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ANTITOXIN IN THE TREATMENT OF ACUTE MENINGOCOCCAL MENINGITIS.

by

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Up to the present no publication has appeared in South China on the use of Ferry's Anti-toxin and its results in Acute Meningococcal Meningitis.

Prior to the investigations of Ferry[1] and his associates dating from 1926 to 1931, the separation of an extra cellular toxin from broth cultures of the meningococcus, which would produce true homologous anti-toxin in an animal, had not been successful.

Until recently the conclusions of Flexner, Gordon and Murray[2] to the effect that the meningococcus did not produce a soluble toxin in culture were accepted with the result that we have been content with anti-serum as the standard therapeutic weapon against meningococcal meningitis.

Studies of epidemics show that the anti-bacterial serum of a polyvalent type, even of the highest titre is disappointing in its results, It must not be supposed however that its use has been without good results.

Flexner[3, 4] has shown that, prior to the Great War and with no serum given, the mortality rate was 75 to 80 per cent. After the war this figure fell to 31 per cent. Further the efficacy of specific treatment was abundantly revealed during that period as soldiers for whom serum was available showed a very much lower mortality rate than affected civilians who received no serum. With type I meningococcus the use of the homologous anti-serum resulted in a mortality rate of 9.2 per cent.

In 1918 Herrick[5] pointed out the greater likelihood of success in the treatment of early cases of epidemic meningococcal meningitis by administering anti-serum intravenously. The possibility that the disease began as an acute systemic infection occurred to him and therefore an early direct attack on the toxins was essential.

Ferry produced clinical evidence that susceptible human beings can be successfully immunised against the meningococcus toxin. As a result of the production of Ferry's anti-toxin Hoyne[6] acting on the same line of thought as Herrick concentrated his efforts on early neutralisation of the toxins and at the same time incapacitating the meningococcus.

In Hong Kong a polyvalent anti-serum prepared from local strains of the meningococcus has, in our experience, proved more effective than the "stock" polyvalent anti-serum obtained from elsewhere.

It has to be borne in mind however that there is great difficulty in assessing the true value of varying methods of treatment.

The virulence of the meningococcus varies in different times so altering the clinical picture and the case fatality.

Certain difficulties are peculiar to South China where the control of epidemic meningococcal meningitis, in fact of all infectous diseases, remains unsatisfactory.

In our opinion after several years of close observation reliable statistical information does not exist. Only those in close touch with the clinical side of the disease both in hospital and outside practice are in a position to appreciate the difficulties of a true assay of treatment and its results.

One powerful factor which militates against success in the treatment of meningococcal meningitis in South China is the frequent long delay in hospitalisation and diagnosis. Many Chinese consult the herbalist and by the time the qualified practitioner is sent for, the infection has had full control for several days. On the other hand the practitioner is at a disadvantage in arriving at a diagnosis because of frequent objections of the Chinese to lumbar puncture. Even if diagnosis has been establishel, superstition and fear of investigations by the Sanitary authorities compels the medical attendant to make what might be best termed a "cover-up diagnosis."

In view of the peculiar circumstances appertaining in these parts it would appear likely that any form of therapy which will appear to relatives to be less drastic and less disturbing to the patient than the present routine method, will be more readily accepted.

As a result of Ferry's researches a few clinicians have adopted the new form of therapy, but, with the exception of Hoyne[7] in America, the numbers treated have been small.

H.S. Banks[8] gives figures for 25 cases treated by anti-toxin. He had no hesitation in stating that anti-toxin in large doses was more effective and more valuable against Group I meningococcus.

His fatality rate of 30.9 per cent. was on the high side because, at the time, it was not realised that wrong storage temperature of the anti-toxin and a period beyond 12 months reduced its therapeutic effect. Better results can be attained if these points are strictly attended to. It has been pointed out that anti-serum quickly deteriorates—in fact is not so effective 6 months after collection.

Hoyne's figures of about 300 cases show a very distinct improvement and point to a great advance in the treatment of meningococcal meningitis.

It has been shown that both a high cell count and the diplococci in cerebro-spinal fluid disappear in cases treated solely by the intravenous method. As Hoynes states "This seems surprising when one considers the long accepted opinion that the specific serum must come into direct contact with the meningococcus."

Brocklebank[9] gives an account of 4 cases, all children, treated with Ferry's anti-toxin.

The results are marred by the fact that in 2 cases the meningococcus was not demonstrated and the total number of cases treated is extremely small.

Hoyne's contribution to the subject in 1936 arouses most interest because of the successful results obtained in patients treated exclusively by the intravenous route.

For 66 patients who received only intravenous treatment the fatality rate was 11.8 per cent. In 43 of these patients 20 years of age and under the fatality rate was 2.3 per cent.

Massive doses are recommended by intravenous route—an initial adult dose of 100 c.c. anti-toxin diluted with 10 per cent. dextrose in physiological solution of NaCl of at least twice the volume of the therapeutic agent, 5 to 10 minims of adrenalin being added to the fluid. For children a smaller initial dose of 60 c.c. is suggested. Such or larger doses are repeated as necessary. The average dose of anti-toxin for each patient was just around 200,000 units. The extreme total dose of 400,000 units was given over a period of 4 days.

Brocklebank gave to 1 case as much as 300,000 units by both intravenous and intramuscular routes and undiluted. This is of necessity a costly procedure and it may be questioned whether just as in the use of diphtheria anti-toxin, such very large doses are necessary. The future will no doubt indicate whether, in cases untreated for 5 to 7 days, very high dosage of anti-toxin is justified.

There is little doubt but that any form of therapy which can replace the frequent lumbar punctures and intrathecal injections to say nothing of ventricular and cisternal puncture, will most certainly result in a much wider and earlier application in South China of a powerful therapeutic agent such as Ferry's anti-toxin appears to be. The clinician will be only too glad to abandon the present disturbing technique as practised by most in the treatment of meningococcal meningitis.

In the past it has been our routine to produce light ether anaesthesia for lumbar puncture. Ether damages the barrier cells of the choroid plexus and contrary to the belief that such a procedure leads to further infection of the central nervous system, it is suggested that the anti-toxin subsequently administered by intravenous route results in more effective access of anti-bodies to the ventricles and cerebro-spinal circulation. In addition anti-serum is given intrathecally. In some cases with thick purulent fluid the spinal canal is gently irrigated from cisternal puncture downwards to the lumbar puncture opening.

When one contemplates such disturbing and energetic methods one cannot but welcome an advance which may ultimately lead to complete abolition of intraventricular, intracisternal and intrathecal treatment and of the necessity to perform lumbar puncture more than once or twice at most.

During the early part of 1937 only 7 cases of acute meningococcal meningitis were admitted to the wards of the Medical Unit.

A supply of Ferry's anti-toxin was very generously put at our disposal by Parke, Davis & Co. and of the 7 cases 3 were treated with Ferry's antitoxin—2 cases recovered and 1 case died.

The amounts of anti-toxin and how administered are shown in Table I.

The fatal case showed a very great initial increase of cells in the cerebro-spinal fluid compared with the cases which recovered.

Exhaustion of the limited supply of anti-toxin resulted in the ment of the remaining 4 cases of the series with anti-serum. Of these 3 died and 1 recovered.

Table II shows the amounts of anti-serum used and how administered. Again the fatal cases exhibited a comparately greater pleocytosis.

We do not suggest that the figures shown in Tables I and II are of any statistical value. The number is extremely small but we show comparative records of the cases treated and the results such as they are, would encourage us to pursue treatment with Ferry's anti-toxin whenever more cases are available.

TABLE I

Case	Sex	Age	Meningococcus in C. S. F.	Antitoxin Units I.V.	I.T.	I.M.	Recovered	Died	Days in Hospital
A	19	F	+ +	70,000	15,000	—	+	. .	30
B	35	M	+ +	30,000	10,000	—	+	—	31
C	9	M	+ +	10,000	15,000	—	—	+	(12 hours)

TABLE II

				Anti-Serum c.c. I.V.	I.T.	I.M.			
A	9	F	+ +	120	120	—	+	—	45
B	19 mos.	M	+ +	—	20	20	—	+	(12 hours)
C	64	M	+ +	60	140	260	—	+	15
D	23	F	+ +	—	32	35	—	+	2

I.V. = Intravenous I.T. = Intrathecal I.M. = Intramuscular

We earnestly hope that other clinicians in South China will publish further data with regard to the value of meningococcal anti-toxin.

We thank Messrs. Parke, Davis & Co., and their Representative in China, Mr. Stokeley, for the anti-toxin so generously supplied.

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PERIPHERAL POLYNEURITIS IN RELATION TO PREGNANCY.

by

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Although the occurrence of peripheral polyneuritis during pregnancy was reported as early as 1889 by Whitefield, it was not until recently that the condition was recognised to be a deficiency disease due to diet imbalance. The early workers presumed the condition to be one of the protean forms of toxaemia of pregnancy. (Whitefield, 1889. Wilson and Garvey, 1932. Berkwitz and Lufkin, 1932) Hoffmann (1924) first pointed out that in the Far East where beri-beri is endemic, polyneuritis might be merely a form of beri-beri associated with pregnancy. Strauss and MacDonald (1933) suggested that pregnancy polyneuritis might be due to a dietary deficiency, and recorded three cases of polyneuritis which they successfully treated with a high vitamin B_1 diet. In all their cases vomiting was present in the early months of pregnancy, and paralysis of the limbs followed very soon after in spite of therapeutic or spontaneous abortion. They concluded that this condition was probably a deficiency disorder similar to Beri-beri, and that it should be treated with large quantities of vitamin B_1. Sze (1934) gave further evidence for the deficiency theory when he reported three cases. These cases had no severe vomiting during pregnancy, and they were successfully treated with high vitamin B_1 and high protein diet. Theobald (1936) also treated five cases, four of which were cured by vitamin B_1 alone. It was interesting to note that patients dying from beri-beri, scurvy, and the polyneuritis of prenancy show similar histological changes in the tissues of the nervous system. (Berkwitz and Lufkin 1932, Luikart 1935, Ford 1935.)

In this communication it is proposed to discuss the conditions which seem to produce or favour the development of avitaminosis B_1 as seen from the investigation of cases of pregnancy polyneuritis in Hong Kong.

During the period from September 1936 to June 1937, twenty-six cases of pregnancy polyneuritis in the University Medical Clinic and the Out-patient Department were studied. Seven cases were treated in the wards, but due to various reasons the remaining nineteen were unable to have inpatient treatment. Complete examination and full treatment were impossible to carry out in the out-patient department, nevertheless many of these patients attended quite frequently to enable a record of progress to be kept. With the exception of one, all the cases were first seen when the condition was fully developed and after delivery. The one came two days after the development of symtoms and five days before the calculated date of confinement.

AGE.

The youngest patient was 22 and the oldest was 40. There was a slightly higher incidence between the age of 30 and 40.

TABLE I.

Age	*No. of Cases*	
22	1	
24	1	
25	2	
26	1	12
27	3	
28	3	
30	1	
31	2	
32	1	
34	2	
35	1	
36	2	14
37	3	
38	1	
39	1	
40	1	
	26	

NUMBER OF PREGNANCY.

The number of pregnancies seemed to have some influence on the incidence of symptoms. There were only two primiparae. The highest incidence fell in the third pregnancy as shown by the following table. Eight cases however, gave a history of similar symptoms during every previous pregnancy except the first.

TABLE II.

No. of Pregnancy	*No. of Cases*
1	2
2	2
3	8
4	2
5	4
6	3
7	2
9	2
15	1

OCCUPATION.

Only 4 patients were working for their living; 2 were maid-servants, 1 was a street hawker, and 1 worked in a rubber factory. The rest occupied themselves with household work.

DATE OF ONSET.

In the majority symptoms developed after parturition, from the third day of puerperium to the third month after delivery. Only 6 cases had their onset before confinement; 1 at the third, 1 at the seventh, 2 at the eighth, 1 at the ninth month, and 1 five days before the delivery.

OUTSTANDING SYMPTOMS.

Anorexia. Dyspnoea. Epigastric Discomfort. Change of Voice. Before the appearance of any neuritic symtoms, many of the patients had anorexia, associated with shortness of breath, palpitation and a sense of depression behind the sternum. This condition usually persisted for a few days before the development of other symtoms, but in two exceptional cases these were noticed for the last two months of pregnancy. In severer cases deep breathing caused discomfort in the epigastric region and the voice became feeble.

Numbness and Weakness of Limbs. Numbness and weakness of the limbs then developed from below upwards. When fully developed, the anaesthetic areas were of the glove and stocking distribution. Tingling was also complained of. In some cases numbness spread upwards to the abdomen and chest. The patient found difficulty in walking and holding chop-sticks, and movements were clumsy. She was also unable to get up from the squatting position. Paralysis of the limbs occurred in two cases at the onset, but improved later with time and under Chinese medication.

Tenderness of Muscles: Pain and deep tenderness of muscles especially the calves were present in nearly every case.

Oedema. Oedema was not a common symptom. It occurred in 3 cases only, and it appeared one or two weeks before the onset of neuritic symptoms. Only the lower limbs were affected.

Vomiting. Morning sickness was common to all the patients for a few weeks during the early months of pregnancy. In one patient, however, severe vomiting occurred after every meal from the second month to the end of pregnancy. The condition was so intractable that the patient was practically starved, and the condition of paripheral polyneuritis was fully developed as early as the third month.

Dimness of Vision. As a rule there was no trouble about the special senses although dimness of vision was complained of in one case.

INTERCURRENT DISEASE.

The case of the patient who had intractable vomiting was complicated by an attack of bacillary dysentery after the puerperium.

One patient was discovered to be suffering from para-typhoid infection during the puerperium.

PAST ILLNESS.

Two patients gave a history of previous intermittent oedema, numbness and weakness of the legs, but not accompanied by pregnancy.

DIET DURING PREGNANCY.

All the patients were poor and their diets were similar. They had two meals daily, one at 7 to 8 a.m. and one at 4 to 5 p.m. Appetite was generally not as good as usual. Cooked, polished rice was the chief food, and the average amount per meal was about 4 to 6 ounces by weight (uncooked). Vegetables included amaranth (莧菜), white sugar beet (甜蓬菜), spinach (菠菜), black and white mustard (芥菜), celery cabbage (白菜), lettuce (生菜), matrimony wine (枸杞), bean sprout (芽菜), melon (冬瓜), cucumber (黃瓜), vegetable sponge (絲瓜), wild cucumber (苦瓜), lily root (蓮藕), sweet potato (甘藷), potato (馬鈴薯), watercress (西洋菜), cauliflower (椰菜花), cabbage (椰菜), and turnip (蘿蔔), etc. In addition to cooked vegetables, vegetable soup is frequently taken. The average amount of vegetables at each meal is about 8 ounces (uncooked). Salted vegetables are also used occasionally in small quantities. Bean curd (豆腐) is cheap and is taken frequently, about 2 ounces at a time.

During the later months of pregnancy all the patients reduce their vegetable intake considerably, and some actually refrain from taking "greens."

Other items of food consist of a small portion of fish either fresh or salted, a few pieces of beef or pork, glandular organs such as liver, kidney, etc., and egg.

Occasionally, besides the regular meals, various other foods such as congee containing rice, mung bean (綠豆) or red mung bean (紅豆), paste made from glutinous rice (糯米), steamed bread (蒸餅), and cakes are taken. Fruit is taken sparingly.

The daily food value of two average meals is shown by Table III.

TABLE III.

		Carbohydrate	Protein	Fat	Vitamin
Rice	12 oz.	288.00gms.	50.80gms.	1.80gms.	
Vegetables	16 oz.	20.16	8.16	0.62	A.B.C.D.E.G.
Bean Curd	2 oz.	0.78	5.40	1.80	A.B.
Potato	1 oz.	5.70	0.35	0.08	A.B. G.
Beef	¼ oz.	0.28	1.24	1.42	A.B.C.D.E.G.

Pork	¼ oz.	0.07	0.66	4.19	A.B.C. E.G.
Fish	¼ oz.	0.07	0.13	0.35	
Peanut Oil	1 oz.	0.00	0.00	28.35	A. E.
		315.06	46.74	38.61	A.B.C.D.E.G.
Calories		1292	192	359	
Total calories		1843			

(All weights stated are that of uncooked food. Calculations are made from "Chinese Medicinal Plants from the Pen Ts'ao Kang Mu" 本草綱目 and "Shanghai Food.")

DIET AFTER DELIVERY.

It was a custom for the mothers to have a special diet after delivery for one month. The individual diets were practically the same. Two meals were taken daily. Polished rice was again the chief food, but vegetables were omitted entirely. Egg, fresh or salted, were taken every meal. Fish, beef and pork again formed a small portion of the diet. A mixture of ginger, vinegar, and pork, was cooked and stored, and some of this taken at odd times.

PHYSICAL SIGNS.

Temperature and Pulse: Except the two cases with intercurrent disease, the temperature and pulse of these patients were within normal range.

General Condition: Generally the patients were medium sized women, rather wasted and poorly nourished. Oedema occurred in two cases, and only of the legs. All of them looked pale.

Muscular System:

(1) *Motor power:* All movements of the limbs were impaired There was early weakness of hand grip and of dorsiflexion of the ankle joint leading to wrist drop and foot drop in the severe cases.

(2) *Gait:* Early cases showed typical high steppage gait, but in the more severe cases the patients either simply dragged their feet along, scarcely raising them from the ground, or were unable to stand without support.

Reflexes:

(1) *Deep:* The ankle and wrist jerks were lost before those of the knee, biceps and triceps.

(2) *Superficial:* The abdominal reflexes were always present. There was no plantar response in the most severe cases.

(3) *Organic:* Sphincters were normal in all cases.

(4) *Pupils:* Reaction to light and on accommodation in all cases.

Cutaneous Sensibility.

Cutaneous sensibility to light touch by cotton wool, to pin prick and to temperature were effected equally to the same extent. The impairment usually appeared first in the fingers, the soles of the feet and over the shins. When fully developed, the anaesthetic areas were below the levels of the wrists and the knees forming the so called glove and stocking distribution. In a few severe cases, the arms and the thighs were also affected. Recovery usually came in the reverse order.

Deep Sensibility.

Tenderness of the calves when pressure was applied occurred in all the cases, but tenderness of the tendocalcaneus was not a constant sign.

Vibration Sense.

Bone conduction present.

Heart.

The heart was affected in half of the number of patients. Increase of the cardiac dullness especially to the right and tic-tac rhythm were the chief signs. Extrasystole was also present in one of the cases. Signs of cardiac failure were not present.

Cranial Nerves.

Not affected.

Electrical Reactions.

No reaction of degeneration in the seven patients tested.

X-Ray of Joints.

Seven cases were x-rayed and two cases showed decalcification of bones of the ankle joints.

Tongue.

In one patient the tongue was red and had many superficial ulcers on the dorsal surface.

LABORATORY FINDINGS.

These were only carried out on the 7 in-patients.

(1) *Blood.* All of them were anaemic when admitted. Except the case with paratyphoid infection which had a polymorphonuclear leucocytosis of 22,000, the white cell count was within normal limits. The average figures were as follows:

Hb.	67.5%	
R.B.C.	3,830,000/cmm.	
W.B.C.	9,900/cmm.	
Differencial count	Polymorph	72.7%
	Lymphocyte (L. & S.)	20.7%
	Large Mononeuclear	4.5%
	Eosinophil	1.6%
	Basophil	0.5%
		100.0%

(2) *Urine:* The urine gave a positive culture of B. Paratyphoid B in the case with paratyphoid infection. In all the other cases, the urines showed a trace of albumen.

(3) *Stool:* In the case complicated with dysentery, microscopic examination revealed pus cells, red blood cells and macrophages. Ova of Clonorchis sinensis were found in the other cases.

(Note.—Infestation by Clonorchis sinensis has a definite pathological effect, producing liver inefficiency, loss of appetite, loss of weight and anaemia of a hypochromic type.)

(4) *Kahn Test.* All of them had negative reactions.

(5) *Fractional Test Meal:* All the acid curves were within accepted normal limits.

(6) *Blood calcium:* No deficiency of serum calcium.

(7) *Blood phosphorus:* Serum phosphorus reduced in 2 cases. One case had 3.6mgm. per 100cc. blood against the average of 5.31mgm. per 100cc. blood.

(8) *Calcium in faeces:* No excessive quantity of calcium found.

(9) *Calcium in urine:* No excessive quantity of calcium found.

TREATMENT.

(1) *In-patients:* Rest in bed with use of a cradle and support for foot-drop. All septic foci were dealt with. The diet included plenty of green vegetables e.g. amaranth, spinach, etc., soya beans, and butter. One orange was taken every day, and marmite one teaspoonful three time daily. Cod liver oil, ostelin, strychnine, arsenic and iron were given in appropriate doses. As soon as the tenderness of muscles became less, manual massage was started, and replaced by electrical massage later. Active movements were carried out by degrees. Betaxin (Bayer) was given to three cases. Two cases had 800 pigeon units daily for 9 days, and the other had 400 P.U. daily for 11 days.

(2) *Out-patients:* The following dietetic changes were recommended to the patients: (a) substitution of polished rice with brown

rice, (b) addition of plenty of green vegetables and marmite, (c) increase of the quantity of protein and fat, e.g. beef, pork, etc., and (d) the use of soya beans and mung beans. Cod liver oil, iron, strychnine and arsenic were given. All patients were sent to the electrical department for manual and electrical massage.

PROGRESS.

Recovery was generally slow, and one patient still remained in hospital after nine months. One case seemed to improve more quickly, and at the end of two months all the symptoms and signs had disappeared except the absence of ankle jerks.

The first symptoms to disappear was anorexia, then shortness of breath and the sense of depression behind the sternum. Voice improved. The patient felt better generally and increased in weight. Pain and tenderness of muscles then disappeared and motor power improved. The finger tips, the soles of the feet and the shin were the last areas to regain sensation, while the ankle jerk was the latest to reappear.

Relapse occurred in 2 patients after discharge from hospital, and relapse was frequent among the out-patients.

DISCUSSION.

The cause of avitaminosis B_1 is a complex one, and it may be conveniently studied under the following topical headings:

(1) Increase demand of vitamin B_1. (2) Deficient supply of vitamin B_1. (3) Deficient absorption of vitamin B_1.

(1) *Increase demand of vitamin* B_1. It is well known that the foetus obtains all nutritional requirements from the mother. It would seem probable, therefore, that vitamin B_1 is also absorbed from the mother, and stored by the foetus all the time during pregnancy. Hence the demand for the vitamin is increased in the expectant mother. During lactation, it is believed that the vitamin B_1 requirements are increased. In studies on the physiology of the mammary gland, McCollum found that vitamin B_1 passes into the mother's milk when it is present in her diet. According to Macy, lactating rats fed with human milk as a source of vitamin B_1 at a level previously ascertained to be adequate for growth and reproduction, showed unsuccessful lactation, in that there was a high mortality of nursing young, and those surviving were much debilitated. The adverse conditions could be alleviated by addition of yeast to the diet of the mother. It was determined that the vitamin B_1 requirement of the lactating rat is from three to five times the growth need.

Cowgill and his associates found that the amount of vitamin B_1 required by the organism was related to the amount of food consumed.

or the total metabolism. They also observed that when the animal was restricted to a diet deficient in vitamin B_1, and its metabolism was increased by forced exercise or by the administration of thyroid tissue, signs of vitamin B_1 difficiency appeared much sooner than otherwise. The indications from such studies are that more vitamin B_1 is required whenever the metabolic rate is raised. It is reasonable to expect, therefore, that during pregnancy when the metabolism is much increased, the demand for vitamin B_1 is many times above normal.

Because of the more rapid production of polyneuritis by carbohydraterich diets, the necessity of the antineuritic vitamin for utilisation of carbohydrates was early emphasised by Funk. He maintained that the greater the amount of protein, the less the amount of vitamin B_1 necessary in the diet, in fact he assumed that protein exerts a sparing action on the antineuritic factor, and concluded that vitamin B_1 requirements rose pari passu with increasing amounts of carbohydrate in rations. Evans and Lepkowsky also came to the conclusion that fat had a sparing action on the antineuritic vitamin B_1. A study of the diets during pregnancy of our patients shows that carbohydrate was the chief food, and that the quantities of protein and fat were low. The minimum requirement of protein in a basal metabolic diet is one gramme per kilogramme body weight per day. The average weight of our patients is 50 kilos, therefore the quantity of portein required is 50 gms. per day. Table III shows that these patients have only 46.74 gms. of protein per day, which is very low for pregnant women. Further, the general ratio (Wright) of protein to fat to carbohydrate in an ordinary diet is 1 : 1 : 5, but in the diets of our patients it is approximately 1.2 : 1 : 8.2. It would seem, therefore, that the requirement of vitamin B_1 of these patients would be much greater than that of a normal person.

(2) *Deficient Supply of Vitamin B_1.* It is generally known that rice polishings contain all the vitamin B_1 of the rice. As polished rice was the staple food of all the patients, it would seem that the greater portion of the food was without any supply of vitamin B_1. Minot has called attention to the fact that the quantity of vitamin B_1 in the diet was as important as the quality. Both from animal experiments and experience with a case of human beri-beri impressed Cowgill of the importance of this. The experience of Goldberger in his study of the diet factor in relation to pellagra also illustrated this point. In our patients the foods containing vitamin B_1 were the vegetables, bean curd, egg, beef, pork, glandular organs and occasionally beans. Except the vegetables and bean curd, the quantity of these foods taken each meal was too small to account for the supply of vitamin B_1. It would seem, therefore, that these patients depended on vegetables for the antineuritic factor all the time. The erroneous custom of reducing the intake of "greens" before, and complete

abstinence from vegetables after delivery deprived them of the supply of vitamin B, which was already too small or barely sufficient.

(3) *Deficient Absorption of Vitamin B*$_1$. Gastric achlorhydria occurs often in beri-beri, but not invariably, and had been reported by Gilman to develop in animals fed with diets lacking vitamin B$_1$. To what extent gastric achlorhydria is a factor favourable to the development of beri-beri or is the result of this disease is difficult to say. Minot, however, reporting two cases of diabetes associated with peripheral neuritis and achylia gastrica, said, "one must wonder if achylia gastrica is not a factor that can inhibit the utilisation of both the P.P. (pellagra-preventive) and antineuritic factor of vitamin B".

Achlorhydria or hypochlorhydria appears to be common during pregnancy apart from anaemia. Strauss and Castle (1932) in a recent detailed study of a series of normal pregnant women found that 18 out of 24 patients showed an acid secretion below the normal range during most of the period of gestation. They found a 50% decline in maximum free acidity from the third to the sixth month, with a rise in the last month to the level observed in the third. The gastric juice after delivery contained three times as much free acid as during the sixth month. There was no correlation between the degree of reduction of gastric acidity and the age of the patient or number of previous pregnancies. Higher acidity values at the end of pregnancy than at the beginning have been reported by other observers. (Nakai, 1925. Smith, 1925. Larrabee, 1925. Hoskin and Ceirog-Cadle, 1927. Pepper, 1929. Mason, 1931.) It would seem probable, therefore, that this frequency of achlorhydria or hypo-chlorhydria is a factor favourable for the development of peripheral polyneuritis in pregnancy. In our patients, the limited number of fractional test meals showed acid curves within accepted normal limits, but these were all carried in the patients with fully developed symptoms and signs of peripheral polyneuritis and some time after giving birth.

Van der Wall noticed that the urine of a dog on a diet free from the antineuritic vitamin had no curative value for the so-called polyneuritic pigeons whereas the urine collected when the animal was subsisting on a normal diet was effective. Curatolo and Gaglio have also reported the presence of this vitamin in urine. Cowgill, Rosenberg, and Rogoff were able to show that in dogs given as large a volume of water by stomach tube as could be tolerated without vomiting and as often as circumstances allowed the experiment to give it, signs of lack of vitamin B$_1$ appeared much sooner than when the animals were allowed to drink water at their free will. They presumed that this condition was due to the loss of the anti-neuritic vitamin in the urine through the induced diuresis. Observations on animals had shown that the faeces contained appreciable amounts of vitamin B$_1$. (Steenbock, Sell, and Nelson, 1923. Salmon, 1925.

Smith, Cowgill, and Croll, 1925.) Arguing from the same principle it is not unreasonable to attribute the development of beri-beri in cases of prolonged diarrhoeas of whatever cause to failure of the individual to absorb a sufficient fraction of the ingested vitamin to meet the needs of the organism. In the same way, gastric troubles such as prolonged vomiting also affect the absorption of the vitamin. This failure of absorption becomes more important as a contributory cause of beri-beri when the amount of vitamin B_1 in the diet is low or only barely sufficient. In such cases the factor of safty against beri-beri is small.

In one of our patients, intractable vomiting occurred from the second to the last months of pregnancy. As expected, the absorption of vitamin B_1 was greatly reduced and the condition of peripheral polyneuritis developed as early as the third month of pregnancy, which was the earliest of the series. Furthermore, the condition was aggravated by an attack of dysentery soon after delivery. The patient was nearly completely paralysed, and recovery was slow and prolonged, over a period of nine months.

It is observed that all the causes discussed may act together in one single case and produce all the symptoms and signs characterising the condition of pregnancy polyneuritis. However, in this part of the world where beri-beri is endemic and where most of the poorer population are having a low supply of vitamin B_1, any one of the factors mentioned may precipitate the development of polyneuritis.

SUMMARY.

(1) An investigation was carried out on 27 cases of peripheral polyneuritis occurring during pregnancy or after delivery.

(2) A slight higher incidence is noticed between the age of 30 to 40 than between 20 to 30.

(3) The number of pregnancies seems to have some bearing on the incidence.

(4) Most cases fully develop after parturition.

(5) The date of onset lies between the third month of pregnancy and the third month after delivery.

(6) The symptoms and signs are similar to those of beri-beri.

(7) Two cases showed decalcification of bone in neighbourhood of the ankle joint but with normal serum calcium and phosphorus blood content and normal calcium and phosphorus excretion.

(8) The patients recover slowly under the routine treatment of supplying vitamin B_1 in various forms, a well balanced diet and electrical massage.

(9) The causes of avitaminosis B, are very briefly discussed:

(a) Increase demand of vitamin B, due to
(i) absorption by foetus,
(ii) absorption by infant through milk,
(iii) increase metabolism during pregnancy,
(iv) high carbohydrate and low protein and low fat diets.

(b) Deficient supply of vitamin B, due to
(i) the use of polished rice,
(ii) the reduction of intake of green vegetables during the later months of pregnancy and after delivery.

(c) Deficient absorption of vitamin B, due to
(i) achlorhydria or hypochlorhydria,
(ii) gastro-intestinal disturbances.

I wish to express my grateful thanks to Professor W. J. Gerrard, Head of the Department of Medicine, for encouragement and guidance throughout the period of this investigation.

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DETERMINATION OF NON-PROTEIN NITROGEN.

A modification of Folin's micro-method, using 0.2 ccs of blood or less.

by

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In our cholera patients during the recent cholera epidemic in Hong Kong, it was found necessary to carry out several chemical estimations on one small sample of blood. For the determination of non-protein nitrogen, Folin's micro-method (1934a) was preferred to the usual titration or gasometric methods which require at least 1 cc of blood. We found however, several difficulties with this method. They were:—

(a) Owing perhaps to the great deviation from the normal pH range of the blood in such patients, a clear filtrate in many cases was not obtained.

(b) The anti-bumping tube does not give enough gas bubbles when approaching the last stage of digestion.

(c) The fumes derived from the sulphuric and phosphoric acid mixture was so irritating that the digestion uprocedure had to be carried out in a fume chamber.

(d) A final clear Nesslerized solution was in many cases not obtained in spite of exercising all the precautions suggested by Folin (1934b), such as the proper reaction of Nessler's reagent and the care taken in the process of digestion (1934c).

(e) The nesslerized solution if clear was so faint that accurate comparison in a colorimeter was very difficult.

The first difficulty was solved by the use of trichloracetic acid as a precipitating agent. The second was overcome by the replacing of the anti-bumping tube with a fine capillary tube attached to a bellows. For digestion we employed Wong's (1923) sulphuric acid and potassium persulphate method. The excess acid is neutralized by NaOH. Gum ghatti solution (prepared according to Folin) and sodium citrate is added. The solution is then Nesslerized. The solution is clear and remains clear over night.

The last and most imporiant difficulty is overcome by the use of a *Photoelectric photometer.

REAGENTS REQUIRED.

Trichloracetic acid	10%
Sulphuric Acid	50%
Sodium Hydroxide	5N

* For this purpose we find the Cambridge Photo-electric Photometer supplied by the Cambridge Instrument Co., Ltd., 45, Grosvenor Place, London, S.W.1., suitable.

Gum Ghatti Solution. This is prepared according the method of Folin (1934). Fill a 500 cc cylinder with distilled water and suspend at the top, just below the surface, in a wire basket of galvanized iron, 10 gm. of the gum. Leave it overnight to dissolve but not for 24 hours. Then remove the wire basket with the remaining undissolved material. A little dirt may escape into the solution when the wire screen is removed, but this material settles and the lear solution can be used without further purification. After the solution has been transfered to a bottle, add 0.4 to 0.5 gm. of benzoic acid dissolved in 2 ccs of alcohol and shake at once. This will keep out moulds.

Sodium Citrate 1.5%

Nessler's. Prepared according to Folin. Transfer 150 gm. of potassium iodide and 110 gm. of iodine to a 500 cc Florence flask; add 100 cc of water and an excess of metallic mercury 140 gm. to 150 gm. Shake the flask continuously and vigourously for 7 to 15 minutes, and until the dissolved iodine has nearly all disappeared. The solution becomes hot. When the red iodine solution has begun to become visibly pale, though still red, cool in running water, and continue the shaking until the reddish colour of the iodine has been replaced by the greenish colour of the double iodide. This whole operation usually does not take more than 15 minutes. Now separate the solution from the surplus mercury by decantation and washing with liberal quantities of distilled water. Dilute the solution and washings to a volume of two litres. If the cooling was begun in time, the resulting reagent is clear enough for immediate dilution with 10 per cent. alkali and water, and the finished solution can at once be used for Nesslerization. From the stock solution of mercuric potassium iodide, made as described above, prepare the final Nessler solution as follows:—

From completely saturated sodium hydroxide solution containing about 63 gm. of NaOH per 100 cc, decant the clear supernatant liquid and dilute to a concentration of 10 per cent. (It is worth while to determine by titration that a 10 per cent. solution has been obtained, with an error of not over 5 per cent.). Introduce into a large bottle 3,500 cc of 10 per cent. sodium hydroxide solution add 750 cc of the double iodide solution, and 750 cc of distilled water, giving 5 litres of Nessler's solution.

Saturated solution of potassium persulphate.

PROCEDURE.

1. Place 2 cc of distilled water in a clean centrifuge.

2. Add 0.2 cc of blood with a pipette calibrated to contain and wash the pipette out three times with the water in the tube.

3. Add 1.8 cc of 10 per cent. trichloracetic acid. Shake vigorously for one minute.

4. Allow to stand for 5 minutes.

5. Centrifuge at 2,500 rpm for 5 minutes or until the supernatant fluid is clear and colourless.

6. Decant the clear fluid into another test tube through a filter paper.

7. Measure accurately 2 cc of the fluid into a pyrex test tube 200/25 marked at 25 ccs. In the absence of a pyrex tube an ordinary thin test tube will serve the purpose.

8. Add 1 cc of 50% sulphuric acid.

9. Insert the tip of the capillary tube to the bottom of the tube and set the current of air going and digest according to Wong's method.

10. Cool.

11. Add 4 ccs of 5N NaOH.

12. Cool.

13. Dilute to about 18 ccs.

14. Add two drops of gum Ghatti solution.

15. Add 2 ccs of 1.5% sodium citrate.

16. Add 4 ccs of Nessler's reagent.

17. Dilute to the 25 cc mark with water and take a reading from the photo-electric photometer, using the blue filter. Deduct from the reading the value of a blank which is prepared as above using 0.2 cc of water instead of blood.

Preparation of the Photometer Reading Concentration Curve.

1. Take 12 test tubes, into each of which put 2 ccs of distilled water.

2. Number the test tubes and put in the standard solution of ammonium sulphate which contains 4 mgs of nitrogen per 100 cc. The amount added is 1 cc in the first tube and 6 ccs in the last with 0.5 cc increments.

3. Add 1 cc of 50% sulphuric acid.
   4 ccs of 5N. sodium hydroxide.
   Cool.

4. Dilute to about 18 ccs and add
   2 drops of gum Ghatti solution.
   2 ccs of 1.5% sodium citrate.
   4 ccs of Nessler's reagent.,

5. Dilute to volume.

Take the Densitometer readings using the blue filter. Plot the graph with the readings obtained, the first tube corresponding to 20 mgs per 100 ccs and the last to 120 mgs per 100 ccs.

DISCUSSION.

We do not claim any improvement in accuracy over Folin's original method. We feel however that the method so modified is more readily successful in our hands, especially with the abnormal kind of blood that we are investigating. The reliability of the modification remains to be proved. The choice of protein filtrates was discussed and studied by Van Slyke (1932A). He finds that the precipitate obtained with trichloracetic acid is less bulky than that obtained with tungstic acid mixture, and hence a larger volume of filtrate is possible. The use of persulphate in the estimation of nitrogen by Folin's direct Nesslerization method was tried by Wong (1923) and found to be accurate. It has a definite advantage over Folin's digestion mixture in that it does not attack the glass and therefore hard glass apparatus is not essential (1932B). The neutralization of the sulphuric acid in the digest was recommended by Van Slyke (1932). We deviate from his method by neutralizing the digest before Nesslerization and use Folin's (1934D) method in the preparation of the Nessler's reagent. The anti-bumping device after Stuck (1927) is found to be more efficient than Folin's anti-bumping tube. The use of sodium citrate as a preventive against turbidity has been proved to be adequate by Van Slyke and Cope (1932C) and later by Barrel (1935). The greater accuracy of photometry obtained by using a photo-electric cell than by using an ordinary colorimeter is discussed by Campbell and Ritchie (1934).

It appears from the above discussions that the modifications will not introduce any appreciable error and hence although the reliability of these modifications remains to be proved, we felt justified in recommending their use. The method has already been found satisfactory for clinical purposes. For determining its limit of accuracy it is proposed to compare the results obtained by this method with those obtained by using the standard macromethods on the blood specimens sent to us from hospital patients, which specimens vary greatly in their non-protein nitrogen content. We propose to publish such results when sufficient data are available.

The method could be applied to 0.04 cc of blood, as only 5 cc of the Nesslerized solution is used for taking the photometer reading, but with ordinary laboratory facilities the larger volume suggested is to be preferred.

CONCLUSION.

Certain modifications with the use of the photometer are introduced into Folin's micro-method for the determination of N.P.N. of blood.

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DETERMINATION OF BLOOD UREA.

A modified micro-method using 0.2 cc of blood.

by

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GENERAL PRINCIPLES.

The usual methods of urea estimation can be generalised under two headings according to the principles involved.

1. Urea is hydrolyzed or decomposed by hypobromite, heat or urease, and the amount of urea calculated from the measured amount of nitrogen gas, ammonia or carbon dioxide evolved.

2. Urea is precipitated (a) by xanthydrol and the precipitate of dixanthylurea estimated or (b) by mercuric chloride and the amount of the mercuric salt measured.

A BRIEF DISCUSSION OF THE PRINCIPLES.

The mercuric chloride method first introduced by Liebzig in 1853 was long ago abandoned. The combining power of the salt is so general that it practically measures the total nitrogen. It has recently been revived by Hench and Aldrich (1926) and White and Ricker (1929). In our own experience we fixed that the end point of the titration is not always sharp, though in a large number of cases is accurate enough for clinical purposes. On this account we consider it reliable only in cases of gross urea retention.

The heat decomposition methods were abandoned even by their originators when the urease method came into existence. Recent work by Folin & Wu, and Clark & Collip (1926) revived this method on the Folin and Wu blood filtrate. They claim an accuracy of 1 mg per cent. The method like the previous two is not applicable to a blood sample of 0.2 cc.

Hypobromite does not yield quite the theoretical amount of nitrogen gas indicated by the equation. It evolves various proportions of gas from creatinine, uric acid and other nitrogeneous material.

The precipitation of urea by xanthydrol is considered quantitative and specific. Its application to micro-methods is however laborious.

Urease is perhaps the most popular reagent among the present day urea estimation methods. The action of urea was once considered extremely specific until the reports of Behre (1923), Kirk (1933), Anderson & Tompsett (1936). It was thought that some "extra urea" arises from the action of an enzyme in the blood on a substrate in

the urease preparation. Damodaran (1937) reported a new source of urease devoid of such substrate. The whole question of this "extra urea" when urease preparations are brought into contact with blood still awaits systematic investigation.

Owing to the present state of our knowledge, it is proposed to adhere to the time-tested urease method for the following two reasons:—First, Van Slyke (1932) believes that the abnormally high values can be avoided at least for human blood by using the appropriate quantity of urease and by the proper control of the temperature and duration of digestion. Second, most of the present data which guide the clinicians when considering their diagnoses and prognoses and when deciding on their treatment, are based upon the action on the blood.

TECHNIQUE OF MEASUREMENT.

The aero-titration of ammonia formed from urease digestion, and the direct weighing of dixanthylurea which is seven times heavier than urea itself, have almost become standardized in micro-methods. When the amount of blood is limited to 0.2 cc the urea involved is so infinitesimally small that these two methods are not practicable. The micro-aerotitration method of Gad Andresen (1922) and the micro-Nesslerization method of Hindmarsh and Priestly (1924) are laborious and in the opinion of Barret (1933) involve the possibility of loss of ammonia, or the introduction of ammonia present in the reagents.

The following micro-methods have from time to time been employed by various investigators:

1. Gasometric measurement by a manometer of the carbon-dioxide evolved, Van Slyke (1927). This method gives an accuracy of within 1 per cent. It must be realized that the apparatus while accurate in the hands of trained workers, may become a source of great error when manipulated by an ordinary laboratory hand.

2. The measurement of a colour produced by the dixanthylurea, as those recommended by Beattie (1928), Yoshimatsu (1929) and Lee & Widdowson (1937); these methods are extremely long and laborious.

3. Obermer (1933) determines the amount of dixanthylurea by virtue of the turbidity. The accuracy of chemical determination depending upon the turbidity of the precipitate is however questioned by Van Slyke (1932).

4. Titration of the dixanthylurea by permanganate has been adopted by Luck (1928). The process is long and it requires 5 cc of Folin's filtrate.

5. Direct measurement of the ammonia formed in the urea and urease mixture by conducto-meter has been worked out by Ranga-

nathan and Sastri (1936). The accuracy of the method does not exceed that of Van Slyke's manometric method. The process is longer. Here again the accuracy of such a delicate electrometric H ion measurement instrument depends too much on the technique of a trained assistant.

6. The measurement of ammonia is used by Conway (1933). The ammonia is first liberated by an alkali and absorbed by standard acid in the Conway apparatus. The idea seems to be very sound but the reliability of such a method remains to be confirmed.

7. Direct Nesslerization of the blood filtrate as those recommended by Archer (1923), Feinblatt (1923) and Karr (1924) etc., excell all the other methods in simplicity and minimum amount of blood required. It is however inferior to Van Slyke's gasometric method in accuracy. The tungstic acid or the trichloracetic acid filtrate contains substances other than ammonia which give a yellow colour with Nessler's reagent. This defect is even admitted by Folin (1934).

OUR PRESENT PROCEDURE.

It seems to be clear that the direct Nesslerization method of Archer etc., combines the advantages of simplicity and minimum blood volume requirement with that of the absence of any instrument which depends so much on the technique of the laboratory hand for its accurate use. In spite of this however, it cannot be considered the ideal method as it is as yet, definitely less accurate than others. We have therefore attempted to increase the accuracy of this method as much as possible and in so doing we have adopted the following modifications:—

(a) The use of Somogy's zinc precipitation of the protein instead of tungstic acid as recommended by Van Slyke and Platzin (1932).

(b) As a preventitive against the unexplained turbidity which usually accompanies Nesslerization, we add gum Ghatti according to Folin (1934) and sodium citrate according to Barret (1935).

(c) We decrease the common source of error in colorimetry by the use of a *photoelectric cell which is, according to Campbell and Ritchc (1934), able to make a much more accurate comparison than the human eye.

The present modified method gives accurate results on aqueous urea solution. We propose to determine the limits of accuracy of this modified method on blood by comparing its results with those of standard macro-methods on many pathological as well as normal blood samples; the results of these experiments will form the subject of

* For our purpose we find the Cambridge Photo-electric Photometer supplied by Cambridge Instrument Co., Ltd., 45 Grosvenor Place, London S.W.1., suitable.

another paper when enough data are available. In the meantime, since all these modifications have been suggested and tried out by other workers it may be assumed that their embodiment in one method does not introduce any appreciable extra error.

REAGENTS REQUIRED.

Urease suspension. Suspend one tablet (20mg) of Urease-Dunning in 5 ccs of 30% alcohol and shake to mix.

Zinc Sulphate solution. The strength of this solution used is about 1.8%, so that 10 ccs will be neutralized by 12 to 12.2 ccs of N/10 NaOH, using phenolphthalein as indicator.

N/10 Sodium Hydroxide.

Gum Ghatti solution. This is prepared according to the method of Folin (1934). "Fill a 500 cc cylinder with distilled water and suspend at the top, just below the surface, in a wire basket of galvanized iron, 10 gm of the gum. Leave it overnight to dissolve, but not for 24 hours. Then remove the wire basket with the remaining undissolved material. A little dirt may escape into the solution when the wire screen is removed, but this material soon settles and the clear solution can be used without further purification. After the solution has been transferred to a bottle, add 0.4 to 0.5 gm., of benzoic acid dissolved in 5 ccs of alcohol and shake at once. This will keep out moulds."

1.5% sodium citrate solution.

Nessler's Reagent. Prepared according to Folin. "Transfer 150 gm of potassium iodide and 110 gm of iodine to a 500 cc Florence flask; add 100 cc of water and an excess of metallic mercury 140 gm to 150 gm. Shake the flask continuously and vigorously for 7 to 15 minutes, and until the dissolved iodine has nearly all disappeared. The solution becomes hot. When the red iodine solution has begun to become visibly pale, though still red, cool in running water, and continue the shaking until the reddish colour of the iodine has been replacel by the greenish colour of the double iodide. This whole operation usually does not take more than 15 minutes. Now separate the solution from the surplus mercury by decantation and washing with liberal quantities of distilled water. Dilute the solution and washings to a volume of two litres. If the cooling was begun in time, the resulting reagent is clear enough for immediate dilution with 10 per cent. alkali and water, and the finished solution can at once be used for Nesslerization. From the stock solution of mercuric pottasium iodide, made as described above prepare the final Nessler solution as follows:—

From completely saturated sodium hydroxide solution containing about 63 gm of NaOH per 100 cc decant the clear supernatant liquid and dilute to a concentration of 10 per cent. (It is worth while to

determine by titration that a 10 per cent. solution has been obtained, with an error of not over 5 per cent.) Introduce into a large bottle 3,500 cc of 10 per cent. sodium hydroxide solution add 750 cc of the double iodide solution, and 750 cc of distilled water, giving 5 litres of Nessler's solution."

PROCEDURE.

1. In a centrifuge tube place 2 ccs of distilled water.

2. Add 0.2 ccs of blood with a pipette, calibrated to contain, and wash the pipette out 3 times with the water in the tube.

3. Add 0.2 ccs of the urease suspension.

4. Place the centrifuge tube in a water bath at 55° C for 15 minutes.

5. Remove the tube from the water bath, add 3.6 ccs of distilled water, 1 cc of 1.8% zinc sulphate solution, and 1 cc of N/10 sodium hydroxide.

6. After standing for five minutes, centrifuge till the supernatant fluid is clear.

7. Draw off 5 ccs of the supernatant fluid and run it into a clean test tube.

8. Add 4.5 ccs of water containing one drop of the above gum Ghatti solution in every 5 ccs of distilled water.

9. Add 0.5 ccs of the 1.5% sodium citrate solution.

10. Add 2 ccs of Nessler's reagent.

11. Place 4-5 ccs in the photo electric Photometer cell and take the reading.

12. Read off the urea value from the graph and deduct from it the value of a blank which is prepared as above using 0.2 cc of water instead of blood.

PREPARATION OF PHOTO-METER READING CONCENTRATION GRAPH.

Dissolve 2.2 gms of pure dry ammonium sulphate in water and make up to 1,000 ccs with water. Dilute this solution 1 in 20 by taking 5 ccs and making up to 100 ccs with water.

Set up a series of tubes and into them pipettes 0.25, 0.5, 0.75, 1, and so on up to 3.5 ccs of the diluted solution. In each case, make up to 10 ccs with distilled water.

Add to each tube 2ccs of Nessler's reagent.

The Photo-meter readings less that of a blank are then plotted out graphically giving a range from 10 mg to 140 mg per 100 cc of blood.

SUMMARY.

A photoelectric method has been described for the estimation of urea in 0.2 cc of blood based on the direct Nesslerization of the filtrate from hydrolyzed blood. Through the embodiment of several modifications the usual difficulties of direct Nesslerization has been removed and the final Nesslerized solution remains clear overnight.

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We wish to acknowledge our gratitude to our chief, Prof. L. T. Ride for many helpful criticisms and guidance in the preparation of this paper.

A REPORT ON THE INCIDENCE OF NUTRITIONAL DISEASES AND FOOD SUPPLY IN THE REFUGEE CAMPS IN SHANGHAI.

by

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This article is an expansion of a short report submitted on September 1st, 1937, to the Shanghai Municipal Council (S.M.C.) on a general survey made last August of the food supply and the incidence of nutritional diseases in the various refugee camps in Shanghai.

The opportunity of making this investigation came to me while I was working at the Lester Chinese Hospital, where I was sent by Professors L. T. Ride and W. C. W. Nixon to study beri-beri and nutritional problems in general. When the war broke out, all research work came to a stand still and the staff of the Lester Institute turned their energies to the welfare of refugees and casualty cases. Through the kind permission of Dr. H. G. Earle and Dr. R. C. Robertson, the latter being then head of the Public Health Department, I was able to study the condition of the camps, their food and their nutritional condition.

For three days before the outbreak, many thousands of residents fled into the safer areas of the International Settlement and the French Concession. The well-to-do accommodated themselves in hotels and boarding-houses, whilst the poor had to be content with the road-sides, alleys and similar places where they could stay without being chased away by the police. This scare was due to the Hungjao shooting incident in which two Japanese Naval Officers, one Paoantui (Chinese Volunteer) and a pedestrian lost their lives. When war definitely broke out on the 12th August, the S.M.C., immediately took cognisance of the refugee problem on account of both public safety and public health.

The second question was no less urgent than the first for this was the period of yearly epidemics of cholera, dysentery etc. Public spirited organizations were encouraged to form camps for these refugees and they were registered at the S.M.C. Within two weeks there were 86 camps established, containing in all about 96,000 refugees.

Segregation of Refugees.

Those refugees without any means of subsistence were either directly rescued from the war zone or rounded up from the road-sides into their respective camps—the Cantonese into the Cantonese Camp, the Fukienese into the Fukienese Camp and so on. Once they were admitted into the camps they were not allowed to leave until they

were shipped off to their respective provincial villages, the expenses being defrayed partly or entirely by the association or by the refugees themselves.

Condition of the Camps.

Without exception, all the camps were overcrowded, dark and dingy, and very poorly ventilated having regard to the number of inmates, all available space was occupied for sleeping. On approaching camps one often had awful warning of the foul air conditions within. Those inmates occupying the centre of the hall (which was seldom left for fear of being taken by new comers) were completely deprived of the beneficial effect of sunlight and fresh air.

The best camp was the Girls' School camp. Here the conditions provided were better and more orderly. The rooms were clean and dry. In the day time the inmates were made to roam about in the school compound whilst the place was being swept clean.

Diet.

Eleven samples of rice received from various camps were investigated for the degree of polishing and the amount of talc. The degree of polishing was examined by Lugol's solution method. The amount of talc was estimated by weighing the rice before and after ashing. (The difference in weight after subtracting the weight of true rice ash gives the rough amount of talc). By these methods the rice was found to be partially polished to varying degrees, and contained a very small amount of talc which could be consumed without danger to the health.

The usual method of cooking rice was adopted by all, that is, soaking the rice with water and stamping it with the hands. This process of washing was repeated 2 to 3 times until the supernatant water was clear. When cooked this turned into soft rice, and was served with a little salted vegetable. Three such meals were served daily.

In one Ningpo camp, sweetened bread and wheat bread to the amount of slightly over 1 lb. were supplied instead of rice for each of the three daily meals. The reason given by the management for supplying bread was that many of the inmates were factory workers having weakness of limbs (beri-beri conscious). The New World Camp (Cantonese Association) supplied rice and salted vegetable to the healthy and milk and biscuit to the sick and babies. This investigation revealed that the diet was similar in all the refugee camps visited and characteristically lacking in certain nutritive elements. Therefore, if the diets were not improved, fresh cases of beri-beri, scurvy and other nutritional diseases might be expected to occur.

Method of Examination.

Refugees of six different camps were examined from the 22nd to 25th August. Four hundred and eight cases were examined

for signs of nutritional deficiency at random as they came for vaccination. In this way the percentage of nutritional deficiency would be nearer to the true percentage than if only cases of beri-beri were examined. A careful search was made for symptoms of avitaminosis, especially for B_1 deficiency. Whenever cases of beri-beri were noticed, their history and duration of illness were ascertained. The presence and absence of symptoms were marked plus and minus on a given printed chart for each patient.

CHART.

Name		Place		Date	
Age	Years	Months			
Sex	M F.				
Occupation					
Family Status					
Economic Status					
Father		Mother			
Sisters					
Brothers					
Children					
Past Illness	Age	Disease	Age	Disease	
Worms					
Eyes					
Bleeding	Nose		Gums		
Previous Health	E.	G.	M.	F.	P. Parb.
Appetite			Sleep		
Crowding	Rooms		Number of persons		
Estimate of Intelligence					
HEAD:—					
Hair	dry		dirty		scanty
Scalp	tinea		eczema		lice
Eyes-expression					
Corneal opacities		Rt.	Lt.		
Scleroties	dry		disease		injury
Conjunctiva anaemic					
Conjunctivae inflamed			diseased		
Ears	discharge		eczema		
Nose	discharge		deformed		
Lips	cracks		fissure		perléche
	pigmentation				anaemia
Gums	colour		pyorrhoea		gingivitis
Tongue					
Mouth					
Teeth	dirty		missing		carious
Fauces					
Breath					
Tonsils					
NECK:—	Pulsation				Thyroid
THORAX:—					
Heart					
Lungs					
ABDOMEN:—					
Liver					Lymph gland
Spleen					Genitalia
MUSCLES:—	Tone				Amount
LIMBS:—	Deformities				
Reflex	K.J.		Rt.		Lt.
Joints					
SKINS:—	dry	cracking	pigmentation	scabies	dermatitis

NAILS:—	Hands	Feet
SUBCUTANEOUS TISSUES AMOUNT:—	Abdominal	Cheeks
INTERDIGITAL LESION:—	Hand	Feet
POSTURE		

This chart is a copy of the charts used and tabulated by Dr. H. S. Platt of Henry Lester Institute of Medical Research, Shanghai.

Types of B, deficiency.

The cases of B_1 deficiency were divided into the following groups:—

1. BORDER LINE cases or minor B_1-deficiency are those having any three of the following signs:—

(a) Neuritis of extremties as revealed by numbness of finger tips and/or toes and peroneal aspect of legs. The nerves are not tender to pressure.

(b) Altered (usually absent) or unequal knee-jerk responses.

(c) Muscular weakness on exertion.

(d) Anorexia.

(e) Tense calf muscles with tenderness on pressure.

2. MILD beri beri cases have in addition to the above symptoms, a, b, c, d and/or e, two of the following signs:

(f) Tachycardia (pulse 90 and above).

(g) The appearance of oedema of ankles and feet after exertion.

(i) Visible epigastric pulsation.

3. SUB-ACUTE beri-beri cases have all the signs of the previous two groups in a more definite form. Thus calf muscles are definitely tender to pressure, there is visible venous pulsation of neck even during rest, marked epigastric pulsation and definite numbness of legs and hands can be demonstrated. The hair on the legs appears dry and fine and is easily pulled off without much pain.

4. ACUTE beri-beri cases are those in the prostrated form having the acute signs of cardiac decompensation, respiratory distress, extreme restlessness with history of beri-beri before onset of acute stage. The patient's mental attitude is alert and the lungs are clear in spite of extreme dyspnoea and cardiac decompensation.

5. PARALYTIC beri-beri cases are those having the characteristic atrophy of extensor muscles of the limbs, foot-drop and/or contracture of fingers with history of beri-beri before the onset of paralysis. Signs of cardiac decompensation are usually absent.

The following table shows the camps visited, the number of refugees present and examined.

TABLE I.

Name of Camp	No. of refugees present in camp	No. of refugees examined
1. Girls' School	448	60
2. Charter Theatre Camp	780	72
3. Western Theatre Camp	832	75
4. Camp No. 27 (3 Roomed house)	190	51
5. Camp No. 5	494	51
6. New World Theatre Camp	13,000	99
TOTAL	15,744	408

These 408 refugees examined consisted of 154 men, 49 women, 107 boys, 78 girls and 20 children. The following are the types of nutritional diseases, eye trouble and skin lesions found in the 408 refugees examined.

Sub-acute beri-beri	3
Mild beri-beri	8
Border-line cases (B_1 deficiency)	106
Sub-clinical A Avitaminosis	6
Sub-clinical scurvy	1
Rickets	0
Pellagra	0
Trachoma	20
Conjuctivitis	60
Skin diseases	204

Discussion.

Of the 408 cases examined, 117 showed signs of B_1 deficiency, giving a percentage of 28.6 of the refugees in a state of B_1 avitaminosis. If this limited number of cases examined at random could be taken as a guide for the percentage of the incidence of B_1 deficiency in the camps, then it is not unduely high, because these camp refugees represent the poorest of the poor; factory workers, artisans and labouring class people who are potentially beri-beri in their normal walk of life.

None of the 408 cases examined suffered from diarrhoea or dysentery. Inquiry from the management revealed that quite a number have suffered from both. No clinical examination was made on these cases.

Remembering that they were only ten days in the camps when examined, the presence of nutritional diseases was not actually due to present conditions, i.e., they suffered from the disease before they entered the camp. This was confirmed by the history and duration of appearance of symptoms.

If the housing conditions of these camps were improved, there is very little danger of beri-beri assuming the acute form. Overcrowding, poor ventilation and high room temperature, are conditions producing sleeplessness and restlessness day and night. These and the presence of diarrhoea and dysentery in the camps present a real danger of beri-beri assuming the acute form, especially from superimposition by the latter.

It may be of interest to record information received from Shanghai that three weeks after my return from the North, acute cases of beri-beri were sent into the Lester Chinese Hospital from these camps. Whether these fulminating cases of beri-beri were the sequence of superimposition by other diseases or were brought about by overcrowding, or continuance of rice and salted vegetable diet, I am unable to say.

The minimum daily requirement of vitamin B_1 for a person of 50 kg. body weight (which is the probable average body weight of Southern Chinese) is 200 to 250 International Units and its vitamin/calorie ratio is 1.35. In Table II are presented estimates of the vitamin B_1 content of the diets fed to these refugees. The B_1 content ranges from 94 to 151 International Units and the vitamin/calorie ratio from 0.75 to 0.77, which is far below the minimum daily requirement of 200 to 250 I.U., and the minimum vitamin/calorie ratio of 1.35. It is obvious that such diet will eventually produce symptoms of beri beri. The vitamins A, D and C are also lacking in the diet. Therefore, one would also expect the appearance of cases of A, D and C avitaminosis. Hence my suggestion for the immediate improvement of the diet to meet these deficiencies.

Gastro-intestinal ailments would also be more prone to take place as the result of lowered body resistance through deprivation of essential food elements. It is to be noted that one week after this report had been forwarded to the S.M.C., a good number of the refugees suffered from dysentery which necessitated the establishment of isolation hospitals. Stool culture revealed that a great number of them were neither of Shiga nor Flexner infection. Bacteriological reports seemed to point that lactic acid fermenting organisms might be the cause of dysenteric stool. The question, whether or not, these commensal fermenting bacteria can exert any pathological effect in a condition of lowered body resistence is beyond the scope of this article. Another interesting point to note is, that the first few cases of cholera were from refugee camps. Again the question whether these cholera cases in the camps were originally carriers succumbing to the organism when their resistence became low, or whether carriers infected their fellow-refugees is not for discussion here. In view of the recent epidemic in Shanghai which seemed to originate in the camps, the urgent need for special refugee-camp doctors is apparent.

TABLE II.

Diet of the Refugee Camps.

Refugee Camp No.	Approximate amount per adult per day		Vitamin B_1 Content			Approximate Calories	Vitamin Calorie Ratio
			Cowgill's mgm-equiv.	International Unit	Total B_1 in I.U.		
1		gms					
4	Rice	500	1280	64	= 94	2860	0.33
5	Salted Veg.	120	600	30			
6							
3	Bread	1360	2720	136	= 151	3900	0.77
	Biscuit	150	300	15			
2	Bread	1000	2800	140	= 105	2705	0.77
	Rice	200	160	8			
	Salted Veg.	50	150	7			

The probable vit/cal. ratio for a body weight of 50 kilograms is 1.35.

SUGGESTIONS.

Owing to the very large number of refugees in each camp and not knowing to what extent these relief organisations are willing to defray expenses on food, suggestions for the improvement of diet to make rather difficult are, especially when one wish to include every essential food element. With due regard to strict economy, the following suggestions embody the minimum daily requirements which will minimise the danger of an outbreak of beri-beri and other nutritional diseases. The cost of the recommended diet as calculated from current market prices is 10 to 12 cents per day per person. This low cost of diet would easily meet the financial requirements of the Refugee Committee which would thus be more likely to follow the suggestion for the improvement of diet.

As stated, the rice samples collected contain very little talc and are partially polished. Therefore the rice can be cooked and eaten without danger to health. Stamping rice with hands as a process of washing should be avoided as this will lower the vitamin B_1 content to half. If washing is necessary to remove the odour of long stored rice, then it should be washed with running water only.

1. Rice 500 grms.
2. Six ounces of green bean or soya bean.

(3) Soya bean sprout or sweet potato (any type of potato) 4 ozs., and if possible fresh leafy vegetables and a little meat should be included.

(4) Cases of avitaminosis may perhaps require drachm doses of cod liver oil.

The bean, potato and green vegetables can be cooked together. This will greatly save time and money and increase flavour of rice.

The caloric value of the above diet is approximately 2,500 calories, the B_1 content in the 6 ozs of bean and 4 ozs. of potato is 4,226 mgm-equivalents (Cowgill), or in terms of International Units, 211. Plus the B_1 present in rice and in fresh leafy vegetables, the total of B_1 consumed will approximately be 300 to 350 International Units and the vit/cal., ratio will be 2.4 to 2.8. This amount of B_1 is more than sufficient for the daily requirements of an adult doing no manual labour.

The vitamin C in bean sprout or sweet potato will minimise the appearance of scurvy.

CONCLUSIONS.

1. Cases of beri-beri and other nutritional diseases found in the camps are not due to the condition in the camps for they already have the disease before they enter the camps.

2. The danger of beri-beri assuming the acute form is from over-crowding and superimposition by other diseases.

3. The first few cases of cholera in Shanghai were from the refugee camps. Gastro-intestinal ailments may be the sequence of lowered body resistance through deprivation of essential food elements.

4. Investigations revealed that the present diet lacks certain nutritive elements and if not improved, fresh cases of nutritional diseases, especially beri-beri, are to be expected.

5. The diet suggested will minimise the danger of an outbreak of beri-beri and other nutritional deficiencies.

Acknowledgments.

Grateful appreciation is due to Mr. E. F. Yang (Biochemist) and his assistants for estimating the degree of rice polishing and the amount of talc in rice, and in assisting the examination of refugees; to Dr. H. G. Earle and Dr. R. C. Robertson for their kind permission to investigate the incidence of nutritional diseases among the refugees; and last but not least to Professors L. T. Ride and W. C. W. Nixon for sending me to Shanghai to study nutritional diseases at the Lester Institute. To Prof. Ride I owe a special debt of gratitude for his constant encouragement and for his help in producing this paper.

A SPECIAL PUBLIC HEALTH COURSE IN NANKING.

by

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During the summer of 1937, a series of lectures, demonstrations, and excursions was specially organized by the National Health Administration (now the Ministry of Health), Nanking, for the Public Health students of the Hong Kong University. This being the first course of instruction arranged by the Nanking Government for the Hong Kong University, the following report is primarily meant to place on record the full details of the course.

Thanks are due to Dr. J. Heng Liu, Minister of Health, Nanking, Dr. C. Y. Wu, Assistant-Director of the National Quarantine Service, a graduate of the Hong Kong University, and to Professor L. T. Ride, Dean of the Hong Kong University Medical Faculty for the origin of the idea which was conceived when Professor Ride visited Shanghai for the Chinese Medical Conference in the spring of 1937.

The following students registered for the course: Miss B. Chu, Messrs. Koe Kheng Loke, Kwan Siu Yee, Lee Ching Ju, P. Moore and Tsang Kwong Kau. Two students of the Arts Faculty, Miss H. Chu and Mr. Lo Hung Chun, also joined the group. As lecturer in Public Health, the writer was assigned to take charge of the group.

THE TRIP TO NANKING.

With the exception of two members of the party, Messrs. Li Ching Ju and Tsang Kwong Kau, who joined the party later in Nanking, the group sailed by the S.S. President Doumer (Messageries Maritimes) on the 26th of June, 1937. Upon arrival at Shanghai, on the morning of June 29th, we were met by two officers of the National Quarantine Service delegated to meet us by Dr. C. Y. Wu, who had instructions from Dr. J. Heng Liu, to make the necessary connections with us on our arrival at Shanghai to render us all possible assistance. We were also met by Dr. C. L. Moore who entertained us at dinner that night. Sir Robert and Lady Ho Tung, who were in Shanghai at that time, welcomed us at lunch at their Shanghai residence. At 8 a.m., June 30, we left Shanghai by the Capital Limited, an express train and arrived at Nanking at 12.45 p.m. At the station, we were met by Mr. K. S. Wang, representative of the National Health Administration, and by Dr. Irene Ho, a graduate of the Hong Kong University, now serving in the Ministry of Education. We were taken to the new students dormitory of the National Health Administration where accommodation was arranged for us. The course commenced the next day.

The following is a schedule of the course and of our activities in Nanking up to July 17th:

THURSDAY, July 1st.

A.M. *Interview* with Dr. J. Heng Liu, Minister of Health.

General Introduction of Central Health Work—Dr. P. Z. King, Vice-Director of Central Field Health Station, and Dr. K. F. Yao, Acting Director, Training Institute.

P.M. *State Medicine and Medical Education in China*—Dr. C. K. Chu, Technical Expert and Chief of the Department of Health Education.

Urban Health—Dr. T. H. Wang, Director of the Municipal Health Administration, Nanking, and Dr. W. M. Li, District Health Officer, Ssu P'ai Lou Health Station, Nanking.

FRIDAY, July 2nd.

A.M. *School Health*—Dr. S. E. Hsu, Technical expert in the Depart of Health Education.

Visit—School for the Sons and Daughters of the Revolutionary Heroes.

P.M. *Visit*—Wu T'ai Shan Primary School.

SATURDAY, July 3rd.

A.M. *Visits*—Departments of Bacteriology, Control of Epidemic Diseases, and of Parasitology.

P.M. *Visits*—Departments of Sanitary Engineering, and of Maternity and Child Health.

SUNDAY, July 4th.

A.M. *Excursion* -Anhwei Province—Places of scenic beauty and historical interest including Tsoi Shih Chih.

MONDAY, July 5th.

A.M. *Visits*—Departments of Medical Relief and Social Medicine, and of Vital Statistics.

P.M. *Visits*—Departments of Chemistry and Pharmacology, and of Health Education.

TUESDAY and WEDNESDAY, July 6th and 7th.

Municipal Health Administration—Lectures and visits.

THURSDAY and FRIDAY, July 8th and 9th.

Rural Health in Kiangnin Hsien—Lectures and excursions.

Excursion to Tongshan Hot Springs.

SATURDAY, July 10th.

A.M. *Visits*—Central Hospital and Central Nursing School.

P.M. *Visit*—Central Midwifery School.

SUNDAY, July 11th.

Sight-seeing in and around Nanking, especially to the famous tombs in the National Park.

MONDAY, July 12.

Visits—The Army Medical Service and the Army Medical School.

TUESDAY, July 13th.

A.M. *Visit*—The Central Army Medical Depot.
P.M. *Discussion*.

WEDNESDAY, July 14th.

A.M. *Visit*—The Academia Sinica.

P.M. *Visits*—Hsia Kwan Public Bath, a Soya Bean-Milk Factory, and Houses for the Poor.

Evening: *Dinner* given by the Hong Kong Group to Drs. Irene Ho, C. C. Chiang, K. F. Yao, W. M. Li and other friends all of whom had shown hospitality to the group.

THURSDAY, July 15th.

A.M. *Visit*—Agricultural Experimental Station.

P.M. *Visit*—Public Health Department of Central University.

Evening: *Boating Picnic* in Lotus Lake given by Dr. C. C. Chiang and friends.

FRIDAY, July 16th.

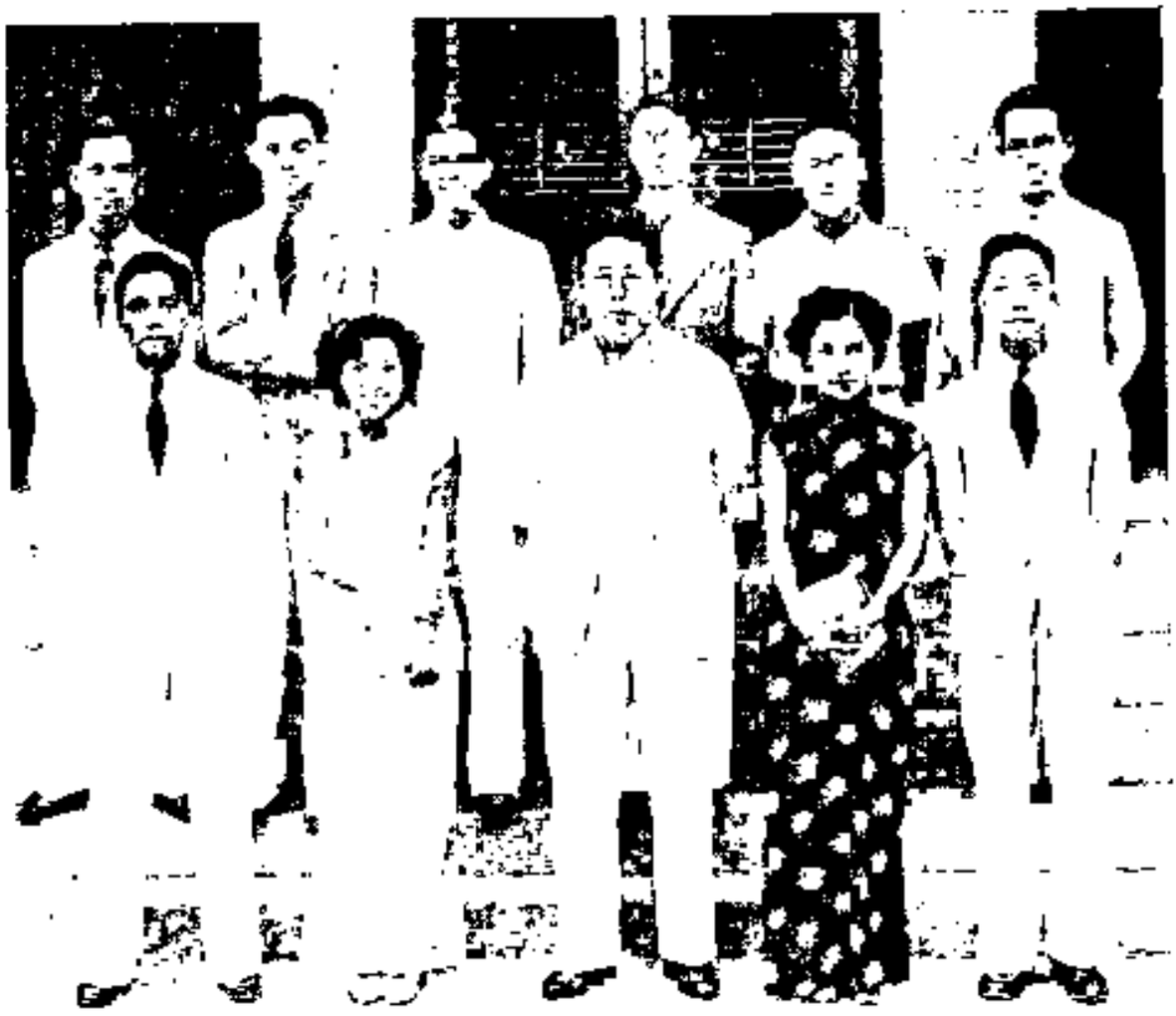
A.M. *Attended Opening Ceremony* of Public Health Training Class.

Visit—Nurses Association of China.

P.M. *Visit*—Ministry of Education.

Evening: *Farewell Dinner* given by Dr. P. Z. King.

On July 17th, we left Nanking: three returning via the Hankow-Canton Railway, two went up north before returning to Hong Kong, and the rest returning via Shanghai.



EXPENDITURE:

The following gives an indication of the expenditure per head (excluding personal expenditure):

Hong Kong to Shanghai: 3rd class, S.S. President Doumer, $40.00 (H.K.) 25% rebate given for return ticket.

Shanghai to Nanking: 2nd class rail, $7.50 (Mex.).

Board in Dormitory, Nanking, $5.00 (Mex.) for two weeks.

No Charge was made for the lectures, demonstrations, or lodging in the dormitory.

The Cost of Transportation during excursions amounted to $7.00 (Mex.) per head. This sum was paid by the Hong Kong University.

REMARKS AND RECOMMENDATIONS:

We were greatly impressed by the warm reception and cordiality extended to us. The course was well-organized and it gave a comprehensive idea of urban and rural sanitation and of the general scheme of State Medical Service in China. We noted with great admiration the spirit of New China—co-operation, self-sacrifice, service—in all the public health workers. The majority are working willingly and cheerfully at very low salaries, especially those in rural areas. To those of us who have visited Nanking five years ago, the visit was an eye-opener, as great strides have been made during that short space of time in public health work and organization.

The course forms a valuable link between Hong Kong and Nanking, and I would like to recommend that other courses be arranged, for example, with the Ministry of Education. Students who are interested in future work in China after their graduation should not miss this good opportunity of making their connections early. There are several Rockefeller travelling scholarships, and government fellowships, awarded every year to those who are selected and recommended by the Ministry of Health.

Review of Books

A Short Manual of Regional Anatory. By J. A. Keen. Longmans, Green & Co., Ltd. Price 5/- net. Oct. 4/37.

This manual is written, to quote the title page, for the medical student as an aid to a rapid revision of the whole subject. An introductory section entitled General Anatomy in parts is highly informatory and gives an impression of being all too short. The subject matter is arranged on a regional basis in much such a way as the student dissected, i.e. by the somewhat artificial if convenient division of the body into the limbs, the head and neck. In addition the author includes a section on the interior of the skull, brain, spinal cord and the autonomic system, another on the orbit, eye, nose, larynx and ear.

It may be questioned if this sort of regional arrangement is what is needed. Experience shows that the region where a student's knowledge is apt to fail him is where the limbs join the trunk or where the neck meets the mediastinum rather than in the middle of a more conventionally described "region".

The whole book is of no more than 167 pages including the index and two appendices. It is well printed and easy to read because of the heavy type given, as one supposes, for the purposes of emphasis. The illustrations are numerous but for the most part purely diagrammatic.

Features of this book which are distinctly unusual are the commencement of each section with an account of the surface markings. The idea is commendable but the result is little more than a list and it is in this place that simple diagrams might be of great value. Only in the section on the abdomen is such a diagram found. At the end of each section is a comparative list of terms belonging to the new English Terminology and to the old Terminology. Such a list has little use for the student; it is far more useful for his teacher, or his examiner, who may have learnt the old Terminology in his own student times.

A list of derivations of anatomical terms from Latin or Greek also follows each section. Again little usefulness is to be seen where the student, or the teacher, has no educational background of the classical languages.

Though some of the diagrams are of undoubted usefulness others are too schematic to be of service. It must be confessed that the diagram in Figure 9 illustrating the interosseous muscles of the hand is difficult to follow. On the other hand Figure 31 showing the boundaries of the perineum and the relations of the perineal membrane is informative. Figure 26 shows the intercostal nerve occupying a plane between the internal and external intercostal muscles, an error trans-

mitted through many editions of textbooks and dissecting-room manuals and now corrected.

The printed matter will be found to lend itself to the purpose of rapid revision. The language used is precise and short and the use of heavy type to catch the eye and arrest the attention is skilfully contrived. Perhaps the sections on the abdomen and on the interior of the skull with central nervous system are the best, though the review of the typical spinal nerve and the autonomic system is so brief that it might have been included in the Introductory Section. Many of the diagrams of the skull venous sinuses and the brain are helpful, precise and informative.

Short notes of advice on the writing of an answer to a descriptive question in an Anatomy paper constitute a novelty. The student may well take a hint that some system is highly advisable, saves time, makes for accuracy and finally gains marks.

The book ends with two appendices; one on the centres of ossification of bones and epiphyses, the other a list of muscles which have a double or a multiple nerve supply.

The book is short and easy to read and may serve a more useful purpose to the senior student who needs a few reminders rather than to the candidate for the 3rd Professional Examination.

Diseases of the Nose, Throat and Ear. By J. Simpson Hall. E. & S. Livingstone, Edinburgh. Price 10/6 net, postage 6d.

To compress the diseases of the nose, throat and ear together with short anatomical descriptions into 423 small sized pages inclusive of index is an almost impossible feat. In spite of the inherent difficulties of so much overcrowding, the manual presents a pleasant, readable and up to date account. The printing is excellently clear. The index is good. There are fifty-five illustrations. Figures 51 and 52 would be more appropriately placed facing one another.

The book "aims to meet the needs of the busy parctitioner and the student. In many instances operations are merely mentioned but particular stress has been laid on minor technical procedures."

Amongst omissions may be noted any account of Gelle's test. A misprint on page 248 spells Hurst's name as Hirst. The description of Ludwig's angina is poor and the treatment recommended namely "free incision of the tissues to promote drainage and retard absortion" is vague to the point of uselessness.

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