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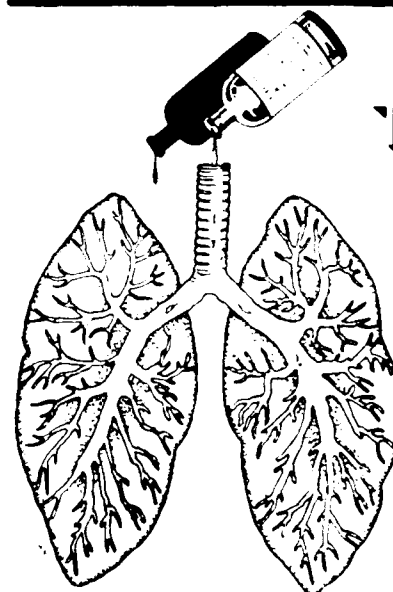
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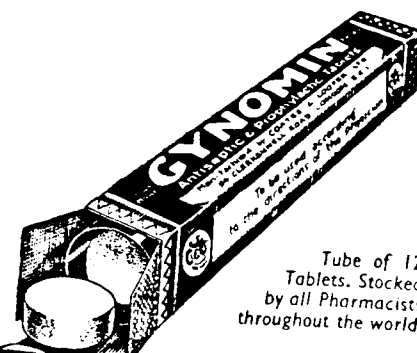
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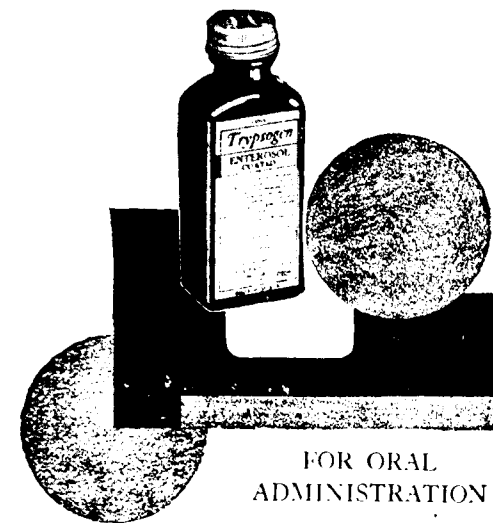
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ADDRESSES AND ARTICLES

Quinine in Solution for Injection

• U. P. Basu, D. Sc., P. R. S., A. Mazumdar M. Sc., and A. N. Bose, M. B. The Bengal Immunity Research Laboratory, Barnagore, Calcutta

Quinine bihydrochloride for its high solubility is preferred for any parenteral administration of quinine. But the solution of quinine bihydrochloride is extremely acidic in nature and it is this acidity which is often responsible for the necrotic action of the drug (cf. Acton 1922; and Acton and Chopra, 1924). Further, during sterilisation this acid salt is partly converted to quinotoxin which lowers the therapeutic efficacy (Bachstsz and de Caro, 1932) of the alkaloid. In the present investigation a systematic work has been undertaken to find out the loss sustained by quinine bihydrochloride by different methods of sterilisation, the change that takes place on exposure to light and the influence of the acidity of the solution on the toxicity of the alkaloid.

EXPERIMENTAL

Extra pure quality of quinine bihydrochloride was dissolved in double distilled water to obtain a 33.0 per cent solution, filtered, filled into neutral ampoules (10 c. c.) and sterilised by autoclaving for 30 minutes at 100°C as well as by the process of Tyndallisation. The following characteristics of the pale yellow solution were then ascertained:

(i) pH from the direct reading glass electrode pH meter as supplied by Leeds and Northrup, (ii) the specific gravity by the bottle method, (iii) the refractive index by Abbe refractometer, (iv) the surface tension by the drop method (all at 35°), and (v) the angle of a rotation in a 2.5 cm. tube from a polarimeter (Precision, Landolt, Schmidt and Haensch).

Effect of Light:—The ampoules were wrapped with just two layers of cellophanes—red, yellow, green, blue and violet. Another set of ampoules were wrapped with sheets of blue, yellow and red cellophane combined. Such a wrapping showed a "brown" shade when viewed through the transmitted light.

All these were then placed in a wooden tray on the table exposed to diffused sunlight. Ampoules covered with black paper and placed in a dark chamber served as control. Within 10—12 days the colour of the solution as noticed from that of the uncovered ampoule, began to intensify and after a month it was found that the ampoules which were exposed to short-wave length (violet and blue) were definitely brownish coloured, but the others were not so effected. Within 3 months the colour of the solution in all the ampoules excepting those wrapped with "brown" (combined) cellophane had altered from yellow to yellowish brown to brown, the intensity gradually increasing from red to violet. Opening another set of ampoules after a year, it was revealed that all the ampoules had undergone same photochemical changes. Those covered with "brown" paper, however, remained practically unchanged, and the ampoules wrapped with black paper and kept in dark had also undergone no change. Exposing all these again to diffused sunlight the intensity of colour was re-established to brown tinge in all the ampoules. This phenomenon was noticed even in quinine bihydrochloride solution to which urethane (1%) or saccharose (1%) was added. The general characteristics of all the solutions were again ascertained but no appreciable difference was noticed. Table I shows the figures obtained from quinine bihydrochloride solutions mixed up with 1 per cent saccharose, after a period of one year.

TABLE I
CHARACTERISTICS OF QUININE BIHYDROCHLORIDE
SOLUTION AFTER EXPOSURE FOR 1 YEAR

Ampoule	pH	Sp. Gravity	Ref. Index	Sur. Tension in dyn/cm	Angle of Rotation
Original	1.7	1.0805	...	91.52	-15.01
Uncovered	1.65	1.0804	1.4078	92.5	-14.88
'Brown'	1.6	1.0804	1.4078	92.2	-14.85
'Black'	1.6	1.0805	1.4076	92.25	-14.85

Effect on sterilisation: The amount of quinotoxin formed after sterilisation by one or other method was then determined from a solution containing 0.5 gm. of quinine bihydrochloride by the method as described in Allen (1929). The change, if any, in its percentage in the quinine solution exposed to light was also noticed. The estimation of quinotoxine was also made by the method as described by Bachstsz and de Caro (1932) by fresh ampoule left aside for one year, but no appreciable difference was noticed. The results are being recorded in Table II.

TABLE II
INDICATING THE AMOUNT OF QUINOTOXIN FORMED

Quinine Bi-hydrochloride (88% solution)	Method of Sterilisation	Quinotoxin in Quinine Bi-hydrochloride %	Increase in the amount of quinotoxin
Original	No.	0.94	...
In ampoule	Through sintered glass (G 5 on 3)	1.08	0.14
"	70° for 45 mins.	3.08	2.14
"	100° for 30 mins.	2.80	1.86
"	100° for 1 hr.	4.90	3.96
"	15 lbs. for 30 mins.	4.60	3.66
"	Tyndallisation	5.60	4.66
After 1 year exposure	100° for 30 mins.	3.0	2.06

Effect of the hydrogen ion concentration in the solution: The acidity of quinine bihydrochloride solution is not only responsible for the necrotic action of the drug, but the enhanced acidity again lowers the toxicity of the alkaloid towards paramoecium (Acton, 1922). Under such circumstances it would also lower the therapeutic activity of the drug (cf. Sinton, 1925; Acton and Chopra, 1925). In practice too quinine has been found to give better results in malaria when administered with alkalies than when given alone (cf. Sinton, 1923). The most widely used soluble salt of quinine is its bihydrochloride as it is extremely soluble in water (1 part dissolving in 0.6 part of water). Recently Johnson (1937) has shown that if the hydrochloride molecule that is attached to the less basic quinoline nitrogen of quinine bihydrochloride be replaced by other weaker acids like lactic acid, the pH of the solution can be increased upto 4.13 without at the same time not decreasing the solubility of the product to any appreciable extent. The pH of the solution can also be increased by adding either alkali or basic quinine to a quinine bihydrochloride solution to about 3 to 3.2. Another method of increasing the solubility and at the same time of obtaining a solution for parenteral administration at higher pH is to add phenazone in suitable proportion to quinine hydrochloride solution. The toxicity of all such solutions was determined against *Paramoecium Caudatum*. For this the paramoecia was cultured on hay infusion at pH ca 8. Equal parts of this culture of paramoecia and the solution to be tested were taken and mixed together. So the strength of the quinine solution given in Table III is half that of the original strength used. The period required for the death of the parasites as indicated by their becoming at first motionless and sub-

sequently disintegrated when viewed through a low power objective, was recorded from a stop watch.

TABLE III
EFFECT OF DIFFERENT QUININE SOLUTION ON PARAMOECIA

Substance	Dilution of Quinine salt in solution				
	1:1000	1:2000	1:4000	1:10000	1:20000
Quinine hydrochloride	D: 5m	D: 15m	D: 30m	No death up to 45m	
Quinine bihydrochloride (fresh solution)	D: 20-24m	D: 45-60m			
'Do' after one year exposure	D: 60 m				
'Quinosin' *	D: 3-4 m	D: 20-25 m	D: 40 m		

D = Death (whole or majority), m = minutes.

* A product of Bengal Immunity (Calcutta) containing 25% solution of quinine at pH 6.6.

DISCUSSION

In British Pharmacopoeia it has been mentioned that quinine, its salt or its solution should be kept away from air and light. Macht and Teagraden (1923) claim that the toxicity of quinine is greater in animals exposed to light than those kept in darkness. From the present investigations (Vide Table I.) it is evident that no appreciable change whether in the physical or in the chemical properties of the quinine salt in solution was being noticed when it was exposed to diffused sunlight. The solutions, however, changed from light yellow to light brown or reddish brown colour. The difference in the relative effect of various bands of spectrum upon the promotion of this change is also negligible. The maximum photochemical effect has been obtained near the blue range of the spectrum. The solution when kept away from light retained its original colour. The exposure to light does not also promote the formation of quinotoxin to any appreciable degree. Thus it would be found from Table II that the percentage of quinotoxin in quinine bihydrochloride in a solution sterilised by heating at 100° for 30 minutes was 2.8 whereas the same solution after exposure over a period of one year showed the percentage of quinotoxin to be 3.0. Such an exposure, however slightly, lowers the toxicity of the alkaloid to paramoecium (Vide Table III.).

It is now generally recognised that quinotoxin which is invariably produced when a quinine salt is subjected to heat treatment is not toxic in comparison with the mother

compound itself. But recently Bachstet and de Caro (1932) have, however, shown that a mixture of quinine and quinotoxin is more toxic than either of the two. This and the fact that the formation of quinotoxin itself would invariably lower the efficacy of quinine, suggest that method or methods must be devised by which a quinine solution meant for injection may be sterilised without any appreciable loss of the alkaloid itself. From Table III it would be found that the formation of quinotoxin in the solution of quinine bihydrochloride sterilised by filtering through sintered glass (G 5 on 3) is only 15 per cent more than the amount that was originally present in the solution whereas the process of Tyndallisation has increased its percentage 500 times approximately.

The local effects on the tissues on intramuscular injection of quinine bihydrochloride are due to the liberation of the acid radicle and subsequent precipitation of the base (Acton and Chopra, 1924). On this basis if the liberated acid may be neutralised by the alkalies of the body tissues, the irritation and other side effects would be considerably lowered. But for this the pH of the quinine solution should preferably be nearer to that of the body fluids as far as practicable. In practice too "Quinosin" (pH = ca 6.6) is being found to be well tolerated by the average patients. The effect of the different quinine solutions on paramoecia (Vide Table III.) again points to the greater toxicity of quinine in lesser acid medium to the parasites. Quinine hydrochloride for its lower solubility cannot be injected in high doses. Consequently the question rises whether a quinine bihydrochloride solution adjusted to a higher pH should be used in its clinical applications. It must be admitted that most of the side reactions of quinine are either due to a defective preparation or faulty technique of injection (cf. Brahmachari, 1922; Murphy, 1925; Macqueen, 1927; and Ahmadi, 1930). A solution prepared away from light, sterilised at a lower temperature and adjusted to higher pH is invariably well absorbed and gives rise to no untoward symptoms. Further work is essential to find out whether the photochemical changes in quinine solution actually increases the side reactions of the alkaloid (cf. Roskin and Ramanowa, 1929).

It may be added here that the strength of the quinine bihydrochloride solution usually injected is 33 per cent, whereas the isotonic solution requires 5.65 gms. per 100 c.c. For better tolerance the solution (say 10 grains in 2 c.c.) should necessarily be diluted with about 10 c.c. of normal saline before injection in order to maintain the tonicity of the solution.

CONCLUSIONS

The quinine bihydrochloride solution on exposure to light develops a colour without any appreciable change in its physical or chemical properties.

Temperature and the period of heating during the process of sterilisation affect the quinine molecule to a certain extent.

The question may be raised whether for increasing the tolerance and potency of the drug the solution of quinine bihydrochloride should be adjusted to a higher pH.

The quinine bihydrochloride solution prepared away from light, sterilised without application of heat and adjusted to higher pH is being well tolerated in general.

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Infantile Biliary Cirrhosis (3) Diet and Habits of Children

● Dr. S. Balasundaram, Director, Ehrlich's Laboratory, Madras

The subject next in importance to the study of environment is the investigation of the reasons for children of lower ages being specially predisposed to this disease. That brings us to the necessity of considering the habits and diet of children at these ages.

The first milestone in the life of a child is weaning which by itself is a stage through which every child has to pass. The number of children who can tide over this phase of their lives without any event is very little. The change from the maternal milk to artificial feeding brings in its wake all sorts of diseases, digestive or otherwise, in many of the children, the reason being that the artificial food is lacking in many of the advantages found in the maternal milk. The human milk contains all the ingredients including the vitamins, salts and other things vital for the child for its growth. It also contains many of the antibodies to resist diseases and in fact all the essential things for the child which can be found in the mother and which can be usefully transmitted through the milk. The quantity and quality of the milk supplied to the child is found by many observers to be independent of the intake of the mother. Thus when a child is weaned a great advantage is lost. Added to this there is a great demand for calcium and phosphorous in the child at this time for the growth of bones and dentition. The demand is greater in male children, as I have described before, on account of their peculiar metabolism. We can easily imagine what a great demand there would be in children who are already experiencing phosphorous shortage from their birth, and counteracting it by their endocrine organs due to their peculiar environment. Such children certainly cannot meet the demand by the available phosphorous and calcium in the artificial food supplied to them. To that extent they are comparatively at a disadvantage than other children in a favourable environment. The problem of successful artificial feeding and regulation of bowels of children has not yet been solved and it is further complicated by the ancient system of giving frequent purgatives to children along with imperfect methods of feeding in our country. Whether

the habit of giving a daily dose of purgative at frequent intervals for children is good or not, it is a fact that it is being practised in many of the households and it may be useful to investigate into that also.

Therefore I thought it necessary first to find out from an enquiry at random the actual and existing state of affairs in households regarding diet of healthy children, their previous illness, general bowel action, usual purgatives given and various other things, taking care to see that various communities and people belonging to various social positions were included in the enquiry. The results of my investigation in this direction are tabulated below. There is another thing which is worth consideration and that is vaccination of children against small-pox. The effects of vaccination while being good so far as the preventive aspect is concerned, it may sometimes produce some unexpected and unforeseen results. A few children were found run down in health from the time of its vaccination. The virus of vaccination is thought by some to be the cause of this ill-health. But in the absence of definite proofs we have to content ourselves by keeping our eyes open to this probability.

ILL-EFFECTS OF VACCINATION

Age	No.	Community				Ill Effects of Vaccination, if any
		Brahmin	Non Brahmin	Muslim	X'an	
Between 1 & 2 yrs.	61	31	12	17	1	Only 3 children were ill in the lot of children studied after vaccination. One suffered from severe diarrhoea, another from bronchitis and the third actually got small-pox.
2 & 3 yrs.	140	50	55	31	4	
3 & 4 yrs.	41	12	22	5	2	
over 4 yrs.	15	5	8	1	1	
Total.	257	98	97	54	8	

DIETS OF CHILDREN UNDER INVESTIGATION

Kind of Diet:	No. of Children	Remarks
Cows' Milk Pure	6	Most of the older children are found to take rice and curry and majority of children between 1 and 2 yrs. are given only diluted cows' milk.
Diluted Cows' milk	128	
Rice and Milk	42	
Horlicks	12	
Barley	13	
Allenburys	3	
Rice and curry	52	
Total	257	

NATURE OF PURGATIVES GIVEN TO CHILDREN UNDER INVESTIGATION

Purgative	No. of Children	Remarks
Castor oil	112	Majority of children are given castor oil of Swastik or Baby Brand or home-made.
Pills	28	
Mixture from Doctors	48	
Gripe water	8	
Powders	18	
Salts	87	
Milk of Magnesia	6	
Total	257	

For comparison with these healthy children, information under the same heads for children suffering from hepatic cirrhosis were obtained. A tabular form showing the kinds of diet given to such children are given below.

Diet	Ages of Children Studied				
	1-2 yrs	2 & 3 yrs	3 & 4 yrs	4 & 5 yrs	Over 5 years
Pure cows' milk	5	1	4	—	—
Diluted cow's milk	11	9	2	—	—
Milk and Rice	10	4	4	2	—
Conjee & milk (Sago etc.)	9	7	2	—	—
Horlicks	3	1	2	—	—
Milk and glucose	1	1	—	—	—
Lactogen, rice & cows' milk	1	—	1	—	—
Rice, milk & Horlicks	1	—	1	—	—
Rice, milk & glucose	1	1	—	—	—
Rice, milk & orange juice	1	1	—	—	—
Total	43	26	15	2	—

From the facts shown above it will be seen that the diet of children with hepatic cirrhosis does not differ to a great extent from the diet of other healthy children. If at all there is any difference, it is in the direction of greater quantity and better quality of the diet given to children who seem to get this disease. At any rate want of nutrition on account of the deficiency in either the quality or quantity of the food is not found to be there. As regards purgatives information on that head could not be got for all the children, but from information obtained so far castor oil either Swastik or Baby brand seems to be the usual purgative administered.

No child in this series gave any history of having had any illness after vaccination and hence this information has not been included in the tabular form.

CONCLUSIONS

1. After weaning, the diet of a healthy child is generally cow's milk, either pure or diluted, till it reaches the age of nearly three years after which rice is usually given.

2. A small number of children get either patented foods or cow's milk in addition.

3. The diet of children who have Infantile Hepatic Cirrhosis does not materially differ from the kind of diet given to healthy children though in some cases the former may be richer in quality or quantity than the latter.

I am much indebted to Doctors K. S. Sivaramakrishna Aiyer, J. V. Badrinayan and others who helped me with their cases and information for my study, and to the parents of all the children who came under my observation.

Modern Conception of Anaemia, Its Causation and Classification, with Special Reference to the Disease as seen in Assam*

● K. P. Hare, M. B., B. S., L. M. S. S. A.,
Hoogrijan P. O., Assam

INTRODUCTION

Till about ten years ago anaemias were classified as "primary" and "secondary". The primary anaemias were those in which no cause could be found: that is, they were "idiopathic". The secondary anaemias were those in which some other condition, which might be casually connected, was also present. This was a most unsatisfactory state of affairs but an even more unsatisfactory feature is that it has, in part, persisted in medical text-books and teaching to the present day.

The modern conception of haematology dates from the spate of research which followed the discovery by Minot and Murphy in 1926 of the effect of raw liver on pernicious anaemia. It is now realised that the marrow, the reticulo-endothelial system and the circulating blood form, in effect, a complete organ, the erythron. Intensive research indicated that the red blood cell is manufactured in the capillaries of the marrow and that, in its manufacture, it passes through several stages, each stage requiring some external stimulus for its perfect completion. From the marrow it passes out into the peripheral blood stream and, when it has completed its useful life, it is destroyed by other cells of the reticulo-endothelial system, probably chiefly in the spleen. The anaemias are now regarded as being specific diseases of the erythron due to pathological influences operating at various places in the organ.

The parent red cell is probably one of the ordinary fixed reticulo-endothelial cells lining the marrow capillaries which becomes detached to form the early megaloblast or primitive erythroblast. It is a fairly large cell with scanty cytoplasm and a large, loosely constructed nucleus. This cell changes into the regular megaloblast of the marrow, a cell with a greater amount of strongly basophilic cytoplasm and a more compact rosy nucleus. Later the cytoplasm becomes haemoglobinised and the megaloblast then changes into the

*A lecture delivered before the Tingri Valley Branch of the All-India Medical Licentiate's Association, December 17, 1939.

fellows, for poverty implies primitive living conditions and those are just the conditions most favourable to the spread of the parasite. It is possible that the chronic blood loss associated with hookworm infection may just turn the scale against a marrow which is fighting hard to make bricks with insufficient straw, but I firmly believe that the primary cause of this anaemia is a lack of minerals, especially iron and calcium, from the diet with, in many cases, an added lack of vitamin C.

Anaemias due to excessive blood destruction are principally represented by the acute anaemia following severe post-partum haemorrhage. Other anaemias of this class are certainly rare.

Mixed Anaemias: In my experience, the second commonest anaemia in Assam is the macro-microcytic anaemia of haemolytic type associated with pregnancy. It is a severe anaemia, often accompanied by extensive oedema and frequently fatal. It appears to be due to a coincident lack of both the extrinsic factor and minerals from the diet together with excessive haemolysis due to over-activity of the reticulo-endothelial cells of the spleen, presumably a legacy from chronic malaria. Also associated with pregnancy in Assam is found the macrocytic hyperchromic nutritional anaemia of haemolytic type. Fortunately it is not so often met with, and it is a very dangerous disease and frequently has a fatal termination.

DIFFERENTIAL DIAGNOSIS OF ANAEMIAS

It is unfortunate but true that the exact differentiation of types of anaemia is impossible without the help of the laboratory. A complete haematological examination includes red and white cell counts, estimation of haemoglobin by some exact method, estimation of the cellular volume by the centrifuge and the Van den Bergh test. In addition stained films must be examined. Such examinations can only be carried out either in the course of research work or, as a routine, in a fully-equipped laboratory. But a great deal of information can be secured by the possessor of a microscope if simple blood counts are made and stained films examined. I would here make a plea for the exact estimation of haemoglobin values. The Tallqvist Scale is valuable for the provision of confirmatory evidence of the existence of anaemia when it has been suspected clinically, but readings on

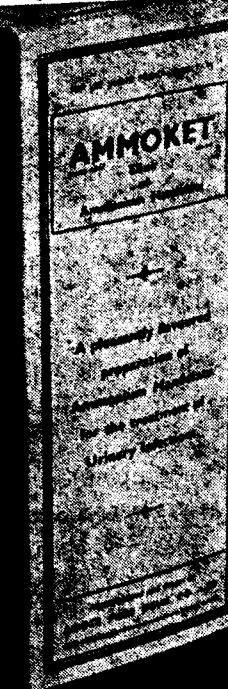
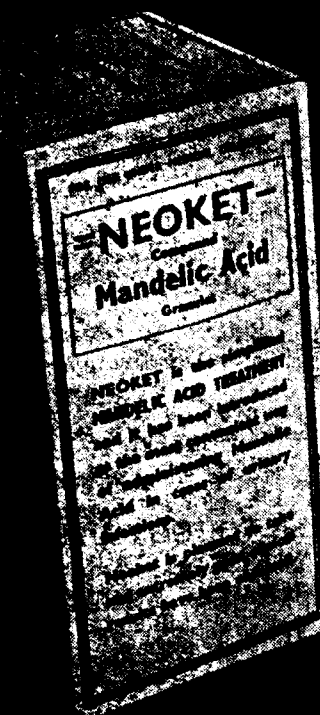
it are subject to such a large margin of error that it is not really suitable for estimating improvement or deterioration in haemoglobin level. Expense, of course, is the difficulty but I assure you that it is worth the while of anyone in private practice to provide himself with a simple haemoglobinometer of the Sahli or Hellige pattern. Moreover you will find that your recording of cases will be made more interesting and capable of correlation with findings on anaemia in the medical literature if you form the habit of expressing haemoglobin values in grammes per 100 c.c. You may not realise it but it is a fact that the term 100 per cent of haemoglobin has no standard meaning, for nearly every different manufacturer of haemoglobin scales decides on a different standard. With one instrument 100 per cent means 13.8 grammes of haemoglobin, with another it means 16.0 grammes and with yet another 17.0 grammes. From the red cell count and the haemoglobin value can be calculated the mean corpuscular haemoglobin in micro-microgrammes. A M. C. H. of 30 or over indicates hyperchromic anaemia, one of 22 to 30 an orthochromic condition and one under 22 a hypochromic state. In stained films you may assess degrees of anisocytosis and search for megaloblasts and normoblasts. The presence of the latter and especially of megaloblasts is indicative, in my experience, of a tendency to the macrocytic hyperchromic type. The greatest degree of anisocytosis occurs in the macro-microcytic anaemia. Bear in mind that the megaloblast which is seen in anaemia in Assam is the basophile megaloblast of the marrow and not the haemoglobinised megaloblast of pernicious anaemia. In the absence of any scientific aids to diagnosis, you must depend on your own clinical acumen. Speaking generally, microcytic anaemia is not a grave condition and the patient will only show such general signs of anaemia as pallor of the mucosa, slight puffiness of the face and some dyspnoea on exertion. The macrocytic nutritional anaemia is a much more serious condition and is usually accompanied by marked oedema of the extremities, probably analogous to famine oedema. In the worst cases there is general anasarca. A majority of these cases show also enlargement of the spleen and many give a history of recent malaria. The symptoms in macro-microcytic anaemia vary according to the degree of nutritional defect and of haemolysis. So far as my own experience goes, I think the danger signs are marked oedema, splenic enlargement and a history of recent malaria.

March, 1940]

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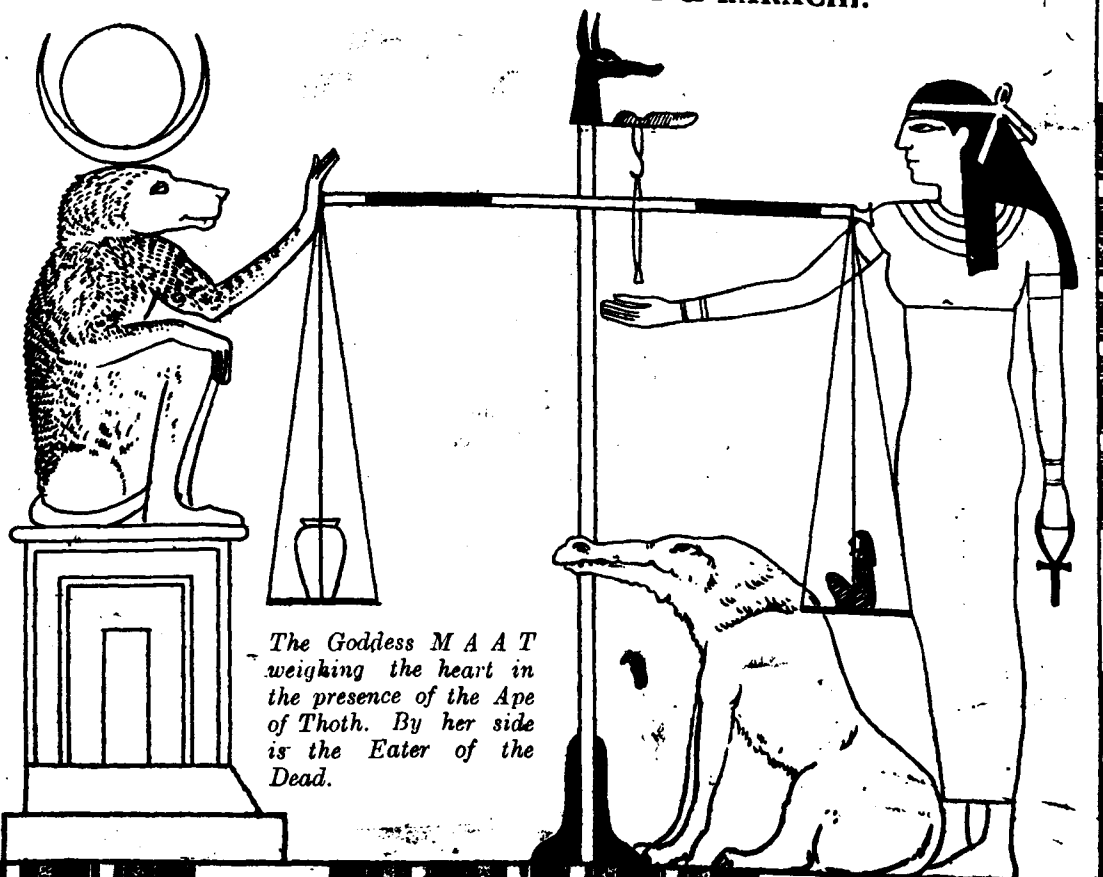
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TREATMENT

Since probably 75 per cent of cases of anæmia in Assam are of the microcytic hypochromic type, due to deficiency of minerals and/or of vitamin C, your first essential is to give adequate iron and to improve the diet. Either iron and ammonium citrate, not less than 90 grains daily or ferrous sulphate, not less than 12 grains may be given, but do not be satisfied with lower doses than these. The use of small doses of iron is a complete waste of effort and money. In the case of many of the proprietary tablets and pills the dosage suggested by the manufacturer is well below this standard so that to give adequate amounts may make the cost prohibitive. If your patient objects to the taste of iron in liquid form your cheapest, and probably most satisfactory, alternative is to give the old-fashioned Blaud's pill. To improve the vitamin C intake encourage your patient to take green leafy vegetables and insist on raw fruit being taken daily. Pine-apples, papayas, limes and oranges will all supply the necessary vitamin and, in their respective seasons, are cheap and plentiful.

Another 20 per cent of your cases will be of the macro-microcytic type necessitating, in addition to the above, the improvement of the vitamin B fraction of the diet. I may have been unlucky but I do not seem to have had the results from marmite which one should expect. I have found rice polishings to be much more effective. This substance, consisting of the pericarp and embryo, can be obtained from the rice mills and may be given to the patient as a paste made up with milk and molasses. Where there is any suspicion of chronic malaria, which there will be in quite a large proportion of your cases, it may be advisable to give also a course of quinine. I think liver treatment should be definitely restricted to those cases which are going downhill and to those with general anasarca.

Of the remaining 5 per cent, the majority will be macrocytic hyperchromic cases and these all require liver treatment. This disease in Assam does not react well to raw liver by the mouth; nor does it react well to the purified liver preparations. One might almost say that the cruder the preparation the greater and the more certain the response. That was the great advantage of Campolon and since hostilities started I have been trying to find a satisfactory substitute. I think I have found one in the injectable liver extract of the Bengal

Chemical and Pharmaceutical Works, an Indian company, which will not be affected by the difficulties of trading on the high seas at the present time.

In the few cases which will not respond to a combination of iron, quinine, fresh fruit, rice polishings and liver extract you may try blood transfusions. But I warn you that it is necessary to give at least half a pint of blood and preferably to give a pint. But to find a donor who is willing to give that amount is not easy; many individuals of the coolie class, too, would become seriously anaemic themselves if they lost that amount of blood. Auto-haemotherapy also has its advocates but I am rather doubtful about some of its claimed successes.

I certainly believe that you will cure the greatest number of cases in the shortest possible space of time if you give all your anaemia cases iron, fresh fruit and rice polishings and, where there is no improvement, large doses of liver extract say 4 or 5 c. c. daily for five or six days, repeating the course later if necessary. But whenever practicable, withhold liver extract until you are certain that the simpler scheme of treatment is likely to fail. Although I think the hookworm has been unjustly blamed for anaemia, I have no particular affection for this parasite and it is advisable always to give these patients anthelmintic as soon as they are fit to take it. There is no point in harbouring hookworm infection when you can easily get rid of it.

I thank you for the patient hearing and hope that this resume of the modern conception of anaemia may help you to take greater interest in what is one of the common diseases which you are most frequently called upon to treat

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CLINICAL NOTES

(Only summaries are published owing to exigencies of space. Ed.).

A Case for Diagnosis

History: Syed Bunyad Hassan, Muslim male, aged 35 years of this place, experienced ten years ago, a fit of yawning lasting for an hour or two in the early part of the night. This continued to recur every night for nearly eight months, and then stopped even without any treatment. Shortly after that, he went on a pilgrimage to Mesopotamia. On his way (at Bombay) he got an attack of nasal catarrh which became worse on reaching Mesopotamia, where he further developed ulceration of the left side of the palate. This gave rise to frequent sneezing and impairment of digestion. In the colder climate of Syria and Iran he felt comparatively better, but on return to India his troubles became worse. The curious thing was that severer the symptoms greater was his appetite. The latest addition to his troubles was flatulence and consequent distension of the abdomen. It is not however a constant symptom, but it attacks in fits, sometimes more severe, at other times less, and again he is symptom-free. During the period of flatulent fits, he is constipated and suffers from polyuria. His urine however is normal in all respects. His normal temperature in mouth is 99°F. A cold bath or a cold drink would afford some relief. Another curious thing: whenever he smokes *hukka*, a number of blue-bottle flies gather about him while they do not pester this patient if he is smoking cigars or cigarettes. If he leaves off *hukka*, they fly away.

But for these symptoms he is practically healthy.

Would your readers be good enough to discuss the diagnosis of this case in your columns?

Zaidpur,
20-1-1940.

SYED ZAHEER MAGURIE,
M.O., CIVIL DISPENSARY.

(These notes are incomplete for diagnosis. The fitful occurrence of yawning and flatulence suggests an allergic cause. Allergic cases are usually characterised by a preliminary nasal catarrh. The allergen may be exogenous or endogenous. Or it may be a case of B vitamin deficiency, particularly B₁, which has been known to cause palatal ulceration, flatulence, constipation, etc.

The clustering of blue-bottle flies while the patient is smoking *hukka*, but not a cigar or cigarette, may be explained by the fact that they are attracted by the sweet smell of *Hukka* smoke, as its tobacco is usually made up of a good amount of jaggery, while the tobacco contained in cigar or cigarette does not contain any sweetening agent.

As for treatment, it would be profitable to try vitamin B preparations for at least a month, and if this does not produce any favourable results, the possibility of an allergic cause must be explored by sensitization tests. Ed., I. M. J.).

An Interesting Case of Haemoglobinuria

A tea-garden cooly, aged 15 years, strong, healthy and hard-working, was admitted into the hospital on 14th July 1939 for the treatment of Black-water fever of two days' duration. He gave a history of frequent malarial attacks (apparently B. T. infection) and suffered once from B. W. fever when he was ten years of age. The history of the present illness was that on the midday of 12th July he had a sudden attack of fever with chill and rigor. On the next morning his temperature came down to normal, but in the evening it rose up to 103°F. and remained so till next morning. During these two days, he took quinine sulphate capsules, 5 grs. each, three times a day, and aspirin twice (5 grs. each).

He came under my treatment on 14th July 1939 when his temperature was 102°F., pulse 120 and respiration 28 per minute. Medicines were stopped to test the urine. At midday, a sample of urine was collected which was tarry coloured and loaded with albumin. He had slight enlargement of liver and spleen. The course of the disease lasted for 51 days and it was characterised by:

- (1) Daily evening rise of temperature with irregular attacks of haemoglobinuria.
- (2) Headache, hepatic tenderness, pain in the loins and calf-muscles, jaundice, bilious vomiting, constipation, etc.
- (3) On the 17th day he had anuria for 12 hours.
- (4) Haemoglobinuria was almost paroxysmal in nature, and urine fairly clear during a-pyrexial periods.

His peripheral blood was examined for malaria parasite on the 8th, 13th and 22nd day of his disease, but none could be discovered.

He was treated first with alkalies, Atebrin and Livadex, but with no effect. Later he was given methylene blue injections and quinine in sensitizing doses. This also proved of no avail, and the patient died on the 51st day of his disease.

Points of interest in this case are:

- (1) Clear malarial history and yet the absence of malaria parasites in the blood,
- (2) The failure of quinine, atebrin and other drugs used,
- (3) The paroxysmal nature of haemoglobinuria.

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Tuberculous Splenomegaly

Leonard Howells¹ reports three cases of tuberculous splenomegaly, two simulating splenic anaemia, and one Hodgkin's disease. The first case was that of a woman who presented the clinical features of splenic anaemia with subcutaneous haemorrhages, uterine bleeding, and a low platelet count. The diagnosis of tuberculous enlargement of spleen was only arrived at by microscopic examination after splenectomy. The second case was due to obstruction to the portal and splenic veins by adhesions formed by a previous attack of tuberculous peritonitis. This obstruction caused splenic enlargement and ascites. The symptoms simulated Banti's syndrome. Unlike in the first case, splenectomy could not be performed owing to extensive adhesions. The third case was a patient suffering from generalised enlargement of the superficial lymphatic glands with enlarged liver and spleen of seven years' duration. The clinical picture was that of Hodgkin's disease,

1. *Br. Jour. of Tuberculosis*, Vol. 33, No. 2, pp. 178-117.

and only when microscopic examination of an excised gland was made tuberculous nature of the condition was revealed.

This report is of exceeding interest to our country, because the more common causes of splenomegaly, due particularly to malaria and kala-azar, are likely to obscure splenic enlargement due to tuberculosis. In fact, the tendency is to view splenic enlargement occurring in the course of tuberculosis as a malarial superimposition. It is to check this tendency that we have chosen to review Leonard Howells' contribution on the subject of tuberculous splenomegaly.

The author admits that diagnosis is difficult, and is rarely made prior to splenectomy or post-mortum, because there are no definite clinical features characteristic of this enlargement. The extreme variation and inconstancy of blood changes is an obstacle to correct diagnosis, and they have been known to simulate pernicious anaemia, polycythemia, aplastic anaemia, haemolytic anaemia, acholuric jaundice, myeloid leukemia and haemorrhagic purpura.

He therefore suggests routine radiological examination of spleen and chest in all forms of splenomegaly of doubtful aetiology. Others suggest that an X-ray of the spleen should be taken in all cases of pulmonary tuberculosis. Tuberculous spleen is however considered to be secondary, and the presence of calcified nodes in the spleen may suggest their tuberculous origin. He quotes Moorman (1937) as having reported 24 cases of calcified nodes in the spleen, as revealed by X-ray, and subsequently confirmed as due to tuberculosis by laboratory studies after splenectomy or at autopsy.

The treatment suggested by the author is splenectomy if there are no extensive adhesions, and deep X-ray therapy or radium as an alternative. The results of splenectomy are reported to be good while those of the latter are said to be unconvincing.

In the differential diagnosis of splenomegaly in India, we think it is important to include tuberculous splenomegaly, for one reason among others that tuberculosis is as common as malaria and kala-azar. This perspective is likely to reveal more tuberculous spleens than is the case at present. At any rate, enlarged spleen proved not due to protozoal diseases should be X-rayed with a view to ascertain the exact tissue changes that had taken place in that organ.

guilty as the importing countries. We hope and trust that the Provincial Governments would take early action under provisions of Section 32 of this bill and bring into existence the necessary organisation to control the standards of drugs and preparations manufactured in their respective areas. Hitherto the Central Government has been blamed for not acting quickly. Let not the table be now turned, and the Provincial Governments criticised for any further delay and inaction.

The medical journals in India should also co-operate in the successful working of the Drugs Act. This they can do in many ways. One of them is to take advantage of Section 25 and expose in their columns such preparations which do not conform to the standards laid down by this Act. The *British Medical Journal* and the *Journal of the American Medical Association*, as has been pointed out by us previously in these columns, have done yeoman service to the profession and the public by systematic exposures of such pharmaceutical and patented remedies which are sold to the gullible public under various pretensions and claims. We should do no less with the aid of the present Drug Act. The Government have now given to the profession what it has been urging for a long time, but it cannot make the horse eat and drink if it does not choose to do so.

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CURRENT COMMENTS

Vitex Peduncularis in Black-Water Fever

Measham⁵ reports 11 cases of black-water fever treated successfully with the infusion of vitex peduncularis and concludes that this is of definite value in the relief of symptoms, such as fever, hepatic tenderness and loin ache. The infusion is said to be well tolerated by the patient. This plant grows largely in Bihar, Eastern Bengal, and the C. P. In the footnote to Measham's article by the editor of the *Indian Medical Gazette*, it is remarked that the drug is by no means a specific either for malaria or black-water fever; that no drug which would not combat the shock and damage of a typical haemoclastic crisis of black-water fever can be considered to be a specific for the disease; and that the clinical trials are confined to too small a series to be convincing. This is quite true from an academical point of view, but we do not feel inclined to dismiss the subject so summarily. The treatment of black-water fever, a fatal case of which is reported in this issue, is so unsatisfactory that even scrappy reports as from Measham have to be taken into account by our pharmacologists with a view to find out the exact therapeutic value of vitex peduncularis, and its alkaloids if any. It was in this way that ephedrine vulgaris and kurchi bark have come into justified prominence in modern therapeutics. Even if it is shown that vitex peduncularis can be trusted to relieve at least the urgent symptoms of black-water fever, it will be no mean gain to the practitioners. It seems to us that the plant is worth re-investigating, and while we say this we are not unaware that the exact aetiology of black-water fever is still shrouded in mystery and that while this is so it is not easy to hit at a "specific".

Fresh Additions to Medical Journalism

Journals devoted to special subjects are comparatively few in our country, and we therefore welcome the enterprise of Poona and Lahore in having ushered the *Indian Journal of Ophthalmology* and the *Journal of the Obstetric and Gynaecological Society of Northern India* respectively. They are indeed costly enterprises in these hectic days of war when printing paper is not easily available even at a high price and medical advertisements are very shy owing to the narrowing of marketing facilities. That they have been started in spite of such unfavourable conditions shows

the enthusiasm and determination of their editors to do their duty by the profession in spheres where their help is needed most. Both the editors are well-qualified and experienced, and this is a guarantee that the standard of these special journals will be kept up, and the field of their usefulness enlarged by the passage of time and gaining of experience. Their first Numbers are good and contain interesting contributions. We wish them a successful career, and as their success depends on the response and co-operation from the profession we would earnestly appeal to the latter to make these special Journals worthy of our country, and to help the editors by all possible means in the discharge of their onerous and sacred duty. Let us not, as is our weakness, be supine and passive in our help to great enterprises of this kind, but share with the editors the difficult task and responsibility of leading them from success to success.

Free Medical Advice

The *National Herald* of Lucknow⁶ seems to be very solicitous to the medical profession by suggesting that the resolution of the last All-India Medical Conference advising the members of the profession not to give free medical advice except to the really needy and indigent persons would deprive medical practitioners much of their clientele. But this solicitude is marred by threats and insinuations which betray a melancholy meanness, and a gross ignorance of facts, both of which could have been avoided if only the sub-editor (we hope it is only a sub-editor) who penned the criticism consulted any local practitioner as to the exact implications of the resolution under editorial scrutiny. We certainly welcome fair criticism, but we resent mud-slinging. It is a vulgar sarcasm to question, as the paper does: *Is the rate sought to be proportionately higher in India because medical men here are generally incompetent?* We can rightly hit back by asking why any editor should be paid for by his proprietors for indulging in unfair and uninformed criticism at the sacrifice of truth and decency. The English of the resolution is so simple that we are amazed to find how a sub-editor of an English daily would find a meaning which its words do not imply or convey, unless it be due to the not un-natural editorial propensity to write something on nothing and give it an attractive colour by unproven hypotheses and untenable insinuations. We are glad at the prompt reply by the *Journal of the Indian Medical Association*⁷

to this curious piece of un-informed and vulgar comment, and we stand by every word of it.

Senile Prostatism

Recent studies have shown that senile hypertrophy of the prostate is endocrinal in origin and is due to the relative decrease of male hormone and increase of oestrogenic substance in the testes. The literature on the subject is ably reviewed by Lahiri⁸, and he says that the successful treatment of senile prostatic enlargement depends on the restoration of normal balance between the male and the female hormone in the testes. This is the rationale of injecting testosterone propionate, by which it is sought to maintain the hormonal balance of testes, and thereby reduce the hypertrophied prostate. The old treatment was by castration which has rightly fallen into disuse today owing to induction of male climacteric. Steinach's operation, consists of ligaturing the efferent ducts. This produces degeneration of the germinal epithelium of the testes, hypertrophy of the interstitial cells, and consequent increase in concentration of male hormone. But there is no need to revive these old operations when there is the chance of supplying the deficiency by injection of testosterone propionate. It must however be clearly understood it is not likely that every case of senile prostatism would respond equally to male hormone therapy, and failures should be frankly expected.

Rural Medical Officer in the Punjab

The lot of rural medical officers in such provinces where the system of rural medical relief has been working for some time, is none too enviable, and they are made to march and work like the dumb-driven cattle. We pointed out last year in these columns⁹ that, unless the personality of the rural medical officer is respected by giving him the advantage of such provisions as reasonable remuneration, leave privileges, unified control and freedom to chalk out his own programme of work within his area, subject to proper guidance and less of the time-worn official red-tapism, what is an otherwise excellent system of rural medical relief is bound to be throttled by defective outlook and organisation. The rural medical officer is today suffering from dichotomy of loyalties and work. He has to serve many masters: the District Board, the Civil Surgeon and the

⁵ *Jr. of the I. M. A.*, Jan. 40, pp. 148-151.

⁶ *Ind. Med. Jr.* Current Comments, Feb. '39, p. 46.

⁷ Monday, Jan. 1, 1940.

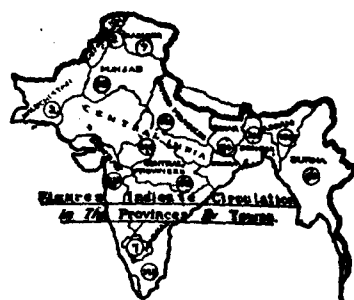
⁸ Jan. 1940, pp. 166-167.

⁹ *Indian Medical Gazette*, Jan. 1940, Pp. 26-27.

District Medical Officer of Health. He has to do every kind of work: health propaganda, health work and dispensary medical and surgical relief. The too comprehensive nature of the work that is allotted to him will by itself mar his efficiency either as a rural health officer or as a rural medical officer if he is made to do both the work at one and the same time. In the Punjab, the anxiety of the Government to improve rural sanitation and to carry medical relief right into the villages has led them to transfer a few rural dispensaries to the control of the Public Health Department as an experimental measure. The arrangement in such dispensaries is that the rural medical officer should tour the adjacent villages in the afternoon for at least five hours on every alternate day and do such work as digging of manure pits, inspection of school boys, health lecture and infinite other sundry public health work which is usually done in every country by the Sanitary Inspector, in addition to medical aid at the villagers' own homes. We are not for a moment suggesting that this kind of work is unnecessary, and the doctors should not be made to do it. But we do believe however that to take away the rural medical officer from his dispensary for an aggregate of 15 days or more in a month on extra duties far distant from his village, and putting the dispensary under the charge of medically unqualified personnel like a dispenser is bound to impair the usefulness, efficiency and popularity of any rural dispensary intended for medical relief. Emergent and serious cases that come to the dispensary during the absence of the medical officer have necessarily to be tackled by the dispenser, often with disastrous results. This is altogether unfair to the residents living within the dispensary area, who expect qualified aid at any time, as well as to the in-door patients, not to say of its also being ethically wrong. We certainly recognise the need and urgency of rural public health work as much as that of rural medical relief, but these works should be kept separate and staffed by different sets of persons, and not by constant and perpetual forking of the duties of the rural medical officer to the detriment of dispensary work to which he is apparently put in charge. The best and effective way out of this tangle is to create a separate Rural Health Cadre in the same manner as its medical counterpart. This division of work is inevitable if either the public health or medical relief is to be rendered to the people with any tangible results and definite advantages. In

any case, if the rural medical officer has to do collateral health work it should be near the vicinity of the dispensary to enable him to attend to urgent cases within 15 or 30 minutes of call. The rural dispensary would never make an impression on our people if it does not serve them, or serve them badly, in such medical or surgical emergencies. We understand that this year's Conference of Civil Surgeons in the Punjab would take place in April next, and we hope that it will review the question of rural health work and rural medical relief in proper perspective and arrive at such conclusions as would make both these two essential parts of rural work efficient, effective and popular. Our suggestions are mainly two: (1) Respect the personality of the rural medical and health officer by giving him reasonable remuneration and reasonable burden of duties. (2) Separate the rural health work from rural medical work instead of the present welter of multiple duties and multiple masters, and of foisting them on the slender shoulders of the poor rural medical officer. There is no use of grinding him to dust in the name of rural public health and medical relief. This has been, in our opinion, the fundamental cause of the very tardy success of subsidized and other schemes of rural medical relief in all our provinces where they have been introduced.

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Cardiology

(15)

CARDIAC FAILURE (continued)

● Dr. Jai Gopal

Right Ventricular Insufficiency

The right ventricular insufficiency is due generally to loss of pulmonary area. Consequently the circulation of blood through the lungs is impeded and the right ventricle in its efforts to overcome the resistance is overstrained and, passing through the stage of hypertrophy, the exhausted pump begins to show signs of failure. It is associated with the following conditions:

1. In most cases the failure of the right side follows on that of the left, as in some cases of mitral stenosis.

2. *Chronic pulmonary affections*, i. e., chronic bronchitis, emphysema and bronchial asthma, are the common causes of the primary right-sided failure. Pulmonary tuberculosis particularly the late stages, and pneumonia when large portions of both sides of the lungs are consolidated also account for several cases.

3. *Congenital heart disease*.—The pulmonary and tricuspid valves are rarely invaded by pathological lesions as a primary feature. Congenital malformations account for most of these valve lesions. Many cases of congenital abnormalities die in early life and seldom reach their thirties. These patients are cyanosed from their birth and there may be clubbing of the fingers. Sometimes there is loud systolic murmur and a thrill in the pulmonary area. Such a murmur when encountered during the course of an infectious disease or in convalescence is liable to be mistaken for an active lesion of the valve, and undue restriction imposed on a child unnecessarily. In severe anaemia a systolic haemic murmur is present in the pulmonary area and is heard only when the patient is lying on his back and disappears on standing, hence it is not of cardiac origin. It disappears when the blood condition is improved.

4. *Chronic tricuspid regurgitation*, the result of rheumatic lesion, is associated in many cases with mitral stenosis, and results in excessive enlargement of the right ventricle. In this early stage of hypertrophy of the right ventricle the first sound in the pulmonary area is accentuated, because the ventricle is beating

forcibly to overcome the increased intrapulmonary resistance. Comparison of the first sound in the aortic with that of in the pulmonary area will reveal the difference in loudness. In the left heart failure the interference with respiration and onset of dyspnoea is an early symptom due to embarrassment of pulmonary circulation; whereas in a right-sided failure the veins and the liver act as a storage. Hence the stage of congestion persists even before the appearance of ascites and oedema.

Failure of Peripheral Circulation

In a severe toxæmia associated with pneumonia, diphtheria and the like acute infections, there is vaso-motor paresis resulting in the dilatation of the vast capillary field and abolition of the tone in the small arterioles. The result is the patient bleeds within his own capillaries. As the bed of peripheral circulation opens out widely, the heart makes ineffectual efforts to maintain the circulation and ultimately fails.

When there is excessive loss of body fluids as in severe diuresis of diabetes or in constant vomiting or profuse diarrhoea as in cholera, the heart fails due to its inability to maintain efficient circulation. In severe loss of blood, similar effect is produced and unless efforts are made to replace the fluids by giving injections of saline with glucose 5%, or the vasomotor tone is stimulated by the use of strychnia hypodermically in 1/20 grain dose or adrenaline sol. 10 m. subcutaneously, the outlook is gloomy.

Physical Signs and Symptoms of Cardiac Failure

In the right-sided failure thrill is seen in the epigastric region. Percussion dullness extends on the right side of the sternum due to the dilatation of the right ventricle. Systolic murmur is heard at the costo-xiphoid angle. Diastolic murmur is present in the pulmonary area. Venous pulsation is usually visible in the veins of the neck. Pulse rate is quickened (90-120). Dyspnoea is the main feature of the disease which in later stages is constant, even in restful condition, and there is markedly increasing cyanosis.

The reserve power of the right ventricle is comparatively less than that of the left ventricle, therefore it fails rather early, death usually takes place within a few months of failing compensation. Patients die of a severe and prolonged attack of cardiac asthma; oedema of the feet and legs is a late manifestation. The cardiac tonics have very little

influence on the disease or in slowing down the pulse.

Physical Signs in Left Ventricular Failure

These will be considered under two headings i.e., local cardiac signs and the vascular signs:

(1) *Local Cardiac Signs*:—In mitral regurgitation the cardiac impulse is displaced downwards and outwards. The systolic murmur is audible at the apex. From here it is propagated outwards and is heard at the axilla and then at the apex of the left scapula. The murmur of mitral stenosis is also heard best at the apex but is propagated inwards towards the sternum and there is often a palpable vibration or thrill. These vibrations which are not only palpable, but are also visible and audible to the ear are commonly known as GALLOP RHYTHM. In this phenomenon, the first sound is reduplicated, i.e., a new sound is heard just before the first sound and it is therefore presystolic in time. The gallop phenomenon carries with it a stigma of grave prognosis, because they develop when the left ventricle is dilated and weak. In the atonic state of left ventricle, vibrations are set up in its wall on the entry of blood from the left auricle.

In the aortic disease, if double lesion is present, both systolic and diastolic murmur commonly known as *to-and-fro murmur* is heard at the aortic area. In the early stage of aortic disease there is hypertrophy of the left ventricle and the volume of the blood is thrown with the force of a projectile into the aorta. Hence the percussion wave in the arterial tracing is very high. In regurgitation the column of blood raised during systole cannot be sustained and is thrown back by the forcible recoil action of the aortic arch. The subsidence of the pulse is equally dramatic and sudden and imparts a peculiar sensation to the fingers. This kind of pulse is known as the WATER HAMMER PULSE.

(2) *Vascular Signs*:—During decompensation, owing to the working incapacity of the left ventricle, there is slowing of arterial circulation and the pulse pressure becomes low with the result that various organs suffer from the effects of reduced quota of blood supplied for their nourishment.

Liver:—Thus the liver is imperfectly supplied with arterial blood. The force of the heart is insufficient to drive the circulation through the liver capillaries. The liver therefore becomes slightly enlarged and tender, and there may even be icterus tinge. This type of liver is commonly known as cardiac liver. Chronic engorgement of the liver due to venous stasis in

the later stage of heart failure is associated with impairment of its function. There is jaundice due to congestion. The derangement of metabolism is associated with faulty oxidation of fats in liver or sets up acetonæmia and constant vomiting.

Diminished arterial circulation through kidneys results in diminution of urine and there is urea retention. During later stages of congestive failure, the output of the urine is diminished due to congestion of the renal veins. The urine is high coloured with high specific gravity and there is thick deposit of urates. In elderly patients there may be fibrosis of the kidneys, therefore diuretics fail to promote the flow of urine. Deficient excretion of urea may precipitate uræmia.

Diminished supply of blood to the brain causes anæmia and sleeplessness.

The most important and the noticeable feature of defective arterial circulation is the peripheral oedema and the pallor of the skin. The oedema commences from the lowest and dependent parts of the body and extends upwards from the ankles to the legs. The cardiac oedema of the feet is worse at the end of the day when the myocardium is exhausted and incapable of maintaining an efficient circulation in the most dependent part of the body where even under normal conditions the velocity of the blood flow is minimum, besides the local gravitative factor being in operation. In cardiac cases this is a common feature for many years. In the later stages of congestive heart failure, there is passive venous stasis resulting from the right ventricular insufficiency and the evolution of oedema has reverse character. Prolonged congestion of the liver and portal stasis lead to ascites with oedema of the legs, and is usually accompanied with cyanosis.

When the left ventricle shows signs of weakness, not only there is defective arterial circulation in the pulmonary area (forward failure), but there is simultaneous slowing of the blood flow behind it, and there is a fall in the rate of circulation in the lungs (back pressure theory of heart failure). The reserve capillaries of the lungs are opened up with a view to maintain the output within normal limits. This opening up of the lung-reserve field which nature has liberally endowed—even a conservative estimate would allow the removal of a 40% of the lung substance before dyspnoea would appear with the body at rest though successful in maintaining the outflow within normal limits—is associated with still further slowing down of the pulmonary circulation owing to an increase in capillary bed.

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Histamine is injected intravenously, the dose being 0.001 mg. per kilo of body weight. For convenience 0.125 mg. is put up in one c.c. ampoules. Four to five minims is sufficient for a dose of half a minim per stone of the body weight. At first a salty taste appears in the mouth followed by a flush in the face commencing around the eyes and is visible in a good light. In a normal individual the onset of flush appears in twenty-five seconds. In a cardiac lesion associated with commencing failure, the flush time is generally prolonged to forty seconds as the delay occurs in the slow rate of pulmonary circulation; whereas in a cardiac lesion unassociated with dyspnoea and without any signs of decompensation, there is no delay in the onset of flush.

Dyspnoea is produced due to inefficiency of the pulmonary circulation. In early stages there is slight breathlessness, but later on the dyspnoea is severe and of grave anxiety not only to the patient himself but even to the relatives also. This breathing difficulty is in direct proportion to the stasis in the lungs. The onset of nocturnal dyspnoea is associated with grave weakness of the left ventricle and it has already been stated that in a severe degree of failure dyspnoea is a constant feature, even when the body is at rest.

The diagnosis of a purely cardiac dyspnoea from that of a pulmonary origin is recognised by a thorough examination of the lungs. In pulmonary tuberculosis and pneumonia, the rate of breathing is advanced, and the absence of cardiac lesion will decide the nature of dyspnoea. In obesity the descent of diaphragm is impeded by the accumulation of fat in the abdomen and there is shortness of breath. In sedentary obesity myocardium may be weak due to lack of activity or there may be fatty infiltration of the myocardium and be responsible for shortness of breath; and the question of weight reduction or advising activity in daily work needs our careful attention. Increase in intracranial pressure in sufferers from brain abscess or tumour interferes with the central nervous mechanism of respiration. Dyspnoea in these cases is a late phenomenon and by the time it is evident, other signs indicative of these conditions are distinctively present. Hysterical women sometimes mask this condition so successfully that it may occasion great alarm.

Orthopnoea, while the person is at rest or sits up in chair, is a sign of grave cardiac failure or diminution of circulation in pulmonary field.

In sitting up position, the respiration is comfortable due to increase in the vital capacity of the lungs depending upon increase in the field of aeration occasioned by the efficient descent of diaphragm and widening of the intercostal angles. This expansion is capable of increasing the aeration field and hence sense of ease and relief from suffocation. Orthopnoea is therefore not only a postural expression of the heart, but also that of reduction in the lung field. It may therefore be seen in hydrothorax, emphysema, asthma and mediastinal growths. In acute abdominal distension, ascites, enlargement of liver due to abscess or hydatids and in some cases of obesity, the descent of diaphragm is impeded and orthopnoea is seen. Treatment will depend upon the elimination of cause and venesection to relieve the venous pressure.

Cyanosis, a bluish discolouration of skin, is commonly seen in fingers, lips, tip of nose and ears. Its intensity is directly proportional with the amount of reduced haemoglobin circulating in the blood. Retardation in the flow of blood results in the excessive loss of oxygen. When the force of myocardium is incapable of maintaining an efficient velocity in the blood stream sufficient for the nourishment of tissues, deoxygenation takes place before the blood has reached the peripheral arterioles or the capillary bed. The extra time taken by the blood flow due to decreased velocity is responsible for the cyanosis. In the final stages of heart failure, stasis in the peripheral capillaries is the result of slowing down of the rate of venous return. Pulmonary changes such as oedema of the lungs and hydrothorax interfere with oxygenation of blood and leads to cyanosis. Congenital heart disease is associated with severe degrees of cyanosis and clubbing of fingers and toes. This is usually due to mixing of arterial and venous blood due to an abnormal opening between the right and the left ventricle or by a communication between the vessels of the heart carrying venous and arterial blood respectively. Severe stenosis of the pulmonary valve leads to cyanosis. The diagnosis of the cardiac cyanosis from that of pulmonary cyanosis occurring in emphysema, bronchiectasis and fibrosis of the lungs is established by the history of prolonged myocardial weakness or bronchial trouble, and the physical signs associated with the heart or lungs, and study of the functional capacity of the heart. In elderly subjects a double cause may be present. Due to fibrosis of lungs there is defective aeration and due to

myocardial weakness there is retardation in the rate of blood flow.

Cyanosis is frequently associated with sulphanilimide therapy. It may be a simple phenomenon due to the circulation of a dark-coloured oxidation product of sulphanilimide and therefore the oxygen carrying capacity of the blood may remain undiminished. It may be of a toxic nature due to conversion of haemoglobin into methaemoglobin or sulph-haemoglobin which is no longer capable of holding oxygen and carrying it for the tissue nourishment. In enterogenous cyanosis, the haemoglobin is converted into methaemoglobin and sulphhaemoglobin in the vessels of the alimentary tract.

In cases of profound anaemia the presence of general cyanosis is impossible due to lack of colouring matter i.e., haemoglobin.

Praecardial pain is the cardinal symptom of failure and, in a heart case, is associated with ischaemia of the myocardium as in angina pectoris or coronary sclerosis. In embolism death may be sudden within an hour or two due to complete occlusion of coronary vessels by embolism. When occlusion is slow due to thrombosis in atheromatous or sclerosed artery, death may occur after several weeks or life may be prolonged though associated with a marked degeneration of cardiac muscle, fatty or fibroid, with permanent incapacity for work. The anginal pain may disappear due to revascularisation of the ischaemic area from the adjacent vessels or when the non-contractile fibrous tissue has replaced the contractile tissue completely.

Praecardial pain in aortic regurgitation associated as it is with defective coronary circulation and insufficient nourishment of the myocardium, leading ultimately to fibrosis, is due to ischaemic patches formed when the terminal vessels are incompletely filled.

Besides ischaemia, another factor responsible for the cardiac pain is hypertension. Angina and high blood pressure are so intimately co-related in many cases that the textbooks seldom fail to stress their association.

Apart from the two preceding possible causes of praecardial pain viz., hypertension and ischaemia, endocrine disturbances occurring in women at the climacteric period is associated with nervous imbalance resulting in pain in cardiac region. These cases are

symptomatically progressive and refractory to treatment unless measures are adopted to restore the endocrine balance.

The extracardiac causes of praecardial pain are various and deserve detailed consideration:—

Gout.—Irregular gout shows signs of breathlessness, palpitation, and pain in the region of heart. The excess of uric acid is responsible apart from increase in blood pressure due either to arteriosclerosis or renal deficiency.

Diabetes is sometimes responsible for the occurrence of violent pains resembling angina, and in one of my patients coma supervened after a severe excruciating pain had lasted for about 8 hours.

Gastro-intestinal conditions, such as gastralgia, sensory neuroses, hyperchlorhydria, and fermentation in the transverse colon or splenic flexure by causing pressure due to accumulation of gases, cause severe pain in the region of heart.

Septic Causes.—Infected gall bladder, septic appendix, nasal sinusitis, and pyorrhoea alveolaris are frequent causes of cardiac distress.

Intercostal Neuralgia.—In this affection there are usually three tender spots—one near the vertebral column, second near the outer edge of scapula, and the third in the praecardial region. Herpes zoster and mediastinal growths cause pain by their pressure effect on nerve trunks. Tabetic crises and myelitis, besides pleurisy and glandular enlargements, are accompanied with plain.

Aortic Aneurysm.—The pain shoots down the left arm; there is dilatation of pupils, and unilateral sweating of neck and face, and other signs of aortic aneurysm viz., a murmur systolic in time, thrill over the growth and dullness on percussion.

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Bombay, Baroda, Madras, Calcutta.

Report of the All-India Institute of Hygiene and Public Health for 1938*

Although it is fully recognised that the country is badly in need of a vigorous and forward policy in regard to public health organisations, even the small number of technically trained personnel is unable to find employment in this national endeavour.

This observation occurs in the latest Annual Report of the All-India Institute of Hygiene and Public Health, just published.

This paradoxical situation, says the Report, arises from the fact that keen though they are to advance health and efficiency of the people, the authorities find it difficult to launch extensive schemes for health protection because they are confronted with the magnitude of the problem on the one hand, and the paucity of funds on the other. Most of the available funds are already appropriated by curative medicine which, as an organisation, is not only well established by tradition, but yields immediate demonstrable results, while the results of preventive medicine are difficult to demonstrate.

Need for Trained Personnel

Whatever scheme is ultimately adopted, the demand for trained personnel will greatly increase. Facilities for field training which are essential for public health students are, however, inadequate. The health organisations, particularly of rural areas, have not yet become stabilized. On the other hand health schemes, which have efficiently worked in one area, may require to be thoroughly modified when applied to another locality, thus necessitating a grounding in scientific principles on which health programmes are based. In the circumstances, training at the Institute has been necessarily more of a general nature, but the necessity of harmoniously supplementing pedagogic instruction with field training is kept in view.

Side by side with training, researches of far-reaching importance to public health are being carried on at the Institute.

Results of practical value have been achieved in investigations into the causation of epidemic dropsy—a disease widely prevalent in the eastern provinces of India, where it is popularly, though erroneously, known as *beri-beri*. Simple tests have been evolved with which it is now possible to detect the poisonous oil, which has been found closely associated with the disease. The poisonous substance in the oil, too, has been followed to its sources, to a weed scientifically called *Argemone mexicana*, but popularly known as *Kata Kar*, *Sial Kanta* and *Odissimari* in different parts of the country.

The Pernicious Seed

The seeds of this weed, which resemble the black variety of mustard seeds, somehow find their

* A summary by the Principal Information Officer, Govt. of India.

way into the stocks of the latter and constitute a poisonous element in mustard oil. The weed can easily be recognised even by the ignorant villagers because of its peculiar thorny leaves and yellow flowers and should be removed from mustard fields to prevent contamination of the oil seeds. Regular examination of stocks of mustard seeds in shops and mills should also go a long way in preventing expression of the poisonous oil and frequent examination of mustard oil exposed for sale should check the use of undesirable supplies for cooking purposes.

The relation between rats and plague is well known but it may be news to many, as has been revealed by investigations at the Institute, that this pest causes epidemics, also, of severe diarrhoea and certain obscure fevers resembling typhoid. A high percentage of rats has been found to carry infection, and the pest must be systematically destroyed even in the absence of plague, and food through which infection is carried to man, must be carefully protected from it.

Remedy for Black-Water Fever

Investigations have also shown that a mild form of scurvy is one of the ways in which the body is left damaged by malaria and that lime juice is a good remedy. The principle has been applied in the new treatment, evolved at the Institute, of black-water fever (a particularly pernicious form of malaria) which has so far proved entirely successful.

A curious phenomenon has been observed, namely, that there is, in epidemics, a preponderance of one type of malaria parasite over another. It is now possible on the basis of this finding to forecast the probable incidence of the disease.

A survey has been made in selected localities of the diets taken by different communities and it has been found that though, as a rule, people who can afford to spend reasonable amounts on food, obtain proper nourishment, this may not always be the case and useful indications have been obtained of the directions in which food in certain communities needs correction.

Investigations have also revealed that though gross defects in diet over a long period cause deficiency diseases, less serious defects in food cause changes in the body which may not be easily recognised, but which it is necessary to correct if actual disease is to be prevented.

New Apparatus for Nutrition Studies

With the help of an ingeniously constructed apparatus evolved at the Institute, with which it is possible to study the effect of light on the deeper membranes of the eye, it has been shown that as many as 17 per cent of men taking what is called an adequate diet and 43 per cent of those taking a poorer diet show signs of deficiency. Only in 16 per cent of the latter group was external evidence of deficiency diseases manifest. Most of them made rapid recovery when the element which was deficient in their diet was supplied.

An apparatus has also been evolved, which is of considerable assistance to the study of different types of anaemia. Though popularly and correctly associated with low vitality, unnatural paleness of the face is not always in direct proportion to the seriousness of the condition of the sufferer. The colour is due to a red pigment contained in minute discs in the blood and depends on the amount of pigment, but does not give an indication of the size of the disc carrying the pigment. Regular and correct size of the discs is just as important as, if not more important than, the total amount of pigment. Just as a bad mint may produce coins of irregular size and shape, so also a diseased system may produce discs of abnormal size and shape. Measurement of the size of these little discs is tedious and difficult but the new apparatus has made it easier.

Teeth and Nutritional History

A simple method has been worked out of studying the structure of the teeth, which gives indications of efficiency in the assimilation of lime by the human being, and the milk-teeth of children when they drop out, can now be utilized for a study of the nutritional history of the child.

Another finding, which has resulted from investigations at the Institute, relates to the vitamin A contents of the liver oil which can be extracted from certain fish found in Bengal. The virtues of cod liver oil as an article of food depend upon its vitamin A contents, but it has been shown that the liver oils of certain varieties of fish found in Bengal waters locally known as "bo-al" and "a-ir" are 25 times as rich in vitamin A as Norwegian cod liver oil, and that oils obtained from "dhain" and "shole" are nearly twice as rich as those of "bo-al" and "a-ir". Industrial exploitation of Bengal fish liver oils may, therefore, well be attempted.

Tuberculosis in Jute Industry

Active research is being carried out to discover the causes of high incidence of tuberculosis in the jute industry, and it is hoped that these investigations will in time lay bare the vital points on which an effective and fruitful attack on the tuberculosis problem can be directed. The incidence of tuberculosis of the lungs was found to be as high as 2 per cent amongst workers in a jute mill near Calcutta, with an additional 5 per cent or more of probable cases. Were it not for the fact that people actually ill dropped out the figures would have been higher still. The seriousness of the problem can be gauged from the fact that industries such as this attract labourers from far and wide and since the labourers return to their villages suffering from tuberculosis, they form a fruitful source of infection for the non-immunised population of the rural areas.

Studies have also been continued on cholera and the conclusion has been reached that cholera incidence is exhibiting a downward trend in some of the worst affected areas of Bengal, and that one is justified in contemplating the future with

FOREIGN MEDICAL NEWS

Our London Letter

(From Our Own Correspondent)

FOREIGN PHARMACEUTICAL PRODUCTS

Many of these products used in this country have been mostly of German origin. Few of us in this island realise that she need not at all depend on German products, and none of us need feel sorry for the inevitable disappearance of German pharmaceuticals from our market. The Association of British Chemical Manufacturers has published a reliable schedule of British products equivalent to foreign counterparts. The *British Medical Journal* also has recently published a list of equivalent British preparations.

BRITISH CHEMICAL INDUSTRY

This leads me to review the note published by Henry Rhodes, Editor of the *Chemical Practitioner*, who confidently asserts that British Chemical Industry is now second to none in Europe. The English chemist Perkin discovered the manufacture of aniline dyes, but the industry has entirely passed out of British hands. The reconquest of aniline dye industry has now been accomplished, and since the raw material of the industry is coal in which Britain is so rich, thousands of chemical compounds from coal can be produced, ranging from benzene at one end of the chain to everyday drug such as aspirin at the other. Remarkable things are being done by biochemical research workers at Cambridge on what are known as "Organiser substances". They are hormones and their exact composition has not yet been determined. They will build up good flesh and bone exactly where it is wanted, and this is likely to be utilized in repairing irretrievable war injuries. It is hoped that before the war ends British Chemical Industry would have contributed not only to the immediate but also to the ultimate and future needs of the country.

EMERGENCY MEDICAL SERVICE

In my last letter I gave you a brief account of the Emergency Medical Service by which the Ministry of Health sought to establish as a war-time measure regionalisation and decentralisation

guarded optimism. Why cholera persists in certain areas in Bengal and flares up in certain other areas at apparently irregular intervals is a matter of considerable importance to India and other countries in commercial relationship with her. Though it is not possible at the moment to give a complete answer to the problem, researches at the Institute have made certain contributions which may help towards a clarification of this question.

of all voluntary hospitals, with a large measure of central control over them. As is natural, a certain amount of discontent and trouble has been felt by the profession, and the Central Medical Advisory War Committee of the British Medical Association has now advised the Ministry of Health regarding the revision of the terms of service of doctors in the Emergency Medical Service. This has been accepted in general by the Minister. We now have three classes of officers: *Class I*—Whole-time officers who would not be allowed to engage in practice but who may hold paid teaching, examining and other academic appointments. *Class II*—Part-time officers who will be free to engage in practice but liable for duty as and when required. *Class III*—Part-time officers on a sessional basis.

I may in this connection draw the attention of your readers to the special article published in the *Lancet*, Oct. 28, 1939 by its Special Commissioner on a "Plan for British Hospitals" and the editorial of the same issue, which are considered on this side as indications of the desire to establish the principles on which the Emergency Service is based on a permanent footing for post-war hospital organisation. "The upshot of it" (which is the *Lancet's* editorial caption) is "that the majority of people realise the folly of existing haphazard distribution of our large hospitals and that every effort should be made to prevent our going back to our old mistaken ways." "The situation is more revolutionary," continues the *Lancet*, "but time is a healer and what now seems a revolution may be seen later to be simply a stage in rapid evolution."

But the article of *Lancet's* Special Commissioner and its editorial comments opened the Pandora's box of warring correspondents for and against the plan proposed by the former, and a few even questioned why the writer of the special article should have been ushered with editorial blessings. Lord Horder's summing up of letters published in the columns of the *Lancet* on this subject at its editor's request is a master-piece of fair judgment, but he also gives no solution to the problem. It is gratifying to note however that he recognises some of the good features of the Emergency Medical Service, viz., regionalisation and decentralisation of all British hospitals. Decentralisation, of course, destroys the last hopes of the honorary consultants. But Sir Robert Hutchison still assures that these war-time arrangements are only temporary, and that the old voluntary hospitals would emerge again in some form or another. This only proves the preamble of the *Lancet's* Commissioner's article, that *English people are not given to looking ahead*. If there is a referendum, I can easily bet that the *Lancet's* Commissioner's plan for British hospitals will be voted for by more than 70 or 80% of the members of the profession. Only the vested interests wobble now, and are determined to frustrate the hopes of the general practitioners who are now suffering the cross.

Our American Letter

(From our own New York Correspondent)

CELLOPHANE AS A WOUND DRESSING

Wounds dressed with cellophane are singularly free of infection and are subjected to little or no danger from cracking of the material, according to new research work of Edward L. Howes, of Washington. Cellophane left on an abdominal wound ten days after operation, failed to break.

There are several advantages for this type of dressing not possessed by ordinary gauze. Among them are, according to Howes: (1) The wound may be inspected repeatedly for evidence of infection without the necessity of changing the dressing. (2) Accurate palpation of the length of the incision may be carried out at any time without contaminating the wound. (3) The cellophane does not stick to the wound crust and consequently may be removed without distressing the patient. (4) It is extremely economical. (5) It resists external bacterial contamination better than gauze. (6) The amount of seepage and hemorrhage occurring during the first 24 hours may be seen and used as a measure to perfect the surgical technic.

Plain cellophane 0.600, with a thickness of 0.0017 inch is the most satisfactory grade and is best prepared by autoclaving. The sheet is cut in a rectangle of the desired size at the operating table and the wound and the surrounding skin swabbed with ether to dry it. The sheet is then placed directly over the incision and fastened by a border of adhesive plaster on all four sides. The adhesive plaster is placed half on the skin and half on the cellophane to seal down the edges.

During the first few hours, droplets of blood and moisture, partly obscuring the vision, accumulate on the inside of the sheet, but drying takes place in the next 24 to 36 hours if adequate hemostasis was observed at the operation. A heat lamp applied to the abdomen not only aids drying and gives comfort to the patient, but also results in vasodilatation which aids healing. If the collection of moisture is excessive, a vent should be made after 24 hours, for the dry state is more conducive to healing than the wet. A small square of gauze is then placed over this opening to prevent soiling of the bed clothes.

SILK IN SURGERY

After more than half a century of use of an absorbable suture, many surgeons now seem ready to discard such materials to return to the use of silk in the repair of clean wounds and incisions. The older masters of the craft who, after unsatisfactory experience, rejected catgut and returned to silk include such leaders as Theodore Kocher, Heidenhain, Hagler, and in the United States William S. Halsted.

Recent clinical and experimental studies, collected in a report of the *Journal of the American Medical Association*, seem to bear out this posi-

tion. Thus, Shambaugh and Dumphy demonstrated in dogs that operative wounds repaired with silk tolerate bacterial contamination better than similar wounds repaired with catgut. Jenkins, in his analysis of 1,294 cases of abdominal wound disruption, mentions among the causes imperfections in the catgut and rapid digestion as a result of sensitivity to catgut protein, to chromic acid and infection. Superiority of silk over catgut, according to Meloney, is due to the following facts: 1. Hemostasis is better, for the silk knots do not become untied as do catgut knots. 2. The cellular and fluid reaction about silk is minimal while about the catgut it is maximal; silk is almost inert in the tissues, while catgut is dead tissue which must be digested. 3. The use of silk automatically requires the surgeon to be more gentle with the tissues.

Whipple stated at a conference that, since silk has been adopted in his clinic, the improvement in wound healing has been so striking as to leave no room for argument as to both immediate and late results. He emphasizes that one should not attempt to use silk unless one is willing to change one's technic and instruments. The essentials of this technic include the use of the finest grades of silk, interrupted sutures, careful hemostasis and a constant effort to tie sutures without tissue tension.

DR. CUSHING IS DEAD

Dr. Harvey Williams Cushing, international authority on brain surgery and neurology, died of a sudden coronary occlusion at the age of 70. He was one of the world's most eminent brain surgeons. His name became almost synonymous with brain surgery the world over, and honours were heaped upon him by learned societies and universities in the whole world. Cushing wrote many monographs on the surgery of the brain and developed the method of operating with the use of local anaesthesia. His work "The Pituitary Body and its Disorders", published in 1912, gave him an international reputation.

Cushing had studied at Baltimore, under Kocher at Berne, Switzerland, and Sherrington at Liverpool. In 1911 he was appointed Professor of Surgery at the Harvard Medical School. In 1932 he retired, but in 1933 he assumed a new post as the first appointee to the Sterling Professorship in Neurology, Yale University School of Medicine. During the world war he was senior consultant in neurological surgery for the American Expeditionary force. During the war years Cushing kept a Journal—it ran to more than a million words before it was done. Parts of the Journal were published under the title "From a Surgeon's Journal" in 1936. His two-volume biography "The Life of Sir William Osler" published in 1925, received the Pulitzer Prize for the outstanding American biography of the year. Yale University, in an official statement on Dr. Cushing's death, lauded him as a "great physician and teacher, the founder of a school of neurosurgery and a humanist of unusual literary gifts".

INDIAN MEDICAL NEWS

(From Our Own Correspondent)

NEW RULES TO CONTROL YELLOW FEVER IN INDIA

The Government of India have promulgated new rules prohibiting air-craft from infected areas in Africa to land at any aerodrome other than Karachi air port. It will also be an offence for anyone to bring into India an air-craft which has on board a case of yellow fever or any person who within 9 days of arrival in India has been in an infected area unless he has been protected by satisfactory inoculation and previous attack of the disease. Rules are also strictly laid down for disinsection of the air-craft before it is allowed in India. And any air-craft which does not satisfy these conditions would be refused entry in our country.

TERMINATION OF THE SERVICES OF A MADRAS DISTRICT BOARD RURAL DOCTOR

The District Board of Tanjore terminated the services of Dr. R. Subbarya Bhut, subsidized rural medical practitioner of Kilayur, on the ground that Kilayur allopathic hospital would be converted into an ayurvedic dispensary by the terms of the District Board resolution. The doctor filed a suit for an injunction restraining the District Board and the Government from giving effect to it on the ground that it was contrary to the terms of the agreement. The District Munsif of Tiruturaipundi, in whose court the case was tried, observed in the course of his judgment that the termination of the plaintiff's service is invalid, as it could be done only on the ground of financial stringency and consequent closing of the dispensary and not for the reason of converting the allopathic hospital into an ayurvedic dispensary. The Government, the Munsif remarked, could not legalise a thing which it had declared to be illegal under the rules, by mere arbitration and by approving of the District Board resolution.

SUB-ASSISTANT SURGEONS CALLED FOR WAR DUTY

It is announced that twelve further reservists of the Indian Medical Department Sub-Assistant Surgeons Reserve have been called to service under the Indian Reserve Force Rules.

THE DRUGS BILL

The import, manufacture, distribution and sale of drugs are sought to be regulated in a Bill published in the Gazette of India. The statement of objects and reasons says:—

In order to give effect to the recommendations of the Drugs Enquiry Committee, in so far as they relate to matters with which the Central Government is primarily concerned, a bill to regulate the import of drugs into British India was introduced in the Legislative Assembly in 1937. The Select Committee appointed by the Legislative Assembly

was of the opinion that a more comprehensive measure, providing for the uniform control of manufacture and distribution of drugs as well as of import was desirable. The Government of India accordingly asked the Provincial Governments to invite the provincial legislatures to pass resolutions under Section 103 of the Government of India Act 1935 empowering the Central Legislature to pass an act for regulating such matters relating to the control of drugs as fall within the provincial legislative list. Such resolutions have now been passed by all provincial legislatures.

Chapter II of the Bill establishes a Board of Technical Experts to advise the Central and the Provincial Governments on technical matters.

Chapter III provides for the control of the import of drugs into British India. The executive power under this chapter will accordingly be exercised by the Central Government.

Chapter IV relates to the control of the manufacture, sale and distribution of drugs and contains the provisions which it is proposed should be enacted in exercise of the power conferred by the resolutions under Section 103 of the Government of India Act 1935 passed by the provincial legislatures. The excessive power under Chapter IV will be exercised by Provincial Governments.

The First Schedule prescribes the standards to be complied with by import drugs and the Second Schedule the standards to be complied with by drugs manufactured, sold or distributed in British India. The standards prescribed in the two Schedules are identical. The Central Government will have power to amend the First Schedule but power to amend the Second Schedule will rest with Provincial Governments.

The Government of India have considered to what extent provision can be made to secure the maintenance of uniformity in standards and in other important matters in which uniformity is desirable. They understand that it would be *ultra vires* of Central Legislature to assign to any authority other than the Provincial Governments the authority conferred by the Bill in respect of matters falling within the provincial legislative field. For this reason it is not possible to assign the power to fix standards and to make rules for any single authority. In order to ensure that before any action is taken due consideration is given to the desirability of maintaining uniformity, provision has been made in Chapter II for a single Technical Advisory Board which both Central and Provincial Governments will be required to consult before modifying the standards set up by the Bill and before making rules under the Bill.

REPORTS AND REVIEWS

Bombay Public Health Report for 1938: This is the 75th Annual Report and contains the activities of the department towards better public health in that province. The compendious nature of the report makes it exceedingly difficult to give an effective summary of the same. As we wrote while reviewing the previous report, we write again suggesting that a readable official summary, either at the beginning or at the end of the report, would be an invaluable aid in understanding the really great work of Bombay's Public Health Department, instead of making its readers or reviewers ramble through the report without any purpose. The population of the province is 19,665 millions; death rate 30.47 as compared to 27.50 of the previous year. Although there is a decrease in the mortality from all the epidemic diseases, yet the three omnibus headings, *fevers, respiratory disease, and other causes* have claimed 90% of the total provincial mortality, and the report points to the lesson that the mortality rate is only slightly influenced by the epidemic diseases. Why it is so is not explained. There is a danger of misunderstanding the figures of incidence and mortality of diseases, and any hostile critic can use them as a big stick with which to beat the P. H. Department which, for aught we know, has endeavoured its best to make things better. Any report which does not carry understanding to the lay man is not worth compiling in these days, and there is no reason why the department should be so modest as to hide its work under the bushel of figures and illustrations, leaving the readers to draw their own conclusions, which more often than not go wrong for the simple reason that it is impossible to make head or tail out of a report of this kind. Bombay is not the only sinner in this respect: every provincial report is of the same kind. The result is that notwithstanding the magnificent work done by Provincial Health Departments, they do not carry conviction to the public, and make them realise the difficulties involved in work of this nature. We hope our remarks will not be brushed aside as a reviewer's jargon.

The Rise and Growth of the Alembic Chemical Works by B. D. Amin, 1939.—The History of the House of Alembic is a history of romance of Indian Pharmaceutical Industry—the romance of troubles and trials, of determination to overcome them, and of the final triumph of a great idea and great endeavour. But for the mighty personalities that guided the destinies of this House, and but for their spiritual and intellectual doggedness it would have joined the majority of frustrated enterprises of this kind. They had to fight unfair competition, the invidious freight charges, the heavy excise duties, lack of inter-provincial reciprocity and yet maintain the standard and purity of their preparations and sell them at competitive rates throughout our country. The Alembic has survived these troubles, although all of them have not been yet overcome, and it has survived because it planned wisely, fought prudently, built slowly, and above all it never sacrificed quality for the sake of winning the market or of covering its losses. The book under review gives an account of its growth in a language of accuracy, and in a truly biographical style. Well may our country be proud of the Alembic, and the contribution it has made to the pharmaceutical industry. It has already reared a reputation for honesty and reliability.

The Human Eye by K. S. Malkani, Oph. D., Hyderabad, Sind. 2nd edition, 1939.

This tiny booklet aims to present "what the eye is, what it is made up of, how we see, how and why we lose our sight, and how again it can be regained or preserved" to the lay public, and we think that the author has successfully accomplished his aim within a brief space of 62 pages. It can be read by even an ordinary man with understanding and some benefit.

Vade-Mecum of Medical Treatment by W. Gordon Sears. 2nd edition, 1940. Price 10/6 net, Edward Arnold & Co., London.

We reviewed the first edition in these columns, and that a second edition has to be issued after only 2 years of the former shows that the book has been in demand and used profitably by the practitioners. Latest therapeutic advances have been included in this new edition. The appeal of the book lies in the simplicity of its arrangement, and the direct method of narrating therapeutic suggestions. The rationale of each suggested treatment is given well and succinctly. The general practitioner would be grateful for such a publication.

Recent Advances in Medical Science—A Study of Their Social and Economic Implication. By Sir Edward Mellanby. Price 2/6 net. Cambridge University Press.

Sir Edward Mellanby is a familiar and popular person in British Medicine of modern times, and this his Rede lecture, delivered before the University of Cambridge on 28th April 1939, reveals the nature and degree of social and economic adjustment as a result of recent advances in medical science. As Sir Edward puts it: "at no time has the average citizen felt so insecure against death by violence; at no time has the same citizen had reason to feel so secure against death by disease". He takes a long view range of the social and economic implications of lowered mortality, longer life and improved standards of health, and believes that medical advances will continue to have a very great effect on the life of the community. His thesis illustrates all these points, and vindicates that medical science has justified itself as a beneficent factor in the life of a nation, and the right use to which it may be put depends on medical leadership, on public health authorities and on the intelligence of the public. On the whole, it is an enchanting little book which can be read pleasantly and profitably by the practitioner within an hour, because the author does not burden him with ponderous statistics or high-browed criticisms. He leads him gently and quickly to the realisation of the up-to-date achievement of medicine and to the happiness of having contributed his best to the country and the community in which he lives and works.

Indigenous Drugs of India by J. C. Gosh, B.Sc., with a Foreword by Col. R. N. Chopra. Second Edition 1940, revised and enlarged. Price Rs. 3/- net. Published by the School of Chemical Technology, P.154. Lake Road, Kalighat, Calcutta.

Sri J. C. Gosh is familiar to the readers of the *Journal* in which he has been often discussing the problems of scientific cultivation and manufacture of indigenous drugs of India. As Chopra says in his preface to the book, he has been making continuous and untiring efforts in enlightening public opinion on the much neglected field of indigenous drug industry. The book under review shows the way to make our country self-sufficient in the matter of drug supply, not only as a war-time necessity

but also as a permanent measure and as the only way to minimise the colossal drain of money out of our country in payment of imported drugs. The author has been writing, speaking and showing times without number how easily and in what valuable directions the Indian drug industry could be built and developed. But his was a voice in the wilderness. The present drug crisis, due to war, has opened the eyes of the Government to the urgent need of developing drug industry in our country. This is evident from the Conference recently held at New Delhi under official auspices for the purpose of taking such measures as would relieve the impending drug crisis. The DRUGS BILL is now notified, and as the author had previously pointed out in the columns of this *Journal*, the Government have now made no distinction between imported and local drugs, and subject both of them to the same control and standards. The publication of the book under review is, therefore, opportune. Many of the author's suggestions and schemes are quite practical, and the working of indigenous drug industry may be well based on the directions given in this book and developed in the light of future experience. We heartily commend this book to all those who are interested in the development of drug industries in our country.

EXTRACTS

The Diagnosis of Vitamin Deficiency

Norman Jolliffe (*Bulletin of the New York Academy of Medicine* July 1939, p. 469) writes that the diagnosis of vitamin B₁ deficiency depends, at the present time, mainly upon a clinical evaluation of the history and the signs and symptoms presented by the patient. The clinical syndrome may be so typical that a positive diagnosis can be made; or so vague that it is difficult or even impossible to diagnose. It is hoped, however, that the clinician will soon have at his disposal a practical laboratory method to aid in the diagnosis.

The signs and symptoms attributed to vitamin B₁ deficiency are legion, the most definite being anorexia, fatigue and a neurological and a circulatory syndrome. Anorexia and fatigue are non-specific. In their presence the possibility of vitamin B₁ deficiency should be considered and confirmatory signs should be sought. When these symptoms occur without supporting objective signs, and do not definitely respond to thiamin therapy within seventy-two hours, they are probably not due to vitamin B₁ deficiency alone.

The neurological manifestations are those of bilateral and symmetrical polyneuritis involving first and predominantly the lower extremities. Peripheral neuritis that involves a single nerve, or that is not bilateral and symmetrical, or that does not involve first and predominantly the lower extremities is, in the author's experience, probably not due to vitamin B₁ deficiency alone. For such neuritides other etiological agents should be sought.

For the purpose of clinical investigation the author has classified the neurological manifestations according to severity into four groups: suggestive, mild, moderate, and severe. Heaviness of the lower extremities, and calf muscle cramps are usually the first symptoms. These are followed by paresthesia in the toes and fingers, burning of the feet, and pain in the legs. It should be emphasized that pain, though nearly always present, can

often be elicited only by a leading question. Calf muscle tenderness and plantar hyperesthesia are as a rule the earliest objective signs. The hyperesthesia may extend up the ankles and legs in a sock distribution. Vibratory sensation may be lost in the toes. These signs are classified as suggestive, and a positive diagnosis of polyneuritis is not made, as circulatory disturbances may cause these or very similar findings. When, however, in addition to these signs, the ankle jerks are absent, a diagnosis of mild polyneuritis can be made. As the deficiency continues, the sensory and motor changes advance, the knee jerks disappear, position sense in the toes becomes impaired, calf muscle atrophy develops, and foot drop follows. This degree of involvement is considered moderate, provided the signs are confined to the lower extremities. When there is also involvement of the upper extremities, the spinal cord, or the cranial nerves; or when a "central neuritis" is present, one has to classify the polyneuritis as severe.

The circulatory manifestations of vitamin B₁ deficiency do not form a rigid clinical picture. They may occur in a person whose circulatory system is otherwise normal, or they may be superimposed on one previously damaged by degenerative, hypertensive, or inflammatory disease. These circulatory manifestations, as observed by Weiss and Wilkins, Jones and Sure, and in the author's clinic, are classified as follows:

(1) Oedema and serous effusions occurring in the absence of congestive heart failure, enlarged heart, or recognized etiologic factors producing oedema and serous effusions.

(2) Oedema and serous effusions occurring with supporting signs and symptoms of congestive heart failure usually with definite roentgenographic evidence of cardiac enlargement.

(3) Sudden circulatory collapse which may be the first manifestation of circulatory failure may occur after other signs of circulatory failure are well advanced.

The circulatory manifestations of vitamin B₁ deficiency occur in about one-third of vitamin B₁ deficient subjects manifesting definite polyneuritis. They are more likely to occur in subjects with suggestive or mild involvement than in those having advanced neuritis. This factor is related to the ability of subjects with mild neuritis to perform muscular exertion.

Some of the more characteristic diagnostic features of the circulatory manifestations of vitamin B₁ deficiency are:

(1) Mild nature of the polyneuritis.

(2) Increased or normal velocity of the blood flow in the presence of congestive heart-failure.

(3) Rapid response to specific therapy with complete and permanent reversibility of the circulatory manifestations.

The Use of Tetanus Toxoid in Private Practice

R. P. Rogers (*Ibid.* Aug. 39, p. 553) writes that two doses of 1 cc. each of alum precipitated toxoid given two or three months apart or three doses of plain toxoid 1 cc., 1.5 cc., 2 cc. at three weeks interval will outside fourteen days after the last doses produce a blood level as high as or higher than 1500 units of the old antitoxin. A boosting dose given several years later will bring this level back to a protective level and often far above in seven days in almost every case tested. The reactions to these toxoids are slight. The alum precipitated toxoid is quite thermostable and therefore keeps well.

To be able to rely absolutely on immunization by toxoid the following things should be done:

(1) A blood titration test should be made two months after the last immunizing dose.

(2) If an injury requiring protection occurs any time after three months after immunization, a boosting dose should be given within twenty-four hours of injury.

(3) Even this should not be relied on in cases of very extensive injury such as would require gas bacillus prophylaxis or injuries where there was extensive haemorrhage. In these cases antitoxin should be given also.

Tetanus rarely develops before five days but it is in this type of case that the incubation is likely to be early. The usual incubation is between seven and fourteen days.

Who should not receive active tetanus immunization?

(1) First of all those who are sensitive to horse serum. That means, of course, those who have had severe and moderate serum reactions from previous serum injections.

(2) Asthmatic patients.

(3) Other allergic individuals if they are in occupations or indulge in avocations that carry with them danger of injury.

It is justifiable to give tetanus immunization to the following on optional grounds:

(1) Children, especially those living in the country or those who ride. Statistical analysis shows that most of the cases of tetanus at present occur from trivial injuries. These cases would very definitely be prevented by such prophylaxis whether a blood titration was made or not.

(2) Individuals, non-allergic, engaged in hazardous occupations or avocations.

Treatment of Angina of Effort

Geffrey Bourne (*B. M. J.*, Nov. 18, 1939, p. 989) writes in the course of his article that the drug treatment of angina of effort is somewhat disappointing except for the effect of nitroglycerin. Phenobarbitone, 1/4 grain t. d. s., p. c., is probably the most useful drug; but it can be given in combination with theobromine or diuretic in some such preparations as theobrominal, 5 grains t. d. s., p. c. In a few cases theobromine alone, 3 grains t. d. s., p. c., or theobromine sodium salicylate, 10 grains t. d. s., p. c., is effective. Nitroglycerin tablets can be taken by the patient as often as they may be required for the prevention or the treatment of pain. They are generally put up in chocolate, so that the patient may be reminded to crush them in the mouth and hold them there for a few minutes before swallowing. If they are swallowed direct, pharmacological action is delayed and sometimes less efficient.

There are three organic diseases which interfere with the coronary circulation and which must be remembered in planning a course of treatment in angina of effort. These are coronary thrombosis manifested by angina of effort; (angina of effort due to syphilitic aortitis, and angina of effort due to anaemia), whether pernicious or microcytic. Where angina of effort follows directly after a coronary thrombosis there is a very good chance of its disappearing completely during the subsequent twelve months or so, and the patient should be so informed. In the case of syphilitic aortitis manifesting itself by angina of effort the cardiac pain can often be cured by thorough antisyphilitic treatment. This should consist of a six-

weeks' course of full doses of potassium iodide, 90 to 150 grains daily, a subsequent course of bismuth injections, and a final course of intravenous injections of neosalvarsan. This programme should be repeated, with intervals of two to three months' rest, until the Wassermann reaction becomes and remains negative. When angina of effort is due to anaemia, the pain nearly always completely disappears with the improvement of the blood count.

The vast majority of all cases of angina of effort respond successfully to treatment on the lines described, but there remains a small group in which the cardiac pain is extremely severe and no improvement follows persistent treatment. In these cases some operative procedure may be justifiable. From a total of about 400 cases of angina of effort the author picked out fourteen as being suitable for thyroidectomy. In nearly every one of these the relief from pain has been striking, and this relief has lasted in the least successful case for a period of six months. The more successful cases have had periods of up to three years, during which time the pain has either vanished or has become so slight as to cause no serious inconvenience. The details of this procedure have been published elsewhere, but it should be remembered that so radical a measure should not be embarked upon without very serious consideration.

The chief indications for thyroidectomy would seem to be that the pain is extremely severe, that previous treatment has failed, that the pain shows no sign of decreasing, that the pain is not the result of a recent coronary thrombosis, that the patient is not adipose, and that there are no signs, clinically or electrographically, of grave disease of the heart muscle. It is possible that in the future omentopexy could be a means of successfully treating these patients, but the evidence available to date has not proved without doubt the usefulness of the measure as a method of general application.

Value of Treatment in Duodenal Ulcer

James Ronald (*B. M. J.*, Nov. 25, 1939, p. 1084) after investigating the results of different methods of treatment in a series of 60 cases, divided them into three groups (those receiving light diet and no drugs; sippy diet with alkalis; and sippy diet with magsorbent) and comes to the following conclusions:

A series of cases of hyperchlorhydria associated with duodenal ulceration has been investigated, and it was noted that:

- (1) The hyperchlorhydria was but little modified by light diet without drugs, but symptoms were relieved.
- (2) The hyperchlorhydria was significantly modified by a sippy regime.
- (3) No special advantage was noted in the use of magnesium trisilicate as compared with alkalis.
- (4) In the absence of vomiting, the risks of alkalosis developing during alkali therapy were slight.
- (5) No distinction could be drawn on clinical grounds between cases in which hyperchlorhydria during treatment is or is not altered.
- (6) Healing of a peptic ulcer and relief of symptoms can take place although the hyperchlorhydria is unaltered or even becomes more severe.
- (7) The "long test meal," lasting at least twelve hours, was of considerable value in the investigation of gastric function and the assessment of the effect of different agents upon secretion.

Relapses after Sulphanilamide Cure of Gonorrhoea

McElligott (*B. M. J.*, Dec. 2, 1939, p. 1080) deals with an important and hitherto neglected aspect of the new chemotherapy of gonorrhoea—namely, the occurrence of late relapses after apparently complete cure by sulphanilamide compounds. He analysed 1268 male and 210 female cases and found that 20% of cases relapsed subsequently which had previously passed tests of cure. This 20% is quite distinct from the incidence of chemotherapy failures and early relapses. And he concludes with a warning that the fact that half of these late relapses occurred more than three months after apparently complete cure throws doubt on the reliability of certain published statistics of results obtained with sulphydrydine and other sulphonamide compounds.

Bacillus Coli Infection of the Urinary Tract

Leishman (*Lancet*, Nov. 4, 1939, p. 971) discussing the paths of infection of the urinary tract with coli-form group of organisms believes that the route of infection varies in individual cases. The proximity of urinary tract to the bowel, which is acknowledged to be the reservoir of infection is a general explanation, but how the organisms migrate is still far from clear. They may spread directly, or through the blood stream or lymphatics. In general, however, the cases in which one or other of these routes of infection can be suspected are rare and uncommon. Neither clinical observation nor experiments, he points out, have as yet established the common path of infection in the ordinary case of primary infection of the urinary tract with *B. coli*. His article, therefore, aims to co-relate the extent of common bowel dysfunction with the incidence of bacilluria, and to find out what type of bowel irregularity is especially to be incriminated. After examining nearly 270 cases with 100 cases as controls, he concludes that (1) a small proportion of apparently healthy subjects have a transient bacilluria (2) persistent loose stools in females but not in males are an etiological factor in *B. coli* infections of the urinary tract and (3) constipation alone is not a factor.

Tonsillectomy and Nephritis of Childhood

Ilingsworth (*Lancet*, Nov. 11, 1939, p. 1018) says that tonsillectomy does not prevent nephritis, and after reviewing nearly 800 cases concludes that (1) tonsillectomy does not prevent nephritis but may predispose to it; (2) it does not cure nephritis or prevent it from progressing into the chronic stage; (3) it may even cause nephritis.

Relief of Pain in Carcinoma of the Cervix Uteri

Todd (*Lancet*, Dec. 23, 1939, p. 1305) summarises his investigations of 51 cases of intractable pain associated with advanced carcinoma of the cervix, 8 cases of rectal carcinoma and 1 of prostatic carcinoma. These cases have been subdivided again into two distinct types: visceral pain (42) and somatic pain (46). He employed presacral neurectomy for visceral pain, and intrathecal injection of absolute alcohol for somatic pain. He believes that this method of treatment gives highly satisfactory results.

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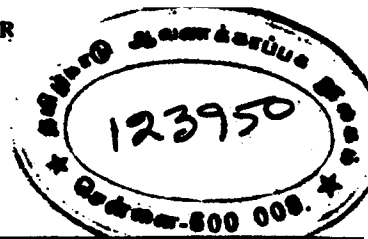
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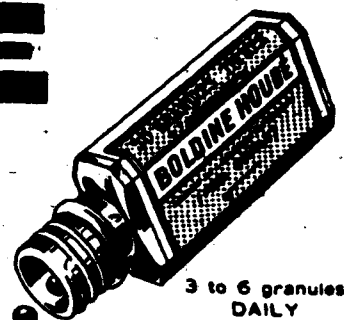
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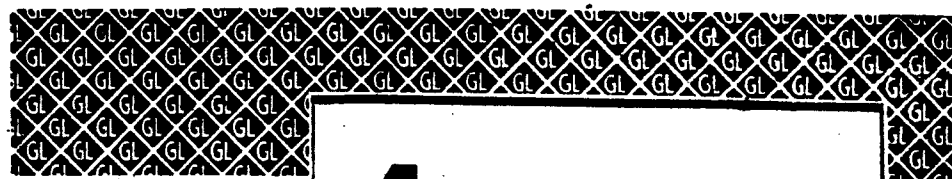
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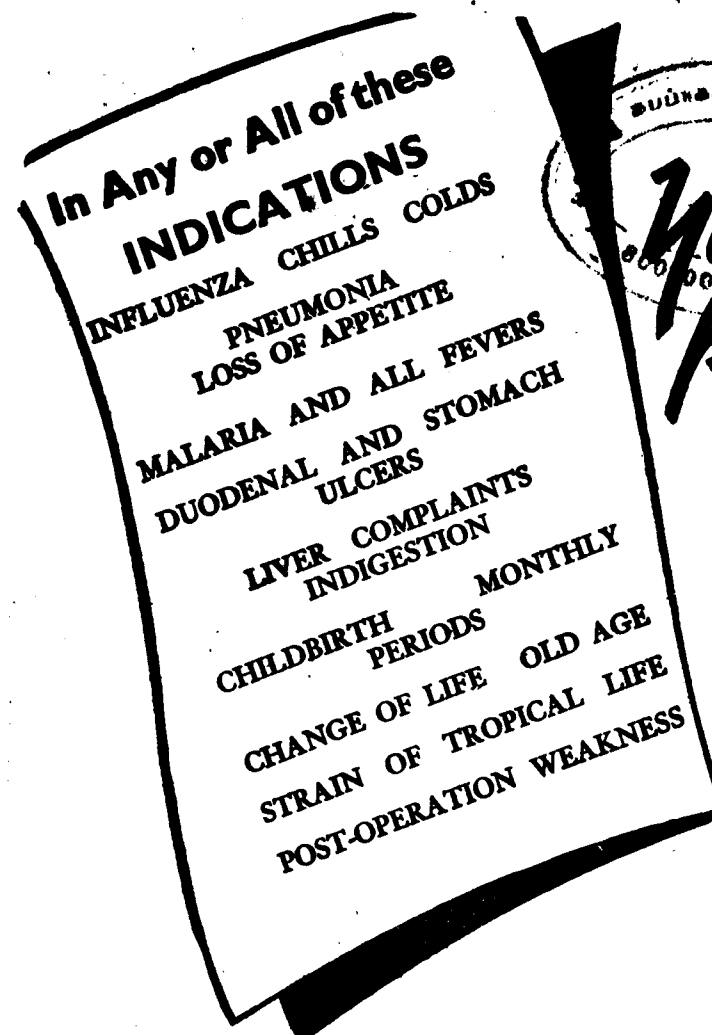
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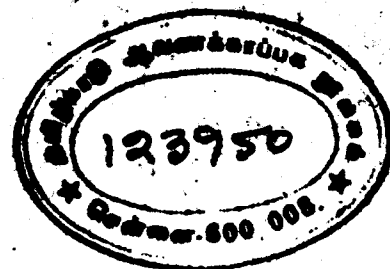
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