia. Narcolepsy occurs mostly in the initial stages of a tumour of the diencephalic region of the brain in and around the area of the third ventricle or during the initial stages of an encephalites involving the hypothalamic nuclei like that caused by the virus of epidemic encephalites or a generalised diffuse encephalites occurring, for example in basal Meningites due to syphilis or other bacterial or viral infections in the initial stages involving the above area as well as the rest of the brain in varying degrees, due to over stimulation of the anterior hypothalamic nuclei in paroxysms due to the constant irritant focus present with consequent suppression of activity of the posterior hypothalamus, containing the waking centre, with some degree of suppression in the initial stages, leading later to a greater degree of suppression, almost amounting to a total loss of functioning of its efferent connections ending around anterior horn cells in the lateral region of the grey matter of the spinal cord (i. e. the tract pathway through which suppressor impulses of the reticulo spinal tracts, controlled by a rea 4a or suppressor strip of the cerebral cortex lying just anterior to primary motor area or area 4) are mediated, with consequent overactivity of the pyramidal tracts, ending in the anterior horn cells of the spinal cord, with resulting epilepti form convulsions etc.

Cataplexy:—In the later stages of the above pathological conditions, producing Narcolepsy with or without convulsive siezures, when degeneration almost amounting to destruction of the anterior hypothelamic nuclei occurs in long standing and severe cases of the disorder, due to the long continued effects of neoplasm or encephalites, Cataplexy results with spread of neoplasm or encephalites due to other causes, and extension of its destructive changes to the posterior hypothelamic area also, leading to very frequent attacks of prolonged somnolence and in some cases to periods of insomnia also alternating with the above, due to cortical centres being affected [illegible]ectly by various special senses and emotional stimu[illegible]producing undue excitability of the person with me[illegible]estations of psycho motor nature also, as also [illegible] effects of degeneration of the normal neuro-m[illegible]ular mechanism of function due to the cerebral [illegible]ortical cells [illegible]eing affected and undergoing dege[illegible]ation, leading to sudden attacks

characterised by loss of tone in muscles similar to Myasthenia gravis, which occurs only when degeneration and destruction of the anterior hypothalamic nuclei has gone beyond a certain stage. That is perhaps the reason for Cataplexy occurring combined with Narcolepsy in most cases, whereas Narcolepsy can occur without Cataplexy, due to the method of affection of the mechanism of the function of the area as given above, by an abnormally strong stimulation of the anterior hypothalamic nuclei alone occurring. Loss of tone occurring in muscles in this condition is predisposed to occur, by any emotion especially mirth and laughter.

Treatment: Benzedrine Sulphate or Ephedrine Sulphate or Dexedrine may be given thrice daily in doses of 5 to 10 mgs. dose of the former and 1 grain dose of Ephedrine Sulphate. Dexedrine is given in doses of 2 tablets (5 mgs) twice daily to thrice daily, the last dose being given before 5 P.M., to avoid insomnia at night. Prostigmin in doses of 15 mgs. twice daily may be useful in preventing the loss of tone in muscles occurring in Cataplexy similar to its use in Myasthenia gravis.

(3) Nocturnal Enuresis in Children, its treatment and the Physiological Basis of Autonomic Nerve Action in Micturition.

There seems to be a widely prevalent view that Nocturnal Enuresis in children is due to increased tone of the musculature of the bladder with the result that parasympatholytic drugs and drugs with a sedative action on the cerebral cortex or both combined, have been recommended for treatment by many. It is also a current belief arising from the frequent reports of observation by certain mothers that children do not wet the bed during deep sleep, but only when they begin to awake (during the so-called waking hours), that hypnotic drugs of the barbiturate group would have a beneficial action in treatment of this condition in addition to the usual therapy.

Both views do not seem to take account of certain facts in the basic physiology of function of the autonomic nervous system. The au[illegible]omic nervous system is based to work in such [illegible]ed manner that both manifest a degree of stimulation [illegible]mplementary to each other's working, in the v[illegible]ous autonomic reflexes involved in the working of [illegible] various organs and systems of the human bc[illegible] as defæcation, micturition, heartra[illegible]e, pilo-erectic[illegible], sweating and the degree of tone of the vasculature of the various parts, an excess of activity of the parasympathetic invariably accompanied by a lowered activity of the sympathetic and vice versa so that it seems impossible either in the physiology or pathology of the human body for both to be stimulated together or for excess or diminished activity of one of the systems to be unaccompanied by an opposite complementary reaction in the other. Nocturnal Enuresis seems to be due more to diminished tone of the sympathetic nerves supplying the internal sphincter of the bladder and sphincter around the ureteric orifices, with consequent increased load in the bladder and involuntary micturition, during deep sleep, which itself is due to suppression of the posterior hypothalamus containing the waking centre and the higher centres for the control of the sympathetic. Children wetting the bed just before waking, does not lend support to the view that enuresis has not occurred during deep sleep, for adults and even more so, children may be in deep sleep even just before waking and so the fact of its occurrence just before waking in children rather than in adults is due to the increased load in the bladder occurring with longer hours of sleep and the lowered degree of the cortical control over the autonomic innervation of the bladder, the parasympathetic innervation being through the nervi erigentes arising from the second and third sacral segments of the spinal cord and the sympathetic innervation through the presacral nerve arising from the first and second lumbar segments of the cord and passing through the hypogastric ganglia to innervate the internal sphincter of the bladder, the parasympathetic innervating the detrusor muscle of the bladder, also through the hypogastric ganglia, which act as the excitor relay station for both sets of fibres.

From the above, it seems clear that parasympatholytic drugs of the belladona group or hypnotics of the barbiturate group are not the drugs of choice in the treatment of Nocturnal enuresis, occurring frequently in some children. Either the condition must be left to nature to cure itself, when not accompanied by any pathological or organic changes in the urogenital or nervous systems, as invariably occurring with progress to adulthood age with greater amount of cortical control over autonomic innervation developing or sympatho-mimetic drugs of the type of Dexedrine or Ritalin should be given a trial in assessing their effects, in cases of frequent nocturnal eneuresis in children continuing to occur between the ages of 7 and 12, but not at an earlier age. It is

also reasonable to administer in addition, to such children, some drug having a stabilising stimulatory action on the neurochemical mechanism of function of the cerebral cortex and central nervous system and developing their psychic and intellectual functions which are turned to good use in cases associated with mental backwardness, as Glutamic acid, contained for example in 'NEURO GLUTAN' (A product of Union Chemique Belge, S. A., Brussels, Belgium) in doses of 1 to 2 tablets or one teaspoonful of the syrup daily continuously for a period of at least 3 to 8 weeks, as it leads to a functional improvement of the activity of the cerebral cortical cells, which in turn, leads to an increase of the cortical control in relation to the Diencephalic centres, which factor is very important in the functioning of various organs concerned in the autonomic reflexes of micturition, defæcation etc. and thereby the condition of the nocturnal enuresis is likely to benefit very much and proceed to an early cure.

As has been advised by physicians from quite a long time, avoidance of abuse and condemnation of children by parents for the fault of nocturnal eneuresis, which has not occurred out of their own free will, and frequent promise with actual award to them of some small reward or prized possession, which children cherish, in case they are able to control nocturnal eneuresis, will go a long way in producing an early cure of the condition.

Influence of folic acid on absorption of iron

Begemann, H., Keiderling, W. and Walter, F., *Klinische Wochenschrift*, Germany, 31 : 881–883, October 1, 1953 ; through : *Journal of the American Medical Association*, 154 : 628, February 13, 1954.

Begemann and associates describe studies on healthy subjects and on persons with various disturbances that were designed to ascertain whether and under what conditions folic acid promotes the enteral absorption of iron. Iron was administered in the form of 200 mg. of ferrous sulphate. It was found that the increased absorption of iron that prevails in conditions of iron deficiency is further improved by the administration of folic acid. The absorption of iron was improved also in patients with gastric anacidity or subacidity, that is, in conditions in which the absorption of iron is greatly impaired. The tolerance for orally administered iron is greatly improved by the simultaneous administration of folic acid. The mode of action by which folic acid improves the resorption of iron, however, is not yet fully explained, but since it is known to promote the absorption of other substances, it is assumed that folic acid acts by modifying cellular permeability. The authors were interested chiefly in ascertaining the influence of folic acid on iron resorption and thus to clarify the indications for its therapeutic administration.

Cardiac arrest after intravenous administration of procaine amide (Pronestyl)

Weingarten, W. and others, *Journal of the American Medical Association*, U.S.A., 154 : 985–986, March 20, 1954.

Procaine amide (Pronestyl) has become widely used in cardiac arrhythmias ; its value in the prevention and control of ventricular arrhythmias has become well established. Some side effects have been noted, however. In this report a 30-year-old negro was treated with Pronestyl, given intravenously in an initial amount of 250 mg., for a condition of multiple premature ventricular contractions. and ventricular tachycardia. QRS complexes widened within one minute. They then returned to their previous duration and additional procaine amide was given because the ventricular tachycardia persisted and the patient's condition seemed hazardous. A total of 800 mg. of Pronestyl (in addition to the initial 250 mg.) was then given over a 15-minute period. This was done in view of the lack of response by the patient. Progressive QRS widening occurred, but five minutes after the last administration of Pronestyl cardiac standstill supervened. The exposed heart was promptly massaged manually and epinephrine was injected into the left ventricle. Within fifteen minutes after the arrest, and initiation of massage and injection treatment, spontaneous ventricular contractions were observed and the electrocardiogram recorded a reversion to normal. Recovery was uneventful, and a few days later an electrocardiogram showed an entirely normal pattern. This is believed to be the first recorded case of cardiac standstill after intravenous administration of Pronestyl, with the exception of three cases recorded by Dr. M. A. Epstein subsequent to completion of this paper. The patient here reported had received a variety of drugs preoperatively, and during anesthesia which may have led to the bout of ventricular tachycardia and contributed to the cardiac arrest. However, the relationship between the intravenous administration of procaine amide and cardiac arrest seems well established here

also reasonable to administer in addition, to such children, some drug having a stabilising stimulatory action on the neurochemical mechanism of function of the cerebral cortex and central nervous system and developing their psychic and intellectual functions which are turned to good use in cases associated with mental backwardness, as Glutamic acid, contained for example in 'NEURO GLUTAN' (A product of Union Chemique Belge, S. A., Brussels, Belgium) in doses of 1 to 2 tablets or one teaspoonful of the syrup daily continuously for a period of at least 3 to 8 weeks, as it leads to a functional improvement of the activity of the cerebral cortical cells, which in turn, leads to an increase of the cortical control in relation to the Diencephalic centres, which factor is very important in the functioning of various organs concerned in the autonomic reflexes of micturition, defæcation etc. and thereby the condition of the nocturnal enuresis is likely to benefit very much and proceed to an early cure.

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