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NUTRITIONAL KERATOMALACIA*

REPORT OF CASES

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Keratomalacia, although not often mentioned in the medical literature in China, is by no means a rare disease in this country. Dr. G. A. M. Hall † found it very prevalent in Tatungfu, Shansi, especially in two institutions for poor children. Dr. H. H. Shih †, of the Shantung Christian University, found a number of cases during one year in Tsinan. She gave the author full reports of four cases under her care. All of them were children under 6 years of age; one was an infant three months old. Since January 1925 we have had sixty-four patients who came to our clinics in the Peking Union Medical College Hospital for treatment. Only those cases which were admitted into hospital and carefully investigated are reported below. If one were to make a careful study of the blindness and leukoma dating from infancy, one might find much of it traceable to keratomalacia.

Keratomalacia has been observed by various workers as a deficiency disease due to a lack of a particular element in the food, namely, the fat-soluble vitamin A. This view has been confirmed by the animal experiments of Osborne and Mendel and also by McCollum and his co-workers. Recently McCollum (1) showed by animal experiments that dietary defects other than vitamin A deficiency may produce the same condition. A thorough review of the literature on this subject was undertaken by Block (2) in 1921 and again by Ross (3) in the same year.

Keratomalacia occurs most frequently in infants and young children who are suffering from severe malnutrition with diminished resistance and vitality. In them the disease is usually severe and runs

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†Personal communication.

a rapid course. If it is not recognized early, the patient usually dies of local secondary infections or of bronchopneumonia. Even in those whose lives are saved, much hazy and opaque scarring of the cornea usually results and the vision becomes impaired. In older patients such as we sometimes have among the young factory workers and poor school students between the ages of fifteen and twenty-five years, the disease is milder and runs a slowly progressive course. Such patients usually recover easily on proper dietetic treatment.

Aside from the well-established fact that the disease is due to faulty nutrition, keratomalacia has been seen occasionally accompanying meningitis, measles, variola and in children with debilitating diseases like diarrhea, tuberculosis and syphilis. In the Peking Union Medical College Hospital we have had five cases occurring in patients with tuberculosis and two cases in patients with kala-azar, one of the debilitating diseases in North China.

REPORT OF CASES

CASE 1. L. S. M. Hospital No. 1915. Chinese male, age 6 months, admitted to the eye service March 20, 1922, because of redness of both eyes. Breast-fed by mother for the first two months. Weaned because of poor health of mother to some milk food and rice powder. No statement in the history as to his health growth and nutrition during period of artificial feeding. Two weeks before admission moderate redness of both eyes, with slight swelling of lids, "white spots" on both corneae noticed at same time; these spread very rapidly, photophobia and profuse discharge from both eyes. All symptoms much aggravated the week before admission.

Physical examination: Very poorly nourished, pale. Weight 5.2 kg. Temperature 38.5° C., R.B.C. 2,540,000; Hgb. 52%; W.B.C. 35,400; Poly. 54%; Lym. 41%; L.M. 2%; Baso. 2%. Dryness and leathery appearance of conjunctiva bulbi on both sides of cornea, haziness of cornea of both eyes and large ulceration of cornea of right eye. The spleen was much enlarged. Lungs, heart, urine, stool and Wassermann normal.

Treatment: Local: hot fomentations, dionin and atropin instillations.

General: At first fresh cow's milk mixture, later, butter-flour mixture of Czermly and Kleinschmidt. He stayed in hospital for one week, during which time he made a gain in weight of 200 gms. although he had irregular fever. He was discharged at the request of his parents. He was seen again in O. P. D. one week after discharge. At that time the cornea of the right eye was becoming clearer and that of the left eye was about the same as before. He has not returned since then.

CASE 2. C. S. F. Hospital No. 5318. Chinese female, age 3 years. Badly cared for and improperly fed since mother's death two years previously. First seen in O.P.D., on March 14, 1923, because of redness of both eyes of about three months' duration. A diagnosis of corneal maculae of both eyes was made and local treatment prescribed. Not seen again until June 19, three months later, when the eye symptoms were much aggravated. Admitted into ward on same day.



Fig. 1. Photograph of Case 2 showing general condition of the patient.



Fig. 2. Photograph of Case 8, taken on admission; shows the general condition of the patient.



Fig. 3. Case 8, taken on admission, shows the eye condition and the enlargement of the cervical lymph-glands.



Fig. 4. Case 8, taken 8 months after the first photograph.



Fig. 5. Case 8, taken 8 months after the first photograph; shows a large adherent leukoma of right eye.



Fig. 6. Photograph of Case 9, showing the opacity of the cornea of the right eye.

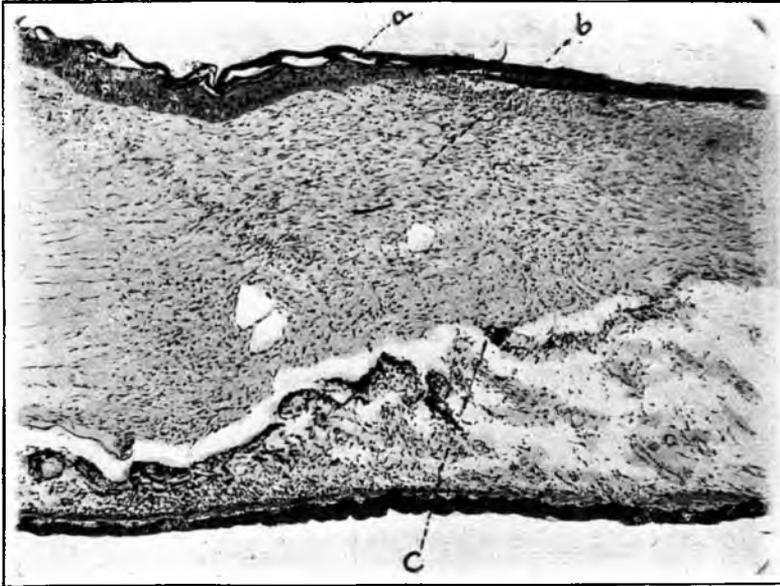


Fig. 7. Case 9. Histological section of right eye. Showing beginning keratinization of the superficial epithelial cells of the cornea with formation of bullae and complete destruction of Bowman's membrane (a). The central portion of the cornea is destroyed and replaced by vasculofibrous connective tissue (b). There is cellular infiltration of the superficial lamellae on either side of the cornea. There is also a moderate adhesion of the anterior boundary layer of the iris to the posterior surface of the corneal scar (c). Magnification $\times 65$.

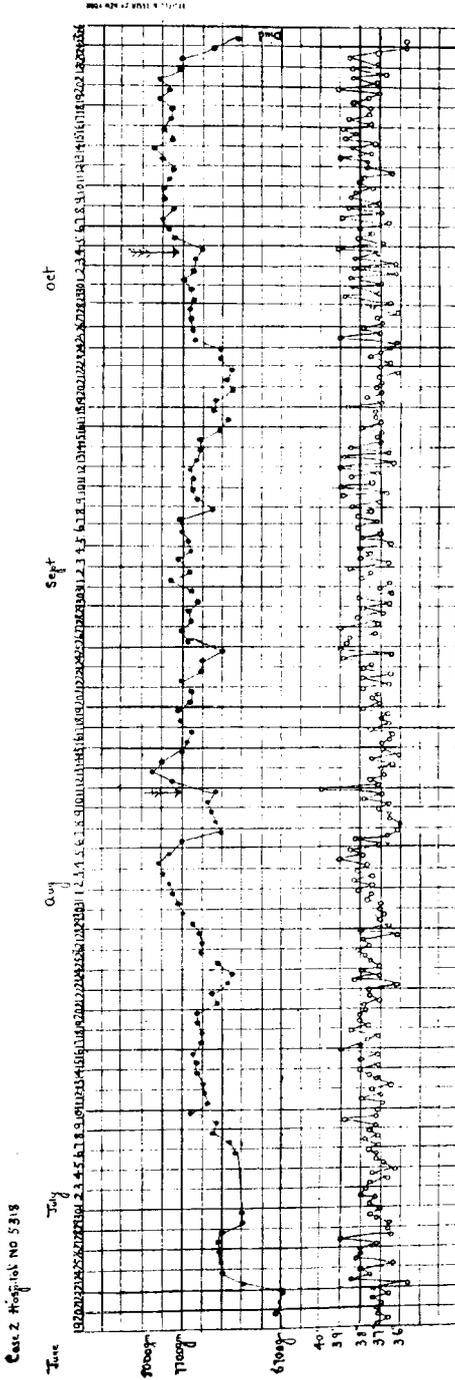


Chart 1. Temperature and weight curve of Case 2.

- represents weight
- represents temperature
- ▲—▲ represents blood transfusion.

Physical examination: Emaciated and irritable. Weight 6.7 kg. Temperature normal. R. B. C. 3,700,000; Hgb. 65%; W. B. C. 24,200; Poly. 72%; Lymph. 24%; L. M. 3%; Eosin. 1%. Slight swelling of lower limbs. Pustular lesions all over body. Right eye-lids swollen, cornea macerated. Leathery appearance of conjunctiva bulbi with opacity of cornea of left eye. Heart, lungs, urine, stool and Wassermann normal.

Course and Treatment. The management of this patient was exceedingly difficult. Cod liver oil and orange juice were given in as large doses as possible. Attempts at adequate feedings repeatedly failed. Several times when the gain in weight was becoming satisfactory distension and diarrhea, with or without elevation of temperature, intervened. Withdrawal of food and giving fluid were the only remedies. Blood transfusion was given twice with the idea of improving the general condition and thus improving absorption and alimentation. This treatment improved her condition considerably but only temporarily. Vision of the left eye was partially saved. The right eye was destroyed. The temperature curve as shown in the accompanying chart (Chart 1) indicates the severity of the disease. Neither the infection of the skin nor of the respiratory tract nor the upset of the gastrointestinal system was responsible for its rise or fall. In spite of all the efforts to rebuild her general condition and in spite of the apparent improvement and a gain in weight (1.2 kg. in 4 months), the child died after staying 18 weeks in the hospital.

CASE 3. T. H. H. Hospital No. 5822, Chinese female, 7 months. The complaints were "losing weight" and "redness and discharge from both eyes." Breast-fed by mother for one week; weaned to rice water only; became emaciated. Admitted to ward for feeding regulation at forty days; stayed five weeks and gained 450 gms. On discharge, weight 3250 gms. During the first three months after discharge, weight 3.9 kg. Mother refused readmission to ward and continued to feed her with small amounts of cow's milk but chiefly with oatmeal. Two months later, at seven months of age, weight 3.5 kg. Restlessness and loss of appetite. Instead of being fed properly, she was given some native medicine day after day. One week before the second admission redness of both eyes developed and "white spots" on the cornea were noticed almost at the same time.

Physical Examination: Emaciated and very small. Weight 3.5 kg., Height 61 cm., middle body 4 cm. above umbilicus indicating poor physical development (4). Temperature, 38°C. Keratomalacia with perforation of the cornea and prolapse of the iris on both sides. Lungs, heart and abdomen, normal, Hgb, 65%; R. B. C. 3,760,000; W. B. C. 20,500; Poly. 65%; Lymph. 28%; L.M. 7%. Wassermann, negative. Urine and stool, negative.

Course and Treatment: Cow's milk (Klim) and cod liver oil for the first five weeks. After the sixth week, breast milk added to usual feedings. Improvement rapid, gain in weight steady. In hospital nine weeks. On discharge, weight 4.7 kg. Acute eye symptoms subsided. Seen in O. P. D. one year later, March 11, 1925; moderately nourished, weight 7.3 kg. Large adherent leucomata of both eyes.

CASE 4. Hospital No. 8415. C. H. K. Chinese male, age 6 months, admitted, July 11, 1924, because of severe diarrhea and vomiting of two weeks duration. Breast-fed by mother for one month, then powdered rice (Kao kan) and condensed milk, without any definite proportion or time of feeding. No gain in weight, rickets. For almost four weeks before admission, trouble with both eyes.

Physical Examination: Keratomalacia and ulceration of the cornea and prolapse of iris, bilateral. Weight, 3.7 kg. part of weight loss probably due to dehydration from diarrhea. Poorly developed and poorly nourished; marked dehydration; head, square; fontanelle, large and sunken; costo-chondral junctions enlarged; lower ribs flaring. Rigidity of neck, no Kernig sign and no ankle clonus. Temperature, 37.5° to 38°C. Stools frequent and watery without blood, mucus or pathological organisms.

Treatment: Protein milk; fluid forced both orally and subcutaneously. Hot compresses constantly on both eyes, dionine and atropin instilled. General and local conditions did not improve and diarrhea could not be checked. Failed slowly, went into collapse and died one week after admission.

CASE 5. Hospital No. 10628, C. T. S. Chinese male, 14 months, admitted April 22, 1925, with a complaint of swelling of both eyes of five days duration. He had never had any human milk. At birth he was fed Lactogen, which gave him diarrhea and distention. Later he was fed with condensed milk and the diarrhea stopped. At the time of admission he was still getting condensed milk and rice occasionally. The swelling and discharge of both eyes started rather suddenly five days before admission and rapidly got worse.

Physical Examination: Poorly developed and poorly nourished. Weight, 4.5 kg. Circumference of head (41 cm.) greater than circumference of chest (37.5 cm.). Height 64 cm. The middle of his body was 3 cm. above the umbilicus (4). Rickets, fretful. Temperature 37.1° to 38.1°C. Eyelids puffy, much

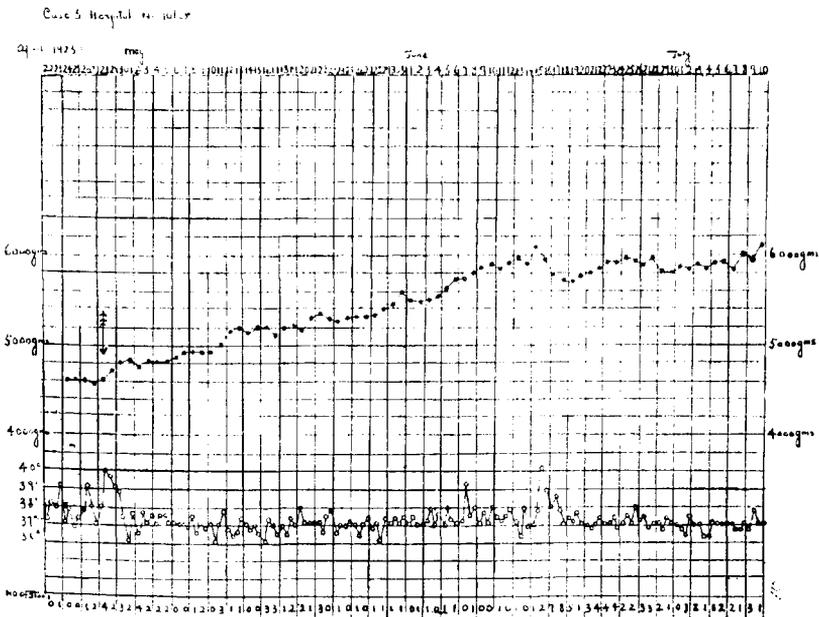


Chart II. Temperature and weight curve of Case 5.
 ●—● represents weight,
 ○—○ represents temperature,
 —▶ represents blood transfusion.

mucoid discharge; conjunctiva bulbi injected, dry and greasy; cornea of right eye hazy and ulcerated; cornea of left eye ulcerated and perforated with prolapse of iris. Lungs, heart and abdomen normal. Hgb. 48%; R. B. C. 3,930,000; W. B. C. 12,000; Poly. 30%; Lymph. 60%; L.M. 10%. Urine and stool normal.

Course and Treatment. The same general treatment of proper feeding and of vitamin administration, and the usual local treatments, were carried out immediately as in the previous cases. During the first week there was a persistent elevation of the temperature and a failure to improve in general and to gain in weight. A blood transfusion was then given. The response was striking, as is shown in the accompanying chart (Chart II). He made steady improvement in his general condition and gained rapidly in weight. The eye condition, however, was very resistant to treatment. It took a little over one month for the acute symptoms to subside. There remained perforation of the cornea of the left eye and scarring of the cornea of the right eye at the time of discharge from hospital. He stayed for fifteen weeks, during which period he developed an acute attack of bacillary dysentery (Flexner), which lasted two weeks. He kept on gaining in weight (though not as rapidly) in spite of the dysentery, and made a total gain of 2.2 kg. during his stay in hospital. He was seen again in O. P. D. October 1, 1926, one year after discharge. He was then in good general condition and was well nourished. He was able to see with the right eye, on the cornea of which there was a large opacity over the lower median quadrant. The left eye was atrophic. There was a large adherent leukoma. Its vision was probably gone.

CASE 6. C. H. E. Hospital No. 10009. Chinese male, 7 years, admitted February 2, 1925, with a complaint of redness and pain of both eyes. The disease had started in the left eye twenty days previously. The right eye had become involved a little later.

Physical Examination. Poorly developed and poorly nourished. Weight 13 kg. Temperature 37° and 38° C. Lungs, heart and abdomen normal. Urine normal. Stool contained the ova of ascaris. Wassermann test negative. The conjunctivae bulbi injected, dry and greasy; cornea of right eye hazy; cornea of left eye ulcerated and perforated.

The same treatment of careful feeding and of increased vitamin intake, as well as the usual local treatment, was carried out in the hospital. The eye condition improved after three weeks in hospital. The ulceration of the cornea healed. There was still some injection of the conjunctiva on discharge. The patient was not seen again after discharge.

CASE 7. C. C. Hospital No. 9907. Chinese male, 10 years, a native of Shantung Province, had been brought to the School for Poor Children, Tzu Yu Yuan, in the Western Hills, Peking, three years before. The daily food intake of the children in that school was rather low in caloric value and consisted mainly of cereal and vegetables, yet it was considered adequate for the maintenance and growth of these children as was shown in the analysis by Hammond and Hsia (5). About three weeks before admission a small wooden splinter stuck in the patient's throat, which became inflamed and swollen. As a result swallowing became difficult. The splinter was later removed and the swelling in the throat subsided. Eye symptoms, however, started (the exact date of onset was not obtained) and were resistant to local treatment. He was admitted to the P.U.M.C. Hospital for treatment on June 20, 1925. In addition to the eye symptoms, he had a brassy cough.

Physical Examination: Fairly well developed but poorly nourished. Unintelligent, some impairment of hearing. Weight 20.5 kg. Slight inflammation of throat, larynx normal. Gingivitis. Lungs, heart and abdomen normal. The conjunctivae bulbi of both eyes injected and dry; cornea of left eye hazy; cornea of right eye clear; marked photophobia and mucopurulent discharge. Temperature 36° to 39.5° C. during first two weeks in hospital. Hgb. 79%; R. B. C. 4,864,000; W.B.C. 15,000; Poly. 85%; Lymph. 15%. Wassermann test, negative. Urine and stool normal.

The usual nutritional treatment with an increase of vitamin intake and proper care of the eye condition was instituted. The patient improved rapidly and recovered entirely in three weeks without impairment of vision or scarring of the cornea.

The temperature chart (Chart III) of this case is reproduced here, with those of Cases 2 and 5, to show the elevation of the temperature which frequently accompanies this disease.

CASE 8. C. A. T. Hospital No. 7296. Chinese male, 4½ years, of a poor family of six children, of whom four were living, the patient being the youngest. Both parents had to work hard in order to make a bare living. Because of lack of care, nourishment and proper housing and hygienic conditions in the family, the boy succumbed to a chronic illness described as follows: weakness, loss of weight and loss of interest in surroundings for two years; redness of right eye for over one year; redness of left eye for a few days; loose stools for half a year; cough and swelling of feet for two months and swelling of the sides of the neck for about one year. He was brought to the eye clinic for treatment on February 27, 1924, when he was admitted into the hospital.

Physical Examination. Emaciated. Weight 8.4 kg. Massively large bilateral cervical lymph nodes; histologically tuberculosis. Small superficial ulcers (impetigo) on buttock and ankles. Moist coarse rales scattered throughout lungs and an increased shadow at the hilum. Conjunctivae bulbi dry and leathery; opacities of both cornea, with a large perforation of right cornea.

Under proper care and feeding and with administration of cod liver oil, the boy's general and local condition gradually improved. He stayed in the ward for four months and made a gain of 3.6 kg. in weight. He has been seen

Case 7 Hospital No 9907

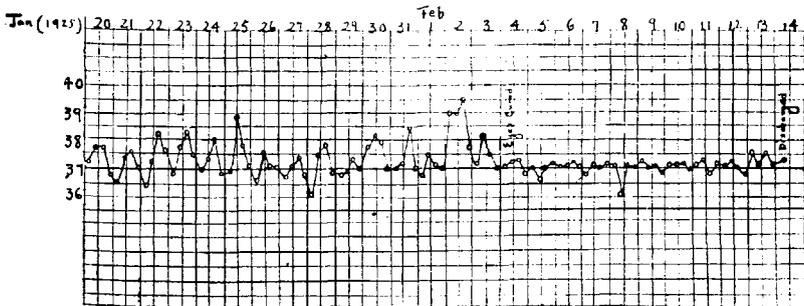


Chart III. Temperature curve of case 7 showing the elevation of the temperature only during the course of the illness and not thereafter.

in O. P. D. several times since discharge. The last visit was on March 23, 1926, twenty-one months after discharge. He was in fairly good general condition and was well nourished. The lymph glands diminished much in size and the tuberculous lesions were considered arrested. The left eye was almost restored to normal except for some superficial opacity of the cornea. There was a large adherent leukoma of the cornea of the right eye. The photographs showing the general and local conditions on admission and eight months later present striking comparisons (Figs. 2,3,4, and 5.).

CASE 9. T.C.E. Hospital No. 14062, Chinese female, 5 months, admitted June 10, 1926, because of "trouble in the eyes." Maternal milk for one month, said to be insufficient. When one month old she was given away because of poverty. At that time the child was very small and very poorly nourished. After adoption she was given skimmed condensed milk diluted with about twenty parts of water, three ounces every three hours. Kao-kan was sometimes used as a substitute. The baby seemed to have gained in weight on the artificial feeding. About two weeks before admission she had increased lachrymation and slight photophobia. One week later there was swelling of the eyelids. Five days before admission a "white spot" was noticed on the cornea of the right eye, which rapidly spread over the whole cornea. In the meantime lachrymation and swelling had subsided. The left eye became affected in the same manner, although to a lesser extent. The baby had lost in weight since the eye symptoms appeared.

Physical Examination: Small and moderately nourished as shown in the photograph (Fig. 6). Weight 2.8 kg. Rickets. Temperature 38.4° C. Bulbar conjunctiva of the right eye, dry and leathery; cornea very dry and uniformly opaque, entirely obscuring the pupil (Fig. 6). A similar condition, though less severe, in the left eye. No photophobia and no sign of marked inflammation in either eye. Lungs, heart and abdomen normal. R.B.C. 2,900,000; Hgb. 75%. W.B.C. 21,500; Poly. 59%; Lymph. 41%. Urine and stool normal.

Course and Treatment. The baby was given lactic acid milk and cod liver oil. She took them fairly well at first. There was a gradual elevation of the temperature during the first week. Signs of bronchopneumonia began to develop on the fourth day after admission. On both general and local treatment the opacity of the cornea of the left eye cleared up entirely, leaving a small macula. The right eye did not improve. After two weeks in hospital her general condition became worse. She developed pyelitis, with a positive urine culture of *B. dysenteriae* and *Staphylococcus albus*. She refused her feedings and finally died with hyperpyrexia and convulsions, after staying twenty-four days in hospital. At autopsy, besides rickets, subacute pyelitis, small abscesses in the kidney and bronchopneumonia, characteristic changes in the cornea of the right eye were found, namely, beginning keratinization of the superficial layer of the epithelium with cellular infiltration of its stroma and destruction of its central portion, which was replaced by vasculofibrous connective tissue as shown in the micro-photograph.

CASE 10. T.T.S. Hospital No. 14609, Chinese male, 2½ years, admitted Aug. 23, 1926, because of diarrhea and impairment of vision. Maternal milk during the first year of life. Weaned to rice gruel, bread and occasionally some green vegetable. The present illness had an abrupt onset two months before admission with a mild fever and frequent watery stools which contained mucus and blood. Two weeks before admission the condition became worse and photophobia, dry-

ness of the eyes and gradual clouding of the cornea with impairment of vision developed. The diet during the period of illness consisted of rice gruel, salted bean curds and a little Chinese noodle.

Physical Examination: Well developed, poorly nourished, recent loss of water and weight. Temperature 38.6° C. Pulse rapid. Lungs, heart and abdomen normal. Conjunctiva bulbi dry and greasy; corneae of both eyes dry and hazy. R.B.C. 4,112,000; Hgb. 65%; W.B.C. 29,680; Poly. 71%; Lymph. 25% L.M. 4%. Stool semi-fluid, containing pus cells but no blood and no pathological organisms. Urine normal save for a trace of albumin.

Course: The day after admission the child became worse and appeared very toxic. The temperature was elevated to 40.2° C. The respiration rate was increased. Rales in the lungs were detected. The abdomen was distended. The urine contained a large amount of albumin, acetone, pus cells and granular casts. He died the same day.

COMMENT

According to the descriptions of previous writers, one of the characteristic symptoms of keratomalacia is the lack of any marked local reaction in spite of the far-reaching changes in the eyes; lachrymation, photophobia and blepharospasm are slight or absent (2), (6). On the contrary, in this series symptoms of irritation were present in almost every case except Case 9 in which, although there was a history of lachrymation and photophobia at the onset, there was no sign of local irritation after admission.

A low fever was of common occurrence. The three accompanying charts illustrate this point. In case 2 the elevation of temperature was certainly unrelated to any secondary infection of the respiratory tract or to the infection of the skin. Case 7 had an irregular fever without any satisfactory explanation, aside from the eye condition, for the first two weeks in hospital but the temperature fell and remained normal as soon as the eye symptoms were gone. It is probable, from the work of Stephenson and Clark (7), Wasson (8), and Mori (9) that vitamin A deficiency leads to a selectively localized, lessened resistance to infection, for in the rat deprived of Vitamin A lesions are found most frequently in the conjunctiva and cornea and are almost always secondarily invaded by bacteria.

Cases 7 and 9 illustrate roughly the time of onset of the disease. The former child was deprived of his food through difficulty in swallowing, roughly between two or three weeks prior to the development of the eye symptoms. The latter was fed four months before his illness with condensed skimmed milk and kao-kau both of which were entirely free from vitamin A. Schwartz (10) reported a case in an infant ten months old who developed the disease three weeks after the apparent deprivation of vitamin A. While this period of three weeks appears to be rather short, yet it is interesting to note how closely it

corresponds to the time of onset in Case 7. This patient always had a minimal amount of vitamin A in his diet at the School for Poor Children. There is evidence in rat experiments that vitamin A, if given in excess of the minimal need, can be stored. Probably this was not possible on his low intake.

That there were four fatal cases among the ten proves the severity of the disease in infants and young children. Cases 6 and 7, on the other hand, represent the milder type of the disease which usually occurs in older children and young adults who live on a poorly balanced diet with inadequate supply of fat soluble vitamin A. These two cases were both over five years old. Their lesions were less severe and recovery was more nearly complete.

In China, owing to the prevalence of breast feeding, little attention has been paid to the diseases of dietary faults or to vitamin deficiency in infancy and childhood. Until recently rickets was considered to be a rare disease (11). In presenting the above cases it is the purpose of the author to call the attention of physicians in China to the significance of vitamin deficiency in the Chinese diet especially for infants and young children who are in the period of rapid growth and activity and for lactating women who are nursing their infants. With the exception of Case 6, in which no history of the nature of the diet prior to the diseases was obtained, all of these patients gave a definite history of faulty feeding or starvation and were mostly emaciated. Case 9 was moderately well nourished as is shown in the photograph (Fig. 6) but she was fed with skimmed milk exclusively. Hence she represents the typical case of Vitamin A deficiency. Cases 1, 5 and 9 had been fed with condensed whole milk, but the amount used was undoubtedly small. Fresh cow's milk was used in Case 3 but only as a supplemental feeding to the main cereal diet when the child was but six months old. It is a popular opinion in Peking that weak and delicate infants cannot take such "strong" food as cow's milk, so they are given rice powder in the form of Kao-Kan (糕乾), which can be obtained easily in the market. This is a dry cake made of finely ground rice powder, sugar and a small amount of Fuhling (茯苓) (*Pachymacocos*) (12). It is dissolved in water to make a moderately thick solution before it is fed to the child. Cases 1, 4 and 9 had been given this food. In Case 4 one may question whether the disease was due to the debilitated condition following diarrhea or to dietary faults. But if one looks into the history carefully it will be seen that faulty feeding, malnutrition and even the eye symptoms started before the onset of the diarrhea, and that the real cause of the diarrhea was malnutrition rather than an enteric infection. Case 8 was a very poorly nourished child with tuberculosis.

Perhaps it may be well to emphasize here that local treatment of the eyes is of little use without first attending to the general supportive measures and vitamin administration. Most of these children were suffering from severe malnutrition with diminished resistance and vitality. The general impairment of function in such children probably involves digestion to such an extent that treatment with proper food or vitamins by mouth is ineffectual. It is in such cases that blood transfusion is of real value. It was used in Cases 2 and 5. In the latter case the response was marked and rapid (see Chart II). In the former, in spite of apparent improvement at first (see Chart I), death finally occurred. Although one may question its value in this case, the patient probably would not have lived so long had it not been given.

In this connection it is interesting to note that Block (13) recently treated two cases with direct exposure to carbon arc light and to natural sunlight without any effect and Powers, Park and Simmonds (14) have shown that neither sunlight, ultra violet light or the anti-rachitic factor in cod liver oil can cure or prevent keratomalacia in rats deprived of vitamin A.

In estimating the etiology and in directing the treatment of these cases one may consider that the vitamin A deficiency is the probable cause of the ocular lesions, for these are quite like those produced in rats by vitamin A deficiency alone and cured by its administration. However, it should not be forgotten that keratomalacia can be produced in rats by dietary faults other than vitamin A deficiency (1). It may also be possible in the case of man. In most of these cases there were other gross deficiencies of diet, of calories, of protein, of salts, and of other vitamins. These defects were necessarily corrected during treatment. Hence it is impossible to evaluate the role played by the vitamin A deficiency in the whole clinical syndrome.

SUMMARY

1. Keratomalacia due to faulty diets is not a rare disease in Peking.
2. Ten cases are reported.
3. Vitamin deficiency in the Chinese diet is of great significance especially for children who are in the period of rapid growth and activity.
4. The value of blood transfusion in the treatment of some of the severe cases is discussed.

NOTE. The writer wishes to acknowledge his thanks to Dr. J. W. Hammond for permission to publish eight of the above cases, which were under his care, and also to Dr. H. J. Howard, Professor of Ophthalmology, for permission to publish the other two cases which were under his care.

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 THE THERAPEUTIC USE OF SODIUM THIOSULPHATE

A REVIEW

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The number of clinical studies recently made of the use of "Hypo" in the treatment of metallic poisoning calls for a review of the properties and known facts concerning this drug. Its extensive use in photography and for gas masks has over-shadowed its therapeutic uses.

Sodium thiosulphate $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$, is official in the U.S.P. X in the form of colorless, odorless, transparent crystals, having a cooling and afterwards bitter, slightly alkaline and sulphurous taste. The crystals are slightly deliquescent in moist air and efflorescent in dry air above 33°C . The cold aqueous solution, neutral or faintly alkaline to litmus, is very gradually decomposed in the cold into sulphur and sodium sulphite. *On boiling the aqueous solution it is rapidly decomposed.* On acidifying the aqueous solution it is decomposed, with the production of sulphurous acid and sulphur, the latter precipitating out. It should be bought fresh in well closed containers, and stored with equal care.

It is very soluble in water, 2 grams in 1 cc at 25°C .

Dosage. U.S. average dose 1 gram; by mouth or intravenously; 5% in normal saline solution.

Action. Although sodium thiosulphate is such a well known drug there is a great dearth of detailed knowledge concerning its action. In therapeutic dosage it is rapidly oxidized to sulphate. Large doses orally may produce local gastric irritation due to the liberation of sulphurous acid. 4 to 6 grams have produced violent colic and diarrhoea. Very large toxic doses which far exceed the body's capacity for oxidation show a lowering of the blood pressure associated with marked depression of the central nervous system especially the medulla. The cardiac and arterial muscle is depressed, though death occurs by paralysis of the respiration.

Holbil recently made a study of the excretion of "thio" by five patients. Doses of half to four grams showed the optimum excretion in twenty minutes, and he concluded that a large amount is destroyed in the organism. The excretion was checked with phenolsulphon-phthalein.

Uses. There is not sufficient critical data to satisfactorily set forth the claims recently made regarding the value of sodium thiosulphate as an antidote to all metallic poisonings, but there is an abundance of indisputable evidence for its use in the treatment of arsphenamine and arsenical dermatitis. Ravaut in 1920 first showed the beneficial effects of its use for the unfavorable sequelae of neoarsphenamine administration. Later Dennie and McBride successfully treated twenty five cases of arsphenamine dermatitis and ten cases of arsenic jaundice. Further evidence was given by Kuhn and Reese. They first employed the same dosage as Dennie and McBride, giving 0.3 gm the first day, 0.45 the second day, 0.6 the third day, 0.9 the fourth day, 1.2 the sixth day and 1.8 the eighth day. They observed no ill effects from daily injections of 1 gram over a period of twelve days. It was given in 5 per cent solution in saline intravenously.

Estimations of the arsenic excreted by the urine, feces and epidermal scales show that there is a decided increase in the output of arsenic as the direct result of thiosulphate medication. Kahn and Loevenhart found that this reduces the therapeutic efficiency of arsenicals in the treatment of experimental trypanosomiasis. Their other findings do not exactly concur with the work of Haag and Bond who found that sodium thiosulphate was unable to save cases given fatal doses of potassium arsenite.

Myer represents another group of workers who consider that the action of sodium thiosulphate is least marked in cases of inorganic arsenic poisoning, it is more effective after pentavalent organic preparations and most efficient with the trivalent organic arsenic group represented by the arsphenamines. After the latter, thiosulphate hastens the excretion of arsenic and clears up untoward symptoms, and it was not found to disturb the therapeutic action of the arsphenamine compound on Trypanosomes *in vivo*.

Kahn and Loevenhart concluded from their work that sodium thiosulphate "does not mobilize arsenic in the body but seems to cause its transformation into a less toxic, less therapeutically efficient and less easily excretable product."

Further observations of McBride are reported concerning the successful treatment of arsphenamine encephalitis with sodium thiosulphate. It suggests the trial of this drug for all post-arsphenamine reactions, especially the nitritoid crises.

The rôle of sulphur as a detoxifying agent is best understood by consulting the work of Voegtlin, who states that the evidence clearly shows that there is a kernel of truth in Ehrlich's theory the SH group as the arsenic receptor. It has been shown *in vitro* that the addition of minimal amounts of various organic sulphydril compounds to a suspension of trypanosomes prevents the action of arsenoxide as indicated by the persistence of the normal motility of the surviving parasites.

The report of F. K. Chen strongly supports the now widely accepted fact that this drug is *good for arsenical dermatitis*. Chen emphasized the need for using solutions prepared from sterile water distilled on the day when used for intravenous injection to avoid severe reactions. Kuhn in giving the drug by mouth uses saline instead of distilled water because it decreases the vomiting which occurs after large doses of sodium thiosulphate, and it decreases the rate of decomposition of the drug in the stomach.

Thorne, Van Eyck and Myers have made an extensive study of the use of this in the treatment of *eczema*. In 104 cases treated with 0.5 gm intravenously three times a week, eighty percent showed a prompt response.

There has been a considerable difference of opinion as to the exact value of sodium thiosulphate as an antidote to general metallic poisoning. The evidence seems quite clear that it is useless for treatment of fatal doses of mercury poisons. Haskell *et al* state that the course of poisoning seemed entirely unaffected. There are too few observations upon its use and worth in treating the toxic effects of non fatal doses of metallic poisons. Kuhn found that it hastened the restoration of the kidneys to normal, and he suggests that it may have significant effect on general intracellular oxidation playing a similar rôle to that of the R-SH group.

Further uses for this drug are in the treatment of *cyanide poisoning* and *coal gas poisoning*. Martinez found in one case of cyanide poisoning that two injections of 10 ccs thiosulphate solution 30% gave immediate relief. The well established fact that the sulphocyanides (thiocyanides) are relatively non-toxic would account for this pleasing result.

It is of particular interest in North China to read of the successful experiments of Zeigler in preventing the sequelae of illuminating gas poisoning by treatment with sodium thiosulphate and calcium salts. Dogs given a fatal dose of gas showed a more rapid return to consciousness, only one of 14 animals died and only one showed mental symptoms. From his experiments he suggests the following treatment for human subjects:—

Remove patient to a proper atmosphere, administer artificial respiration and inject intravenously 2% solution of sodium thiosulphate, 5 ccs for every 25 lbs of body weight. Then give subcutaneous injection of 4% solution of calcium lactate, 5 ccs for every 25 lbs of body weight.

LITERATURE UPON SODIUM THIOSULPHATE

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**A CRITICISM OF THE GENERAL TREATMENT OF CHOLERA
BY INTRAVENOUS HYPERTONIC SALINE INJECTIONS**

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The claim that intravenous saline injections in themselves constitute a self-sufficient treatment of cholera is wholly irrational, since such injections are logically indicated only where collapse has already set in, or is impending from excessive loss of fluid from the system.

Cholera is clinically divided into two well marked and distinct stages, the primary stage of evacuation and the secondary stage of collapse from loss of fluid. This being so the treatment of cholera naturally resolves itself into:—(1) the medical treatment of the stage of evacuation by intestinal astringents, with the object of arresting the diarrhoea and thus preventing the onset of collapse; and (2) the surgical treatment of collapse by intravenous saline injections in an effort to restore and maintain the circulation until the loss of fluid from the bowel spontaneously ceases.

As most cases of cholera, owing to the fulminating character of the disease, come under notice only when collapse has already set in or is impending, by which juncture the time for medical treatment is past, the great value of such treatment appears not to be adequately realised.

The teaching (Rogers 1921, p. 152) that in the stage of evacuation in cholera no medicinal measures should be instituted to check the diarrhoea, and that an expectant policy should be adopted until collapse manifests itself and saline injections become imperative is both mischievous and erroneous; experience in the Balkan War, the Great War, and elsewhere, having definitely proved that remedies such as kaolin, morphia, and the essential oils are all of the greatest value in the treatment of this stage of the disease (1).

From the returns of the Director of Public Health with the Government of India, it is seen that amongst 2,153 cases of cholera treated solely by intravenous hypertonic saline injections (Rogers) in the army and jails of India over the decade 1912-21 (2) 1,060 deaths occurred giving a mortality rate of 50 per cent. That the general treatment of cholera by intravenous hypertonic saline injections presents in practice no superiority over treatment of the disease by the common carminative "cholera mixture" containing chlorodyne or other preparation of opium is also proved by the results of treatment over many years by various methods of many hundreds of cases of cholera* in the coalfields of Bengal, the mortality rate being approximately 50 per cent in both cases.

*By the term "cholera" is here meant a disease characterised by the passage

Consideration of these facts has led the writer to enquire critically into the arguments advanced by Rogers in favour of the use of intravenous hypertonic saline injections as a general treatment for cholera (Rogers 1911, p. 155 et. seq. and Rogers 1921, p. 85 etc. etc.) (3) & (4). Having studied the arguments there put forward in support of the use of hypertonic salines, the writer is of the considered opinion that they are untenable and unsound.

The theory of the necessity for the use of hypertonic salines in collapse in cholera instead of physiological salines would appear to be based on two assumptions:—(1) that in cholera the serious symptoms are in part due to excessive loss of salt from the blood and tissues, and that this excessive loss requires to be made good to the system in the form of intravenous hypertonic saline injections; and (2) that by oversalting the blood by means of such injections the flux from the bowel will be arrested through osmotic attraction of fluid from the intestine into the circulation, and blood pressure thus more adequately maintained.

We shall now examine the grounds on which these assumptions are based so far as it is possible to follow Rogers' reasoning, which is often involved and obscure.

Rogers records that the average quantity of chlorides in cholera stools examined by himself was 0.53 per cent and that a still smaller amount was found by him in the watery evacuations from the stomach. (Rogers 1911, p. 155).

This he states "would mean a loss (from the blood and tissues) of half-an-ounce (i. e. 240 grains) of chlorides with every 100 ounces of stools". The loss of 240 gr. of chlorides would, however, be much more than replaced by the injection of 100 ozs. of isotonic saline solution which contain 400 gr. of chlorides. The loss of half-an-ounce of chlorides in every 100 ozs. of stools does not, therefore, in any way necessitate the use of hypertonic saline injections.

It is difficult to understand Rogers' reasoning in the statements (loc. cit. p. 156) that "in the most severe fatal cases of cholera in which on the average two-thirds of the fluid of the blood has been lost, the chlorides in the serum were slightly lower than normal (i. e. 0.79 as compared with a normal of 0.80) *instead of being three times as great as would have been the case if no salts had disappeared from the circulation*" and that "it is clear that in the most severe cases (of cholera) over

of profuse watery stools accompanied by copious vomiting of watery fluid, muscular cramps and suppression of urine. Cases of choleraic diarrhoea (vomiting and diarrhoea only) are not included.

two-thirds of the salts of the blood may have been lost from the circulation, and presumably almost as great a proportion from the whole system" since, so far as the writer is aware, it has never been asserted or assumed that "no salts" are lost from the circulation in cholera, but, to establish the physiological necessity for the use of hypertonic salines, it would be necessary to prove that the loss of salt from the system was proportionately greater than the loss of fluid, which, on Rogers' own showing, is not the case. Moreover, if by the expression "the fluid of the blood" Rogers here means the blood alone and not also the fluid of the tissues, then no salts whatever can have been lost from the tissues (Rogers' "whole system") but if, on the other hand, the fluid of the tissues is included in the expression, the loss of salt from the tissues as well as from the blood would still be much less proportionately than the loss of fluid, since the dejecta of cholera, whether derived from the blood or tissues, are strongly hypotonic.

Isotonic saline injections in such cases would not only equally well replace the fluid lost but would actually provide a considerable excess of salt, one-third of the original amount of salt according to Rogers' argument) being retained in the system.

Rogers states (loc. cit. p.156) that "in some of the worst cases the percentage of chlorides was actually below normal, as little as 0.6 per cent, having been met with, while the serum showed distinct haemolysis, which however, immediately disappeared on the chlorides being raised to a little over the normal point by a hypertonic injection". That such cases are much too rare and infrequent to justify the foundation on them of a universal treatment for cholera is clearly shown in Table X" (loc. cit. p. 148) where the average percentage of chlorides before injection "in seven fatal cases" was found to be 0.79 per cent, as compared with a normal of 0.80 per cent, the two percentages being identical within the limits of experimental error.

Table X*

	Normal.	Average of 12 fatal cases.	Average of 7 cases requiring transfusion.	Average of 5 cases not requiring transfusion.
Chlorides before injection.	0.80	0.79	0.90	0.92

The statement that "in the recovering cases, the percentage of chlorides was slightly above normal, although owing to the great loss

*Blood changes in Cholera with the effect of Hypertonic Saline Injections .

of fluid, the total amount of salts in the circulation must have been reduced" is scientifically meaningless.

These observations Rogers asserts "clearly indicate the necessity for replacing the salts as well as the lost fluid (in hypertonic form) and furnish a complete scientific basis for the use of hypertonic saline transfusions in cholera." The observations referred to undoubtedly would indicate the necessity for replacing both salts and fluid—but in physiological form—and furnish no argument for the use of hypertonic saline injections.

If we take the salt content of the blood as a guide to the salt content of the tissues, then from Table X (Rogers 1911, p.148) we find that not only is the percentage of salts in the blood not lowered in cholera but—as might be expected from the loss of so much hypotonic fluid—that it is considerably increased (0.90—0.92 per cent. as compared with a normal of 0.80 per cent). Rogers himself states (*loc. cit.* p.157) that "in all except the most severe cases of cholera, the percentage of chlorides in the blood is slightly *increased*"—the increase amounting, as we have seen above, to 15 per cent. He also states (*loc. cit.* 155)—"For rectal injections I use 90 grains of sodium chloride to the pint which makes a 0.95 per cent solution or *just above the amount I found in the blood in the milder cases of cholera*" [normal = 0.80 per cent]

It is clear, therefore, that the assumption that in cholera there is an excessive loss of salt from the blood and tissues which requires to be made good by intravenous hypertonic saline injections is erroneous.

In a paper published in 1893 on the effects of the injection of hypertonic salt solution into the jugular veins of dogs Gaertner and Beck (5) found that oversalting the blood leads to absorption of fluid into the circulation from the gut and serous cavities, with consequent increase in the watery part of the blood. They also expressed the opinion that if the collapse and other serious symptoms in cholera are due to loss of water from the blood, then injection into the veins of concentrated salt solutions might bring about resorption of fluid from the intestines into the blood vessels with consequent improvement in the condition. They also mention a personal communication from Dr. G. Topfer, who stated that in an epidemic of cholera he had found good results to follow this line of treatment.

Rogers (1911, p.181) states "on thinking over the possible causes of the generally admitted failure of isotonic* saline injections in cholera

*The context shows that the word "isotonic" is misleadingly used here for "normal" or "hypotonic", no "generally admitted failure" of isotonic saline injections being recorded.

it occurred to me that *if the salts of the blood become concentrated* as a result of the great loss of fluid, then the injection of the so-called normal saline would once more reduce the proportion of salts in the plasma, which in its turn might restart the outflow through the damaged intestinal mucous membrane; when it had been previously *checked by the concentration of the salts of the blood.*

If, as Rogers here states, the salts of the blood become concentrated in cholera as a result of the great loss of fluid from the system, all his previous arguments purporting to prove that the salts of the blood-serum are diminished in cholera must go by the board.

To those familiar with the use of intravenous hypertonic saline injections in cholera, it is a matter of common knowledge that the assumption put forward originally by Gaertner and Beck in 1893 and subsequently by Rogers, that by the use of such injections the flux from the bowel will be checked and blood pressure maintained is erroneous, experience in India over many years having proven that hypertonic salines possess no such specific action, and that repeated injections of these, as of isotonic salines, are necessary if blood pressure is to be adequately maintained.

That this is also Rogers' own experience is manifest, for under the caption of "Repetition of Intravenous Injections", he writes (Rogers, 1921, pp.176-7) "It is clear from the above analysis that the frequent repetition of (hypertonic) saline injections, whenever a fall in the blood-pressure indicates them, is not only perfectly safe, but is clearly of the greatest advantage to the patient, total quantities of over 20 pints in the course of several days having proved successful in saving very severe and prolonged cases, and even over 30 pints have been administered with recovery of the patient".

The statement is made by Rogers that "if blood pressure be fully restored (by hypertonic saline injections) rapid excretion of the toxins by the kidneys takes place" (Rogers, 1921, pp.93-4), but, we also read that "rectal injections every two hours of isotonic alkaline salines should be regularly continued after collapse has been overcome until such a time as two pints of urine are excreted in twenty-four hours" (loc. cit. p.197) which may not occur for an interval of two or three days (loc. cit. p.108), "the injections are then reduced from every two to every four hours and are omitted the day after. If in spite of these measures the urinary flow is scanty, slow intravenous injection of a pint of alkaline saline is indicated".

McLaughlin and Sellards investigated the comparative merits of hypertonic and isotonic intravenous saline injections in cholera and

found no difference between the two solutions in their effects either on the course of the diarrhoea, the maintenance of blood pressure or the secretion of urine (6).

On the other hand Ross (7) and others have found that in ileus and paralytic affections of the bowel the intravenous injection of strongly hypertonic saline solution constitutes the most effective known agent for producing copious watery evacuations from the bowel.

It is clear, therefore, that hypertonic saline injections possess no specific action in cholera, the role in cholera of intravenous saline injections in general being purely symptomatic and non-specific, viz. to replace, as frequently as may be necessary, the fluid lost from the circulation until the flux from the bowel naturally ceases, as many as 20 to 30 pints of saline in some instances having to be injected over a period of six to eight days before cessation of discharge from the bowel spontaneously occurs.

The "frequently recorded" instances of failure of treatment by "normal salines cited by Rogers (1911, pp. 158 and 181-2) will, on examination, be recognised to be instances of failure of treatment by hypotonic salines and not by physiological salines of which Rogers made no recorded trial.

From the statistics cited by Rogers (1921, Pp. 885 & 189) it is of interest to note that the recorded mortality from the treatment of 589 cases of cholera in villages by potassium permanganate pills alone was considerably lower (22.25 per cent) than that from treatment in hospital of 294 cases by hypertonic salines alone (32.6 per cent), and of 858 cases by hypertonic salines plus permanganates (25.9 per cent) and was practically as low as that of treatment of 1429 cases by hypertonic salines plus alkalies plus permanganates (20.80 per cent).

With regard to the use of potassium permanganate pills it would appear to be uncertain whether Rogers now attributes such action as he alleges they possess to the permanganate or to the kaolin which they contain. Referring to the successful use of kaolin in cholera by Stumpf and others Rogers writes "Bolus alba consists of kaolin powder which has always formed the basis of the author's ²permanganate of potash pills" (Rogers 1921, p. 189).

Reference to this original paper (8) shows that Benjamin Moore's speculations on the supposed specific action of hypertonic saline in the elimination by the bowel of the hypothetical toxins of cholera, which are cited by Rogers (Rogers 1921, p. 178) as supporting his theory, are based on the presumed validity of Rogers' arguments regarding the alleged excessive loss of salt from the blood in cholera which have

been shown above to be untenable. Moreover Rogers' avowed object in advocating hypertonic salines in cholera in preference to physiological salines was thereby to check the "elimination" by the bowel of fluid (as well as of toxins and their causative organisms). He writes "By the use of hypertonic salines the saline content of the blood is raised very considerably with the result that the osmotic currents tend to carry more fluid into the blood rather than allow it to escape from it and thus diarrhoea ("elimination") is *checked* instead of encouraged as by "normal" (hypotonic) salt solutions" (Rogers 1921, p. 93). Referring to the use of hypertonic salines of 150 grs. of salt to the pint of water Rogers also writes "these (by stronger osmotic attraction) may produce a more violent reaction possibly *due to increased absorption of toxins from the bowel*" (Rogers 1921, p. 168). Furthermore if the theory of the necessity of "elimination" of toxins by the bowel in cholera were correct then the "eliminative" treatment of cholera by purgatives would be the treatment of choice, whereas, as we know, it was so disastrous that it had to be abandoned (Rogers 1921, pp. 147-8). *Per contra* universal experience has proved that by checking the "elimination" not only of the alleged toxins, but also of the vibrios from which these toxins must originate, we cure the disease.

In his detailed account of "The Chemical Composition of the Blood in Asiatic Cholera" (9) H. Aron quotes the prior investigations of Schmidt with which his own are in accord. Both Schmidt and Aron found that the chlorides of the blood serum in cholera are constantly increased by 14 to 20 per cent and that the blood in cholera is never hypotonic.

Notwithstanding our criticisms of Rogers' reasoning and the unsoundness of the hypothesis on which his treatment of collapse in cholera by intravenous hypertonic saline injections indisputably is based, we desire to acknowledge the service which he has rendered by his demonstration—albeit under highly organised hospital conditions which can never be approached in private practice—of the great value of *repeated* intravenous saline injections in the treatment of collapse in cholera continued where necessary over many days, until such time as the loss of fluid from the bowel spontaneously ceases, and the circulation is once more satisfactorily established.

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INTESTINAL PARASITISM IN TSINAN*

AS OBSERVED IN 1273 ROUTINE FECES EXAMINATIONS
DURING A PERIOD OF 17 MONTHS

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The present paper constitutes an analysis of laboratory findings in feces examinations in Shantung Christian University Hospital for a period of seventeen months, from Mar. 1, 1925 to July 31, 1926. Only the examinations made in the staff laboratory are included. These comprise mainly the routine examinations of in-patients in the hospital, but also a number of examinations of patients, Chinese and foreign, seen on out-calls, who have had laboratory work sent in to the hospital. The examinations made in the dispensary laboratory and in special laboratories are not included. The examinations in the staff laboratory are made by (1) students of the fifth year class in medical school, (2) internes (3) a competent technician, (4) residents and foreign doctors. The majority of the examinations are made by the students and technician.

During the period mentioned a total of 1273 examinations were made, 297 of which were re-examinations, leaving a total number of 976 patients examined. Of these 614 patients or 62.9% were negative; 362 or 37.1% had positive findings. The percentage infestation by the various parasites is shown in the accompanying table (Table I). The 297 re-examinations gave 220 examinations with negative results.

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TABLE I

Findings	1925												1926												Total Examination	No. of individuals infested with each parasite (including analys. of multiple inf.)	% of individuals infested with each parasite
	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June	July										
Neg.	68	20	41	66	32	2	48	71	98	63	16	18	74	60	87	48	19	834	614	62.9							
Ascaris	30	21	28	11	11	7	14	32	28	18	5	3	28	13	35	17	13	369	295	30.2							
Ent. Aya.	2	1	2	4	5		3	6	8	3	1		1	2	13	4	7	55	69	7.1							
Band. coli	1			1			1				1		1		1	1		7	15	1.5							
Trichostrongylus	1						1	1										5	11	1.1							
Hook-worm	1				3		2	1	1	1			1		1			10	11	1.1							
Trichinosis	1														1			3	7	.7							
Tape-worm			1			1				2			1				1	6	6	.6							
Giardia			1									1						4	6	.6							
Iodamoeba butchlii					1													2	7	.7							
Ent. canna			1															1	2	.2							
Multiple infestation	3	1	2			1		1	4		1	4	1	1	3	2		37									
TOTAL	107	52	76	86	49	10	71	112	139	87	18	27	101	81	149	75	33	1273									

Total No. of persons examined
976

TABLE II

Parasites first found on re-examination. Figures refer to no. of individuals.

No. of examination on which first found	2nd	3rd	4th	5th	6th	Total
Ascaris	12	3	1		1	17
End. coli	1					1
End. dys.	7	5		1		13
Trichomonas	1	1				2
Hook-worm	1					1
Giardia	1	1	1			3
End. nana	1					1
Total no. of parasites not found on first exam.	24	10	2	1	1	38

TABLE III

Number of persons showing duplicate findings on re-examination among 57 persons examined twice or oftener.

	2×2	2×3	3×3	2×4	4×4	2×5	3×5	4×5	2×6
Ascaris	17	3	3	1		1	1	3	1
End. dys.	3	1			1	1			
Hook worm	1								
Giardia						1			
End. coli	1								
Trichiuris	1								

2×2 = " twice found in 2 examinations

2×5 = " " " " 5 " etc.

These are not referred to further in the present study. There were 77 positive findings. These 77 examinations were made on 57 individuals, of whom 38 persons had two examinations each, 11 persons 3 examinations each, 2 persons 4 examinations, 4 persons 5 examinations, and 2 persons 6 examinations. Of the 362 persons with positive findings in the stool, 36 required more than one examination to find the parasite. In one case of amoebiasis, the parasite was found first on the fifth examination; in one of ascaris, found first on the sixth examination. Table 2 shows the number of examinations required to get positive findings in the 36 persons (38 positive findings, including multiple infestations).

Among the 38 persons who had one re-examination, both examinations were positive for ascaris in 17 persons, for end. dys. in 3, for hookworm in 1, for end. coli in 1, for trichiuris in 1. Of the 11 persons examined 3 times, 3 were positive for ascaris on 2 examinations, and 3 on all 3 examinations; one person was positive for end. dys. in 2 out of the 3 examinations. Of the 2 persons examined 4 times, one was positive for ascaris twice, the other positive for end. dys. on all 4 examinations. Of the 7 persons examined 5 times, one showed ascaris twice, another end. dys. twice, a third giardia twice, and a fourth ascaris three times. Three showed ascaris on 4 out of 5 examinations. One person showed ascaris on two out of six examinations. See Table 3.

In 6 of the 57 re-examined patients with positive findings, additional or different parasites were found on one of the subsequent examinations. Of three patients with ascaris on the first examination, one showed end. dys. on the second; another end. dys. on the fifth; a third, giardia on the fourth examination. One patient with end. dys. on the third examination showed ascaris on the sixth; one with end. dys. on the first examination showed ascaris on the second. The sixth patient showed on first examination a triple infestation with trichiuris, end. coli, and iodamoeba butchlii, while a second examination showed trichiuris, end. coli and end. dys.

Among the total 362 persons with positive stool findings, multiple infestations were found in 36, and in one individual twice, making a total of 37 such findings. Of these, 32 showed double infestation, and 5 triple infestation. With two exceptions, all showed ascaris of end. dys. as one of the parasites, a fact not surprising when one considers the great preponderance in the incidence of these two parasites over all others. The combinations in which the parasites occurred are given below (Table 4).

SUMMARY

1. Analysis is made of 1273 feces examinations made during 17 months on 976 persons. 30% were found infested with ascaris, 7% with endamoeba dysenteriae, and in lower percentage endamoeba coli, trichomonas, hook-worm, trichiuris, tape-worm, giardia, iodamoeba butchlii, endolimax nana and oxyuris were found.

2. 36 patients required more than one examination to find the infesting parasite.

3. 40 patients showed the same findings once or oftener on re-examinations.

4. In 6 patients with positive findings additional parasites were found on subsequent examination.

5. Analysis is made of 37 multiple infestations as noted in 36 patients.

 THE THERAPEUTIC VALUE OF CARBON DIOXIDE*

By C. LANGTON HEWER, M.B., B.S. (Lond.)

There are few remedies which have sprung into greater prominence in a short time than carbon dioxide, and it was thought that a brief outline of its action and value in pathological conditions might be useful.

Carbon dioxide was first distinguished from air by Van Helmont in the seventeenth century. It is a colourless gas, with a rather pleasant pungent odour, and is one and a half times heavier than air. It does not support combustion or life. Carbon dioxide was first liquefied by Faraday, and is now stored in cylinders in the liquid state, a pressure of 52.1 atmospheres being necessary for liquefaction at + 15° C.

SOLID CARBON DIOXIDE

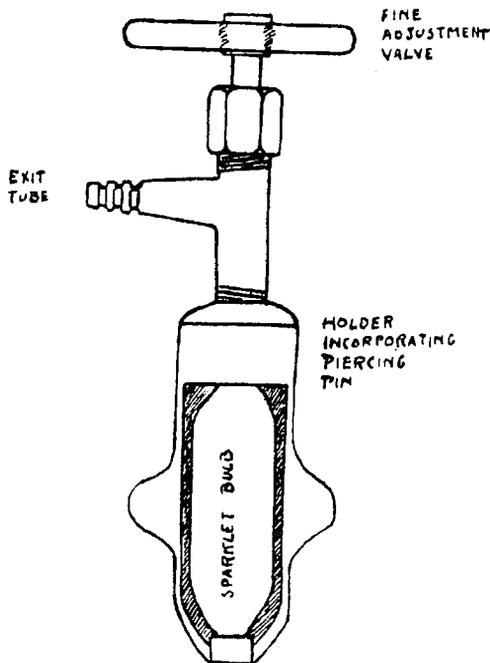
In the first place brief reference must be made to the action of solidified carbon dioxide or "carbonic acid snow." This is prepared in the form of "pencils," and is used in various skin diseases by a few seconds' firm application to the affected area. Refrigeration, followed by hyperæmia, occurs, and surprisingly little pain is caused.

*By kind permission of the Author we are permitted to reprint this article which appeared in the St. Bartholomew's Hospital Journal of April 1927.

References to complicated anesthetic apparatus not usually found in China are cut out, and a note from the Author in regard to the practical use of the simple apparatus described is inserted.

EFFECTS OF INHALATION OF CARBON DIOXIDE MIXTURES

Man normally breathes air which contains about 0.04% CO₂. An average adult at rest consumes about 7 litres of air per minute. Under inhalation anaesthesia the consumption is slightly greater, and under endo-tracheal anaesthesia is slightly less. If, however, 5% CO₂ is added to the inspired air, an immediate increase in the depth of respiration takes place, and in about 20 seconds the volume per minute of inspired air rises to about 30 litres. This increase will continue, within limits, for as long as the mixture is inspired unlike the transitory effects of other gaseous stimulants such as ammonia. We know of no other drug which even approaches this result either in speed or intensity, and this increase in respiratory depth is obtained without any marked increase in metabolism, such as obtains with lobeline, strychnine and other similar drugs. Furthermore, carbon dioxide has the supreme advantage that it is the normal stimulus of the respiratory centre. Occasionally one meets with patients who react in a different manner to 5% CO₂, in that the rate of respiration is greatly affected while the depth remains unaltered or even diminished. This reaction of rapid shallow breathing must be taken as a contra-indication to the



PORTABLE CARBON DIOXIDE APPARATUS (ABOUT HALF SIZE).

use of CO₂ and incidentally shows that the patient is in a very unstable respiratory condition, and that great care must be exercised during a general anaesthesia. An *overdose* of carbon dioxide is indicated by pallor, fibrillary twitching of the facial muscles and rapid or irregular breathing. An immediate reduction in the percentage of the gas must be made under these conditions. It is impossible in the scope of this paper to mention all the extremely complicated effects of CO₂ on human metabolism, but our attention must be mainly directed towards its principal action as a respiratory stimulant.

THE TECHNIQUE OF CARBON DIOXIDE ADMINISTRATION

It is rarely necessary to administer a mixture containing more than 10% CO₂, while 5 is usually sufficient. The balance may be composed of air, oxygen, or mixtures of nitrous oxide, ethylene or ether vapour with air or oxygen, according to circumstances.

For short inhalations a simple method is to use a "sparklet" bulb in a special holder with a fine adjustment valve. At least two patterns of this handy apparatus are manufactured, and owing to the fact that 10 grm. of liquid CO₂ provide about 4 litres of gas quite a large supply is available. The whole outfit, with several refills, only weighs a few ounces and can be carried in the pocket.*

If no apparatus of any kind is available, it should be remembered that CO₂ is present in expired air to the extent of 4.4%, so that simply blowing down a small tube into the pharynx may stimulate respiration. Naturally this is not an efficient method, if only for the fact that the oxygen content in expired air does not exceed 16%.

Whatever method is being used, the aim of the administrator should be to give the minimum amount of the gas which will yield the maximum respiratory effect. The addition of 2 litres per minute to the mixture which a patient is breathing generally fulfils this condition.

Let us now consider *the conditions in which carbon dioxide inhalation is beneficial.*

(1) *In the induction of anaesthesia.*—The value of CO₂ in the induction of anaesthesia has been recognized since the first closed inhaler was invented by Clover about the year 1876. The fact that "closed ether" produces surgical anaesthesia in a shorter time than

*In the absence of complicated apparatus for the administration of gaseous anaesthetics a "sparklet" holder connected to a soft rubber nasal catheter or to a metal tube in the mouth is quite satisfactory. If open ether has been given a rubber tube can be made to deliver the gas under the mask.

does "open ether" is largely due to the increased depth of respiration caused by the high CO₂ concentration in the rebreathed air. In most cases the patient's own breath supplies an adequate mixture, but sometimes—particularly in people whose larynxes are exceptionally sensitive to ether vapour—a small amount of added CO₂ conduces to a quicker and smoother induction, owing to the increased pulmonary ventilation allowing a smaller concentration of ether vapour to be employed. Carbon dioxide is also useful in inducing anaesthesia in highly nervous patients. These individuals almost invariably breathe deeply while they remain conscious, and thus deplete the CO₂ in their alveolar air and blood, so tending to pass into a condition of acapnia, with consequent shallow and irregular breathing. The addition of CO₂ rapidly restores deep, regular respiration. Again, if a closed inhaler is not available, the time of an open ether induction can be materially shortened by introducing CO₂ through a tube under the mask.

(2) *In the course of an operation under general anaesthesia.*—If we exclude respiratory obstruction, irregularities of breathing during general anaesthesia are generally due to one or both of two factors. In the first place excessive surgical stimuli may produce a temporary hyperpnœa, often accompanied by laryngeal spasm. This may deplete the pulmonary carbon dioxide sufficiently to produce shallow breathing or apnœa. Thus an irregular or even a Cheyne-Stokes type of respiration becomes established. Such stimuli as stretching the sphincter ani for hæmorrhoids, or distending a sensitive bladder for cystoscopy or everting the liver in cholecystectomy may be cited as examples. Secondly, the sensitivity of the respiratory centre to the CO₂ stimulus may become diminished by the action of the anaesthetic circulating in the blood, so that a higher CO₂ concentration is required to produce a response. This explains the spaced and sighing type of respiration characteristic of prolonged ether anaesthesia. Irregularities in breathing due to either of these causes will be corrected by the addition of CO₂ to the anaesthetic mixture. Again, in the course of a prolonged or severe operation the patient may drift into that unsatisfactory state conveniently described as "surgical shock," and characterized by pallor, sweating, lowering of temperature, shallow and irregular respiration, a feeble pulse, rising in rate and tending to become irregular, while the systolic and diastolic pressures are falling and approximating to each other. In this condition a carbon dioxide-oxygen mixture is a valuable aid to other anti-shock treatment. Its use will deepen respiration and thus re-establish the action of the "respiratory pump," so that the filling of the heart becomes more efficient and the blood-pressure will rise. The direct action of CO₂ upon the vaso-motor

centre will also raise the blood-pressure. Furthermore, the high oxygen content in the alveolar air will ensure a supply of fully oxygenated blood to the coronary arteries and thus improve the tone of the heart muscle, so that more forcible contractions will ensue and the systolic blood-pressure will again tend to rise, or alternatively the diastolic pressure will fall. The general improvement in a patient's condition is usually rapid and marked.

(3) *In the course of an operation under local analgesia.*—In most types of extensive regional analgesias the blood-pressure tends to become lowered, and, when this is marked, a condition very similar to that described above as "surgical shock" becomes established. If the patient is having no general anaesthesia in addition, he usually complains of nausea and may vomit. Spinal, splanchnic and sacral blocks are particularly liable to be associated with abnormally low blood-pressures, and in these cases a carbon dioxide-oxygen inhalation usually has a pronounced beneficial effect.

(4) *In de-etherization.*—If, at the end of a general anaesthesia, the patient be made to inhale a carbon dioxide-oxygen mixture with no re-breathing, the increased pulmonary ventilation will eliminate the anaesthetic much more rapidly than would normally be the case. Consequently the liability of post-anaesthetic vomiting will be diminished. Furthermore, the hyperpnoea will cause expansion and full aeration of the bases of the lungs, thus minimizing the risk of subsequent congestion and consolidation. It also seems reasonable to suppose that pulmonary embolism would be less likely to follow, while it has been demonstrated by Yandell-Henderson that a normal acid-base balance in the blood is restored more rapidly than if the patient were simply left to recover consciousness by himself. It should be noticed that in de-etherization an inhaler embodying an expiratory valve is essential, as if re-breathing takes place, the anaesthetic vapour will be re-inhaled instead of being eliminated. If an endotracheal anaesthetic has been given the CO₂ - O₂ mixture can be given through the catheter at the conclusion of the operation. This is, in fact, the most efficient means of its administration.

Thus we see that carbon dioxide has given us an almost complete control over respiration, so that general anaesthesia can be made a reversible condition. We can induce deep narcosis rapidly and we can restore consciousness almost equally rapidly, while rendering the effect upon the organism slight and transitory. In this connection, however, a word of warning is necessary. In most major operations it is unwise to continue giving the CO₂ mixture after the reflexes have returned. It is better to let the patient alone after most of the

anæsthetic has been eliminated. He will then doze, and remain free from pain for a longer period than if the administration were continuing until full consciousness returned.

(5) *In persistent hiccough.*—Hiccough is a combined laryngo-diaphragmatic spasm, and it seems reasonable to expect that if the diaphragm could be made to contract regularly and strongly, as in hyperpnœa, its spasm would cease. This supposition is fully borne out in practice. The writer has given several patients with most distressing hiccough a 90% O₂ - 10% CO₂ mixture to inhale, and in every case the spasm has ceased within twenty breaths. The cure may be permanent or a relapse may occur an hour or so later, but as many inhalations as necessary may be given without risk. This method of treatment is of especial value in the intractable type of hiccough sometimes occurring after high abdominal operations, particularly in cases of peritonitis or distension.

(6) *After tracheotomy.*—It has been observed that certain patients upon whom tracheotomy has been performed for chronic laryngeal obstruction have stopped breathing and died for no adequate reason. This has usually occurred when the operation has been performed under local analgesia. Negus has recently pointed out that chronic laryngeal obstruction causes a rise in the CO₂ percentage in the alveolar air (normally 56%). When tracheotomy has been performed this immediately falls to normal, so that the respiratory centre, which had previously been accustomed to respond to a higher CO₂ concentration in the blood than normal, no longer receives the necessary stimulus, with the result that apnœa occurs and the patient may die of anoxæmia. Haldane has described a similar condition in animals when the CO₂ in the tissues and blood is greatly reduced by prolonged and forced artificial respiration. When this is stopped, apnœa occurs, and the animal may die from oxygen deprivation without attempting to draw a single breath. This conception of the condition immediately following tracheotomy suggests that a small percentage of CO₂ added to the air inspired through the tracheotomy tube will prevent apnœa while the respiratory centre is becoming used to the diminished CO₂ concentration in the blood, and it is recommended that this should be a routine proceeding in all cases in which the alveolar CO₂ before operation exceeds 6%.

(7) *In pulmonary diseases.*—Reference has already been made to the prophylaxis of *post-operative pulmonary complications*. Carbon dioxide-oxygen mixtures are also extremely useful in *atelectasis* and *asphyxia neonatorum*. If a child is born in asphyxia it will usually breathe regularly within a few minutes if a 10% CO₂ - 90% O₂ mixture

is administered under slight pressure. The frequent success of "mouth to mouth" artificial respiration depends upon the CO₂ in expired air. Again, in cases of *emphysema* and *massive collapse* the increased depth of respiration will help to expand the collapsed lung. Encouraging results have also been obtained in *asthmatical attacks*, but an insufficient number of cases have been treated so far to permit of any definite statement upon the results in this condition.

(8) *In cases of poisoning.*—All poisons which act by depressing or paralysing the respiratory centre and those which are excreted wholly or partly by the lungs should be treated by the inhalation of a CO₂ - O₂ mixture. Common examples of such poisons are coal-gas or carbon monoxide, hydrocyanic acid, morphia and alcohol. However drunk a man may be, if his stomach be washed out and he be given a CO₂ - O₂ inhalation, he will almost certainly be sufficiently sober to walk within an hour. Again, suppose that a man is overcome by exhaust fumes inside a closed garage. He will be breathing so poorly that the inhalation of oxygen will have practically no effect. Directly CO₂ is added, however, the pulmonary ventilation increases, the alveoli become filled with oxygen, and the carboxyhæmoglobin of the blood is replaced by oxyhæmoglobin. Haggard has shown that the rate of elimination of carbon monoxide in gassed dogs is slowest in the untreated animals, slightly faster if pure oxygen is inhaled, a great deal faster if air + 10% CO₂ is breathed, and most rapid of all if the mixture is 90% O₂ - 10% CO₂.

(9) *In suspended animation.*—The rather curious group of cases of suspended animation in catalepsy, trance, partial drowning and lightning or electric shock should be treated on similar lines, as the increased depth of respiration and raising of the blood-pressure are powerful factors in recovery.

It is hoped that the above brief account of the action and uses of carbon dioxide may prove of some value to those who have not, as yet, availed themselves of this stimulating gas.

NOTES ON THE STRIPED HAMSTER (*CRICETULUS GRISEUS*,
THOMAS)*

A. B. DROOGLEEVER FORTUYN

The striped hamster of North China (*t'sang shu*) has been introduced by Hsieh (1919) as a laboratory animal and since that time it has shown its usefulness as such several times. Therefore it seems desirable to know more about this animal.

In view of this Dr. E. D. Congdon, assisted by Dr. Ma Wen-chao, collected in the years 1924 and 1925 in the neighborhood of Peking a large group of hamsters and on this material the following notes are based.

The material was collected on the following dates: March 3, 7, and 8; May 18 and 23; June 29; July 31 and November 1, all of the year 1924 and February 2, 4, 12, 16, and 19; March 12; April 10, 18, and 27, all of the year 1925. The collection consists of 350 animals of different ages and sexes among which are 39 females with their litters and in addition some sexual organs of other animals. The animals were fixed in toto in formalin or in Zenker's fluid, usually after the sexual organs had been removed from the body and fixed separately in formalin, Zenker's fluid or Zenker-formol. The material fixed in Zenker's fluid or in Zenker-formol was preserved in alcohol 70%.

As a rule Dr. Congdon measured the length of the animals, taking as such the distance between the tip of the snout and the root of the tail. In order to determine from this the average length of the adult male and female we must know when the adolescent period of the animal may be considered to have reached its end. For this the material gives three indications.† In the first place the length of the smallest pregnant female is 8.0 cms. In the second place the largest young found with their mother in one burrow measured 7.8 cms, but in one case 7 animals measuring 8.0 or 8.1 cms were found in the same hole. Probably they belonged to a litter the mother of which escaped. This too would indicate that by the end of the adolescent period a length of 8 cms is reached. In the third place in one case which will be mentioned more in detail on p.862 the growth of a single young animal was followed by Dr. Congdon. After having reached a length of 8.5 cms it stopped growing.

If we consider all animals of 8 cms length or more to be adult we get the following information about the length of the adult male and female.

*From the Department of Anatomy, Peking Union Medical College, Peking.

†A fourth may be derived from the work of Chung Shih-fan, p. 864

LENGTH OF ADULT MALES

Length in cms	8	9	10	11	12
Number of animals	29	16	12	2	

The average length of these 59 males is 9.28 ± 0.11 cms. (± 0.11 indicates the mean error).

LENGTH OF ADULT FEMALES

Length in cms	8	9	10	11	12
Number of animals	47	31	20	1	

The average length of these 99 females is 9.24 ± 0.08 cms.

In the case of the females we have a means of knowing with certainty that the animal is adult, i. e. pregnancy. I therefore calculated also the average length of 27 pregnant females and found it to be 9.61 ± 0.13 cms.

We may therefore say that the length of the adult hamster varies between 8 and 12 cms with an average of 9.5 cms. The two sexes do not differ in length*.

The material also gives some information about the number of young in the uterus and the number of young in the nest. According to Hsieh (1919) the litters consist of over a dozen young. This estimate is certainly too high. In 27 cases in which the uterus was visibly pregnant and in which the number of the egg-chambers (and therefore of the embryos) could be counted the following range of variation in the number of the egg-chambers was found.

NUMBER OF EGG-CHAMBERS IN THE PREGNANT UTERUS

Number of egg-chambers	3	4	5	6	7	8	9	10
Number of uteri	1	2	2	9	5	6	1	1

This gives an average of 6.55 ± 0.29 egg-chambers or embryos per uterus. Empty egg-chambers, so common in rodents and described by me (1919) in the mouse, were observed in a number of cases, but they deserve a special investigation.

As to the number of young in the nest we can expect this to be less than the number of egg-chambers because losses by death will act continuously to diminish their number. Dr. Congdon counted the number of young in 39 litters and found the following figures.

NUMBER OF YOUNG IN THE LITTER

Number of young	2	3	4	5	6	7	8	9	10
Number of litters	1	2	6	9	14	4	1	1	1

*Hsieh (1919) said that the adult was about 10-12 cms in length and that the male was much larger than the female.

The average number of young per litter is therefore 5.39 ± 0.23 . Generally speaking it may be said that the hamster produces 2—10, on the average 6 young at a time.

As Hsieh (1919) remarked, the female produces several litters a year. Pregnant females with litters of young (i.e. pregnant and lactating) were collected by Dr. Congdon in both April and November.

The hamster is supposed to hibernate in wintertime. Hsieh (1919) tells us that during the winter the animals retire to their burrows, sleeping the greater part of the time, but awakening about February or March. Because animals collected on February 2nd and on November 1st were visibly pregnant the time for "sleeping" can not be very long. It is very likely that the young animals after having been born in November require for some weeks the care of the mother and are thus not in a condition to hibernate immediately whereas sexual activity begins at least in the middle of January. It would therefore seem that the hamster does not hibernate at all, but, during the coldest weather lives quietly on supplies of grain collected in the burrow.

An actual growth-curve of the hamster can only be constructed when the age as well as the size of many animals before as well as after birth is known. Until now it has not been possible to breed the hamster in captivity and therefore at least the growth-curve before birth cannot be given with complete accuracy. But a provisional growth-curve (Fig. 1) may be based on the material studied here.

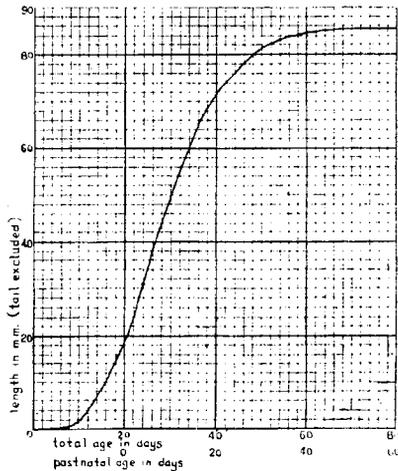


FIGURE 1

Provisional growth-curve of the striped hamster

In this curve we must distinguish between the portion below and above the point corresponding to a length of 31 mm and 24 (4) days of age. Above this point the curve is based upon data which Dr. Congdon collected. He reared a young animal from the 12th of March to the 17th of June when it died. Its length on March 12th was 31 mm., on March 25th 67 mm., on April 8th 82 mm., on April 22nd it was 85 mm. and this length was retained on May 6th, May 20th, June 3rd and June 17th. This animal therefore stopped growing after having grown from 31 to 85 mm. in 41 days.

The lower end of the curve is based upon a comparison of the striped hamster with the white mouse. This revealed a close resemblance in the development of both as will be shown in a later article, only the white mouse is always somewhat larger than the hamster. As in the white mouse the embryo reaches a length of 20 mm. just before birth, whereas the young animal (not including the tail) reaches a length of 24 mm. on the 2nd and of 34 mm. on the 4th day after birth, the hamster of 31 mm. length was supposed to be 4 days old, whereas the length at birth was taken to be 18 mm. The latter point is in accordance with the fact that the largest embryos of the hamster in the collection had a length of 16 mm. and, compared with the white mouse, they were not quite at term.

The striking resemblance between the hamster and the white mouse in their development was a reason to assume the duration of pregnancy to be in both cases the same and therefore 20 days. The growth-curve of Fig. 1 during that time is based upon data for the white mouse as they were found in the literature (Duval, 1891; Burckhard, 1901; Sobotta, 1903, 1911; Asai, 1914) but verified by my own material. Probably they are also right for the hamster.

Those hamsters which are pregnant and have young at the same time allow a certain control on this growth-curve. It is obvious that the embryos in the uterus can never be older than the age of the young after birth. The material contained 8 such hamsters. The following table gives a summary of the data which they yielded.

It is very remarkable that in 2 out of 8 cases only empty egg-chambers were found in the uterus whereas in 2 other cases the empty egg-chambers were much more numerous than the normal embryos. This would suggest that the time following the dropping of a litter (i.e., the normal time of lactation) is unfavorable for the development of the embryo. But it must be stated at once that uteri with nothing but empty egg-chambers were also found in hamsters without a nest of young. I will come back to this point in another article.

No. of mother	Length of the young in mm.	Diameter of egg-chamber in mm.	Embryo
225	63	7.5	7 mm. long
90	64	4	1 embryo (blastula) and 5 empty egg-chambers.
224	65	2.5	blastula
227	66	—	only empty egg-chambers
241	70	—	only empty egg-chambers
276	71	5	younger than No. 225
277	72	5.5	younger than No. 225
89	78	8	younger than No. 225 (2 embryos and 6 empty egg-chambers)

As a control on the growth-curve of Fig. 1 only the first hamster is of importance. Here the young have a length of 63 mm. which would correspond with an age of 15 days after birth, whereas a length of 7 mm. in the embryo would correspond with an age of 14 days. Therefore it seems as if in this case the mother would have been fertilized by the male immediately after the birth of the young in the same way as often happens in the white mouse. In the other cases fertilization must have taken place a longer time after the birth of the young.

Finally there is still another point on which the material throws light. Hsieh (1919) states that the young are driven out of the burrow of their parents when they are 3 weeks old. It would seem probable that the approximate age at which the young are forced to become independent should rather be taken as about 4 weeks since we know that young of 7.8 cms length are still living with the mother when their age according to the growth-curve of Fig. 1 would be 26 days.

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**NOTE ON THE DEVELOPMENT OF THE TESTIS IN THE
STRIPED HAMSTER (*CRICETULUS GRISEUS*)**

CHUNG SHIH-PAN.

The department of anatomy of Peking Union Medical College has a large collection of striped hamsters (*Cricetulus griseus*) obtained some years ago by Dr. E.D. Congdon and Dr. Ma Wen-chao. I have had an opportunity to study in this material some details about the development of the testis.

For my purpose 78 male hamsters were available which were caught at different times of the year in the fields around Peking. Usually the testis and epididymis were removed from the body and fixed in formalin, Zenker's fluid or in a mixture of both whereas the body itself was preserved in formalin.

The first fact to which attention may be drawn is the relatively enormous size which the testis may reach. As will be shown more in detail by the accompanying table the male hamster may reach a length of 115 mm. (excluding the tail) whereas the testis may be 16 mm in length.

In order to see whether the size of the testis was due to its functional stage or merely more or less correlated with the size of the body the following correlation table was constructed. In the vertical columns the variation of the total length of the animal is expressed, based on measurements previously made by Dr. Congdon. In the horizontal lines the variation of the length of the testis is recorded based on my own measurements.

Correlation table of the length of the body and of the testis.

Length of body of mm.	LENGTH OF TESTIS IN MM.															Total
	3	4	5	6	7	8	9	10	11	12	13	14	15	16		
60-65	1															1
66-70	1	5	1				1									8
71-75				1	1		2									4
76-80	1	3	6	2	2	3	1	2								20
81-85			1	2	1		1	1	1		1					8
86-90				1					2	3	1				1	8
91-95										1	1	1	1			4
96-100											1	3	4	1	1	10
101-105												1		1		2
106-110											1		7	3		11
111-115												1	1			2
Total	3	9	11	4	2	7	2	5	4	6	6	6	12	6	1	78

The arrangement of the figures in this table shows in the first place that there is a certain positive correlation between the length of the body and that of the testis. Generally speaking the length of the testis increases with the length of the body. Closer inspection shows that the figures may be divided into two groups occupying roughly the upper left and the lower right quadrant of the field, the two groups touching one another in the figure 2 common to columns 10 and 86-90.

This observation suggested that the material might be composed of two groups of animals, young and adult ones. The young animals would then have a body-length of less than 90 mm and a testis not more than 10 mm. long.

This assumption with regard to body length is in accordance with the conclusion reached by Dr. Fortuyn in his paper on the same hamster material (Fortuyn, See page 859) that hamsters with a length of 80-85 mm may be considered to be adult.

The material was further investigated by making microscopic sections of many of these testes of different sizes and by studying the spermatogenesis with the following results: In testes of 3 or 4 mm length spermatogenesis had not yet begun. Testes of 5 mm length showed the first mitoses. In testes of 6-10 mm length spermatogenesis was going on actively, but no mature spermatozoa were found in the epididymis. Testes of 11 mm length or more showed mature spermatozoa in the epididymis.

Therefore we are justified in considering that the male hamster becomes adult when its body has reached a length of 90 mm and its testis a length of 11 mm.

A further study of this material was made to determine whether or not there were evidences of a seasonal difference in spermatogenesis. This proved not to be the case. Testes with a greater length than 11 mm contained mature spermatozoa and showed active spermatogenesis February, March, April, May, and November, that is in all the months in which such material was collected.

Clinical Notes**TUBERCULOUS MENINGITIS***An Atypical Case*

W. H. TURNER JR. M. D. Nanking, China.

The statement usually seen in textbooks is that tuberculous meningitis rarely lasts longer than three weeks. The case reported below is of interest on account of the long duration of the disease, the slow development of typical symptoms, and the difficulty of early diagnosis.

REPORT OF CASE

History: A male American child almost four years of age living with his parents in Nanking, China. The family history was negative for tuberculosis and no history of contact was elicited.

Past history: The child was said to have had heart trouble at the age of two years, and about the same time developed cervical adenitis which healed promptly following incision and drainage. About six months later he had amebic dysentery which was successfully treated with emetine hydrochloride. Following this the only other troubles were two attacks of bronchitis during the winter preceding the present illness, each lasting three or four days and accompanied by a low fever.

The present illness began on June 1st, 1925, with loss of appetite, fever between 101 and 102 F. rectal, and some general lassitude and lack of interest in play. Physical examination done at this time revealed a moderately well developed and nourished male white child of about four years of age, mentally bright and alert, complaining of no pain and apparently not very sick. Aside from moderate enlargement of the tonsils and some redness of the throat the examination was negative.

Course: During the next few days there was apparently no change in child's condition; at the end of this time he began to complain of a dull frontal headache, and this continued throughout the illness, at times becoming severe. Aside from this and increasing weakness and anorexia there were no leading symptoms during the first two weeks. The temperature was not recorded above 103 F. A blood examination on June 9th. showed. W. B. C. 16,000, Widal weakly positive for B. typhosus, (mixed typhoid vaccine had been given about two months previously), negative for malarial parasites. Repeated urine and stool examinations were negative.

On June 16th a fainting spell lasting several minutes was reported by the parents and on the 17th. a tonic spasm of the lower extremities lasting a few minutes. Examination at this time showed a slight stiffness of the neck and a slight Kernig sign. The following day the patient was admitted to the University Hospital, Nanking, and a lumbar puncture done. The spinal fluid was clear and flowed from the needle in fast drops, cell count 230 per cmm., mononuclears 86%, polys. 14%, globulin not increased, sugar negative, no organisms found. Examination of the eye grounds on the same day showed a papilledema of one to two diopters in each eye, no tubercles were seen in the choroid.

The course following this was somewhat irregular, the patient gradually becoming more drowsy but sometimes rousing and talking with intelligence. At times he was restless and required sedatives. There was little or no change in the eye or superficial reflexes until the fifth week of the disease. The temperature ranged between 100.4 and 103.4 F., until June 30th. when it rose to 105.4, and on July 2nd to 105.6 F. Light spasms of the muscles of the left arm were noted from time to time during the last weeks of the disease. These became more frequent toward the close and the left leg was later involved, also there were twitchings of the muscles of the face and a rolling upward and outward of the eyes, usually to the left; at no time was there a generalized convulsion. On June 28th. the eye grounds were reported as showing less papilledema than on the previous examination. A cough developed during the last week of the disease. (The patient's sister at the time was suffering with whooping-cough).

Blood examination on June 22nd. showed W. B. C. 16,900, differential; neutrophils 65%, eosinophiles 5%, lymphocytes 22½% and large nonnuclears 7½%. The Widal was unchanged. Lumbar puncture was done every second day after admission to the hospital. The cellcount gradually dropped to 57 on July 2nd., with 88% mononuclears. No organisms were found in the spinal fluid until the last examination when the tubercle bacillus was found. The patient died July 2nd, 1925, thirty two days after the onset of active symptoms. No autopsy was performed.

Some of the atypical features of this case were, the difficulty of early diagnosis due to the slow development of symptoms, the absence of vomiting, the absence of definite convulsions, and the long duration of the disease.

Hospital Technology Section

DEVOTED TO THE GENERAL INTERESTS AND PRACTICAL
NEEDS OF THE SMALLER HOSPITALS

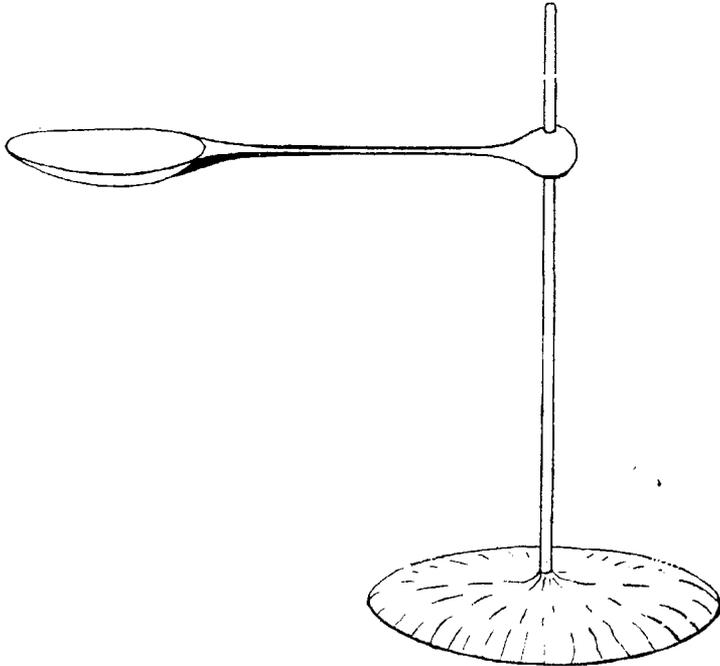
Edited by the Institute of Hospital Technology

A STERILIZING SPOON FOR HYPODERMIC SOLUTIONS

E. G. B.

Whatever care is taken in the preparation and storing of hypodermic solutions (See the Inquiry Service in this Journal), it is well to resterilize them by boiling immediately before use.

For this purpose the sterilizing spoon here illustrated is invaluable. There ought to be some such thing ready for use in every ward, or wherever hypodermics are apt to be required. It is locally designed, and made by the local copper-smith.



The spoon handle is level with the upper surface of the bowl, and it sends a supporting keel underneath nearly to the deepest part of the bowl. This is important. The ordinary Colles-fracture shape

sooner or later breaks off where the handle joins the thin metal of the unsupported bowl. The bulbous end of the handle slides freely up and down the stem of the stand. No screw is needed to keep it at any desired height, because the mere leverage of the spoon will be found to jamb the edges of the bulbhole against the stem, and fix it there. The spoon would break before it would move if pressure were applied only to the bowl end of it.

The spoon is about the size and length of a dessert spoon. The bulb is about half an inch thick. The stand foot is about $2\frac{1}{2}$ or 3 in. in diameter and a little thicker than a dollar, increasing in thickness towards the centre. The stem is about 5 in. high, and as thick as a slender bone knitting needle. All the dimensions will vary according to the size of the spirit lamps to be used.

The solution to be sterilized is taken from the bottle the exact dose of it in the syringe, and ejected into the spoon for boiling. A little evaporation of the water is unimportant; it does not affect the amount of the drug present.

If need be, the syringe and needle can themselves be boiled in the spoon before beginning.

I. H. T. INQUIRY SERVICE

To the I. H. T. What is the usual procedure in the preparation of stock solutions of the hypodermic alkaloids? Are they sterilized in the autoclave? How are they preserved for use? If gauze plugs are used, will not the solution still become contaminated in use? We have hitherto evaded the problem by using tablets, but it seems an unjustifiable expense. J. McD.

Answer,—This is rather a difficult question to answer out of hand. Solutions are certainly more economical to use than hypodermic tablets. During the last three years our method in the P.U.M.C. has been to make up our alkaloidal solutions in quantities of 500 C.C. at a time,—sterilizing all the glassware in the usual manner, by boiling it in double distilled water. The solution is prepared by dissolving the requisite amount of alkaloidal salt in the boiling distilled water transferred to a glass-stoppered bottle. This makes our stock solution for approximately three weeks, and from it we fill the ward wants,—usually 30 c. c. bottles,—after, of course, having sterilized both bottles and corks by boiling.

In making up the solutions it is essential to use freshly distilled water, and alkali-free glassware,—or you will get some precipitation or discolouration within fourteen days. If such a precipitate or cloudiness is observed in the ward bottle, something has gone wrong, and solution should be discarded.

We use no preservatives. Gauze plugs are no good for stock solutions.

As for the actual sterilizing, solutions of Novocaine, Cocaine, Pilocarpine, Morphine, and Adrenaline may be sterilized in the autoclave at 115°C for 15 or 20 min. Salts of Atropine are sterilizable at 100°C. Solutions of Gum Acacia may be sterilized by boiling in a hard-glass flask for 5 min, or by heating at 75° for three hours.

Statements that Cocaine would be decomposed in solution on boiling probably depend on a slight alkalinity in the glass. A temperature of 100°C on the water bath in glass vessels causes only the barest trace of decomposition. Adrenaline chloride can be sterilized at least twice under a variety of conditions without loss of activity.

Such things as will not stand boiling may be pasteurised by heating to temperatures between 60—70°C (140—150°F) for from half an hour to an hour on six successive days, keeping the solution during the resting stages at about 20°C. J. C.

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To the I. H. T.—Can you supply me with a soap formula using local oils? I have experimented with lye, and every local oil I can get; but the result is sticky, almost resinous,—anything but soapy, and quite useless. P.W.

Answer,—Try,—Caustic Soda (Brunner Mond, in 1 Picul kegs) 9 lbs.
Dissolve in 38lbs. water, and heat to about 100°F.
Then add Oil (Bean, Linseed, Vegetable, or even Wood) 60lbs.
Stir till thoroughly mixed, and allow to cool. J.S.

The product is a creamy yellow, of the consistency of train oil. It is stored in kang. It may be supplied to the laundry either in jars or in solution. Home laundries use solutions only. If made up to a definite formula, it can be given out by measure instead of by bars.

Practical laundresses tell us that a piece of hard soap should be on hand for rubbing into extra dirty patches in the clothes. E.G.B.

Editorials

MORE ABOUT CHOLERA

In a recent number (July 1927) we called attention to some of the problems regarding the treatment of Cholera and especially to the doubts thrown on the scientific accuracy on which Roger's hypertonic infusion theory is based. We have recently received a revised and enlarged version of Dr. Tomb's previous criticism of this system of treatment for publication in the *China Medical Journal*.

After India there is probably no country in the world from which Cholera takes a heavier toll than it does from China and we are very grateful to Dr. Tomb for his contribution.

In view of the questions that have been raised out here with regard to the Tomb treatment by a mixture of essential oils, about which considerable interest has been roused, we wrote ourselves to Dr. Tomb asking for fuller information. He has kindly replied to our letter as follows :

"As you will appreciate from perusal of the enclosed reprint ('Treatment of Cholera', *Lancet*, "Modern Technique" October 2nd 1926, p. 721) I am of the opinion that the action of the Essential Oils Cholera mixture is non-specific, the mixture being mainly an intestinal astringent which arrests diarrhoea as do kaolin and morphia. It possesses however certain advantages over these latter for general use as it is non-poisonous and there is no tendency to relapse after apparent cure. Its value in collapse is problematical but I see no theoretical reason why the mixture should not continue to act as an astringent in the stage of collapse and thus limit the loss of (injected) fluid from the bowel. The mixture is a powerful diffusible stimulant and should also I think, be of use in this regard in collapse."

In the paper referred to, Dr. Tomb emphasizes the value of the essential oil treatment in the following words :

"As the mixture contains no opiate it can safely be placed in the hands of any intelligent person for administration. For this reason it is particularly valuable in the treatment of cholera during epidemics, when large numbers of cases have to be treated simultaneously. It is a powerful carminative, stimulant and astringent, quickly arresting diarrhoea and thus aborting the disease. Relapses after its use are unknown, and no serious restriction of diet is necessary on apparent recovery. In my experience the mixture of essential oils taken three times a day in doses of a drachm during epidemics affords almost absolute protection against the disease."

CARBON DIOXIDE IN ANAESTHESIA

The progress of inhalation anaesthesia in China has largely come to a standstill. This of course is not true as regards a few of the leading hospitals in two or three of the largest cities but in all the smaller places and the inland towns the difficulty of obtaining gaseous media in suitable containers together with the cost of transportation and of refilling empty containers has made the use of such anaesthetics practically impossible. We have therefore a special pleasure in publishing this month an article by Dr. Langton Hewer on the use of Carbon Dioxide. The article originally appeared in the *St. Bartholomews' Hospital Journal*, but the Author has kindly given us permission to reproduce it with a few slight changes that make it more applicable to conditions out here.

The gas can be used as an adjuvant to the ordinary inhalation anaesthesia methods by the use of an apparatus simple and inexpensive, and free from the inherent difficulties of ponderous gas containers, and it is thus brought within the reach of every anaesthetist in China however isolated his hospital may be.

Dr. Hewer also indicates other possibilities in the use of Carbon Dioxide which will be of no little interest to doctors in general hospital practice.

SODIUM THIOSULPHATE

A little while back it was hardly possible to take up one of the larger medical journals without noting an article on the use of Sodium thiosulphate for some or other medicinal effect. Many of these seemed to base their arguments for the exhibition of the drug on very flimsy evidence. Feeling personally a good deal confused and believing that he would not be alone in this position, the Editor appealed to our faithful and valued contributor Dr. B. E. Read for a short paper that would clear up the situation in the minds of those who were perplexed by the many articles referred to above.

In this number of the *Journal* we are publishing the kind response of Dr. Read to this appeal. If, after all the promises of almost unlimited possibilities, we are rather disappointed over the hard facts of the case, we are at least given clear indications for the use and methods of administration of the drug and in the name of ourselves as well as of other perplexed medical journal readers we would express our thanks to Dr. Read.

THE FUTURE OF MISSION HOSPITALS

The Members of the Missionary Division are referred to an article on this subject in the *Missionary Section*. The paper is intended only as an expression of personal opinion and to open a discussion on an extremely important subject. There is often considerable hesitation on the part of our readers in taking part in such discussions, but we hope that this will be overcome in this case and that those who have had personal experience of the problems to be met will not shrink from making their views public for the common good.

SHANGHAI MEDICAL SCHOOL

Not a little interest has been aroused by the proposals for reorganisation of the Union Medical School in Shanghai. In this number of the Journal we are publishing a brief note of the present arrangements. It must be understood that this constitutes only a provisional scheme to make it possible to get to work without delay. We welcome it heartily and trust that it will be but the beginning of a school that will become one of the leading medical colleges in China.

China Medical Association Section

SHANGHAI UNION MEDICAL SCHOOL PRELIMINARY ARRANGEMENTS

St. John's University having closed its Collegiate Department for 1927-28 found itself unable to offer courses for the first and second year medical students. An effort was made to secure the assistance of the Yale Board of Trustees in America and an emergency grant from the Rockefeller Foundation. When these efforts failed representatives of the Medical College of the Fourth Chung San University (the provincial University of Kiangsu) offered to come into the proposed union and contribute the sum expected from the Yale Trustees. This offer was accepted by St. John's University and a Board of Managers for this year has been organized for the purpose of supervising the co-operation between these two medical colleges, for the administration of the funds held jointly, and for the purpose of establishing a Union Medical College in Shanghai of grade A standards. Four members were appointed by Chung San and four by St. John's University and these eight are given authority to add to their number. The following are now members of the Board.

E. S. Tyau—Chairman—Acting Dean St. John's Medical School.

H. H. Chao—Secretary—China Christian Educational Association.

- K. P. Chen—Treasurer—Mng. Director Shanghai Commercial & Savings Bank.
- F. C. Yen—Vice Director, Peking Union Medical College.
- V. T. Loh—Acting Dean Fourth Chung San Medical College.
- C. V. Yui—Professor of Terminology.
- C. L. Kao—Editor-in-Chief, National Medical Journal.
- S. C. Chu—Manager Transportation Service.
- Y. J. Cieh—Shanghai Municipal Council Medical Officer.
- T. K. M. Siao—Business Manager National Medical Association
- O. S. Lieu—Manager Kailan Mining Administration.
- W. S. New—President National Medical Association, Shanghai Branch.
- A. W. Tucker—Supt. St. Luke's Hospital.
- J. C. McCracken—Professor of Surgery, St. John's University.

Already five thousand dollars have been subscribed in Shanghai and the Rockefeller Foundation has made an emergency grant of twenty thousand dollars.

Chung San University will become responsible for the teaching of the first and second years classes which will be conducted in a spacious building at Woosung. Dr. F. C. Yen has been appointed Dean and Dr. W. C. Loh Acting Dean of this School. St. John's University will continue to be responsible for the third, fourth and fifth year classes. The enrollment in the five classes will be near sixty.

SUSAN TOY ENSIGN MEMORIAL HOSPITAL

(NANCHANG HOSPITAL)
KIANGSI

Since the Nanking affair March 24th., we have suffered tremendously by the sudden loss of our Missionaries Dr. G. T. Blydenburgh, Dr. W. E. Libby and Miss E. K. Pennepacker. Their departure meant naturally a sudden shortage of working efficiency with the result of heavy burdens being placed upon the shoulders of Chinese staff members. At that time it was all dark before us and even now we still do not know what will happen in the future. Nevertheless, we kept pushing on steadily to resume the normal routine as closely as possible.

Of course, time and again, we encountered difficulties from without; but they were readily readjusted. One of the difficulties we met was the "strike" held by hospital cooks on June 3rd., because they objected to our ways of cutting down the kitchen expenses. At that time the Labor Union seemed to be a menace. Yet, fortunately, we succeeded in getting rid of these cooks by appealing to their headquarters for justice. So they left disappointed and their selfish ends failed. To meet the emergency during this "strike", we managed to run the kitchen ourselves for two days under the leadership of our matron till we secured new cooks. Almost every one of the staff and the ladies gave help in the kitchen. The pleasure we felt in kitchen work and in serving patients was really a new experience for us and we thoroughly enjoyed it.

Toward the end of May soldiers began to bother us. Three times they wanted our hospital for their barracks. Fortunately we succeeded in refusing them each time. The recent fighting on July 31st. gave us another opportunity for service as well as the usual excitement which you would naturally expect in Missionary hospitals at this particular time. About one hundred and twenty wounded soldiers were taken care of by us in the hospital. It so happened that fighting took place on the third day after the arrival of Dr. Tsen who had newly joined our work. With the help of our head nurse, Mr. Wang, Dr. Tsen was enabled to take care of many wounded soldiers and the civilian cases as well in spite of various limitations during my absence. Besides the enormous amount of time we put in for our professional work, we were annoyed by soldiers who continually kept asking for our hospital in which to station troops. Through the diplomacy of Dr. Tsen and Mr. Wang and with the help of police at the gate, we finally succeeded in keeping the soldiers out. Our success in refusing them was I believe, due to the many wounded soldiers we had taken in, who filled our wards, otherwise the soldiers would probably have taken the hospital.

Ever since March, our work has never been interrupted for a single day except for the temporary closing of our Out-Patient-Clinic in the latter part of July, when I was away in Shanghai. During this time dozens of patients came to hospital every day to inquire when our clinic would re-open, and it is to be deeply regretted that so many patients went away disappointed. One woman with nephritis, whom I had treated earlier told me that she waited and waited with patience for our clinic to re-open. She sent a messenger daily to hospital to find out whether our clinic was opened or not, as she refused to be seen by any other doctor in the city. This woman came at once on the first day of our clinic, and she said to me, "I hope

that your hospital will never close". This is, perhaps, one genuine example of what many patients feel. Though we may not realize the importance of our service at ordinary times if for any reason our doors are closed the result will probably endanger the lives and health of the vast population of this city. Although we cannot prophesy for the future, we feel as long as this hospital is of benefit to the needy and sick, our work must go on. I am glad to say that, throughout this whole time of chaos and apprehension, our object in Christian service through the art of healing has not been defeated. Now we are left peacefully at work and hope that a brighter period will come for us soon.

S. C. WU, M.D.

Missionary Section

THE FUTURE OF THE MISSION HOSPITAL

JAMES L. MAXWELL

Executive Secretary

Our President has handed me a letter written to him by a well known member now on furlough. The letter contains passages of such general interest and importance that Dr. Fowler suggests that a discussion in the *Journal* would be timely. This paper is therefore intended merely to open such a discussion and we hope that the members, and especially the Chinese members, will frankly give us their views on the problem.

The passage in the letter to which attention is called reads as follows:—

"One of the strongest leaders in our Mission and a keen observer after her generation of time in China writes that she fears that the hardest job ahead (now in hand) is for the Chinese to take over the medical plants,—especially those that are distinctly "foreign," for her feeling is: (A) that the Chinese do not want a "foreign" hospital: and (B) they are not prepared to support so expensive an institution as a really modern hospital plant,—the local public as a rule not being educated to the point of either endowment or annual contributions sufficient for support. May I ask for your reaction to this attitude and feeling, please? My own feeling has been that it should be the

aim of every medical plant to construct and maintain any such plant as nearly as possible along Chinese lines, avoiding as much that is "foreign" as possible. I know of a plant that is constantly in financial trouble because, though up-country, it is too expensively run, and postpones thereby the desirable day when it can be an "all Chinese" plant. Surely the greatest care should be taken to keep a high professional standard, and often the local make-shifts may not lend to finesse, but the aim for missionary physicians is to show how much may be done with the materials in hand. Especially if the spirit of the Master is interwoven is there thus the greater likelihood of the work being multiplied in various other nearby regions,—one of our essential aims."

The Association has not been altogether forgetful of these problems heretofore and a few weeks ago a letter was sent round to a number of our Chinese physicians requesting an expression of their views with regard to some of the points that are here raised.

As this letter emphasizes some points of this problem we reproduce the bulk of it here.

It reads as follows:—

Dear Doctor:

The present period of troubles in China is, we all believe, but a prelude to an all round advance and not least in the realm of medicine.

It is evidently desirable therefore at this time carefully to consider some of the problems that must be met in the coming years, and among these are the problems of future hospital construction.

For the past century the modern science of medicine has been considered "western" and this name has been attached both to the physicians and their hospitals. Doubtless this was inevitable in the early days but with the growing number of modern medical schools in China such a term is now out of date. The fact remains that the present system of medicine has come from the West and with it the ideas of construction of modern hospitals in China. To some extent this is again inevitable as the construction of modern hospitals has been evolved through a long period to meet the needs of modern medicine.

We feel however that the time has now come when more definitely Chinese ideas of construction should be incorporated in the plans of all new hospitals. Further we believe that our Association could through the pages of the *China Medical Journal* give expression to these ideas and bring them to a focus in specific suggestions for future hospital building.

We are therefore asking a number of our Chinese members who have had personal experience in the management of hospitals to let us have their views in short articles for publication. These will be published either as a series of articles in consecutive issues of the *Journal* or, should the contributions seem to warrant it, in a Special Number of the *Journal* devoted to this subject.

Hospitals in this country naturally group themselves under two headings:

1. The City Hospitals in the larger and more wealthy cities where the demand for better accommodation and more specialised treatment will have to be met, and where considerable support from wealthy citizens may be expected.

2. The Country Hospital to meet the needs especially of village populations where the standard of living is low, the people poor and illiterate, and where outside support is not easily obtained.

There is a further grouping which unfortunately has not in the past been at all adequately realised, that is the grouping according to climate. It is reasonable to suggest that three styles of hospitals are required in China:

1. In the South, where other requirements have to be sacrificed for the sake of coolness, where for most of the year little or no bedding is required, and where at no time of year is there any call for artificial heat.

2. In the North, where other requirements have to be sacrificed for the sake of warmth and protection from the extreme cold of the many winter months, where warm bedding for most of the year is a necessity, and where artificial heating is essential.

3. In the Centre, where the winter may be very cold and the summer correspondingly hot and where allowance must be made for both these conditions.

We suggest that two points should be separately dealt with:

(a) Dispensary construction to cover the requirements of the Out-patient Department.

(b) Hospital construction to cover the requirements of the In-patient Department.

I am,

Yours sincerely,

James I. Maxwell.

This letter deals of course with only one side of a complex problem but I print it here because it does emphasize that side, viz that western medicine in China is a foreign importation and can only gradually take on a fully Chinese form.

The other and even more important question raised is as to the general suitability of the hospitals built in recent years for the positions in country and city where they are placed. Purely as a personal reaction my own answer would be that while the large bulk of such hospitals are well suited to the areas in which they are placed a few of them are on a scale and in a style that will make it extremely difficult for the Chinese to take over. This applies however more especially to a few buildings in the country or in comparatively small cities, and I doubt whether it can be fairly applied to hospitals in the large cities. My reason for saying this is that the Chinese themselves are building or running in a few of the cities hospitals as large and as well arranged as the hospitals run by foreigners, and there certainly would have been more of these but for the economic difficulties of the past few years.

As examples of the above I would give the Central Hospital, Peking, the Eastern Hospital, Moukden and the Red Cross Hospital Shanghai. The latter though the original building was foreign has been largely added to and in any case as to management and support is entirely Chinese.

The problem before us is therefore by no means as simple a one as would appear at first sight.

In dealing with it there is still another method of approach viz., as to how far the difficulties raised in the letter have actually in practice prevented our hospitals being taken over by the Chinese. Is this actually a serious difficulty?

An extremely interesting commentary on this problem is afforded by the happenings of the past year. Three groups of hospitals are now in Chinese hands.

1. Hospitals seized by the military and still used for medical purposes. This happily is a very small group and without exception, I believe, the experiment has been an entire failure. Such hospitals are now quite unworthy of the name.
2. A large group from which the medical superintendents have been driven by the political disturbances and for which temporary arrangements have been made with the existing staff. It is perhaps too early to pass any serious judgement on these and in any case the conditions differ so much in different places that perhaps no opinion can be fairly given. My own impression is that for the most part these hospitals have suffered very considerably in standards and efficiency and in their power for service among the people, but that this has been much less the case in some than in others depending largely on the education, experience and spirit of the men who have of necessity been put temporarily in charge.
3. We have a small group, unfortunately only small as yet, where by deliberate plan and arrangement the superintendence of the work has passed into Chinese hands. This includes both hospitals in the country and in the smaller cities. Where the men that have taken over these hospitals have been the right type the results have I believe been excellent. Some of them are located in fine plants that have done splendid work in the past and are going to do even finer work in the future.

It seems to me that after all the problem is not so much the buildings as the men. Undoubtedly buildings may be made more Chinese in style and atmosphere but in the end the diseases to be dealt with are

the same as those met with abroad and the methods of treatment can only be varied within narrow limits so the problem cannot be very greatly simplified along this line. The real difficulty is the supply of Christian doctors of high standard of training and ability and to reach this there is no short cut. We are taken back to the old problems of the lack of adequate medical schools to provide the necessary staff.

The conclusion sounds rather depressing but it is absolutely necessary to face the truth that there is no short cut to handing over of the hospitals and that any attempt to devolve them on insufficiently educated and inexperienced men can only end in disaster.

Current Medical Literature

THE MORBIDITY AND MORTALITY OF CESAREAN SECTION

T. L. MONTGOMERY, M.D., Philadelphia, Pa.

CONCLUSIONS

The study of these statistics and the results of our rather bitter experience of the past year lead unswervingly to certain conclusions.

1. Early or elective cesarean section has a low mortality, 2 to 3 per cent. Late cesarean section of the classical type has a high mortality, 20 to 30 per cent.

2. Delayed operation in cases of disproportion is dangerous. A more earnest effort must be made to reach a decision for or against cesarean section either early in labor or before its onset.

3. These statistics raise the question whether in late operation for any indication the classical cesarean section alone meets the need of the case.

4. The operative results in fibroma uteri complicating labor are not particularly good. There are problems in the conduct of labor of these cases which are open to discussion.

5. In placenta previa the collected maternal mortality is higher for cesarean section than for the other commonly accepted methods of delivery. The operation appears best in the case of central placenta previa with a nondilated resistant cervix. In such a patient the maternal mortality is as good or better than that of other methods of delivery and the fetal mortality considerably less.

6. The question of applying cesarean section in certain cases of premature separation of the placenta is still under consideration. From our experience we feel that it is the best method where most of the bleeding is concealed and the cervix not dilated, provided the condition of the patient warrants interference.—*Am. Jour. of Obs. and Gyn. May, 1927.*

CLINICAL AND THERAPEUTICAL ASPECTS OF
INFLUENZA — FROM 1889 TO 1927:

The Value of Salicin in Treatment

E. B. TURNER, F.R.C.S., London

The essentials of the treatment by salicin are: first of all to give the salicin as soon as ever there is a definite rise of temperature; keep the patient warm in bed, on light simple food; give 20 grains of salicin every hour for the first twelve hours, then 20 grains every two hours for the next twelve hours. When I first gave it I used to administer it in powder, but it is much more conveniently given in cachets. In many cases this is sufficient, but if not the dose of 20 grains may be repeated four, five, six, seven, or eight times a day, as may be necessary, and should there be any relapse repeat the treatment.

For young persons the dose must be reduced. I found that 1 grain for each year of the patient's age, with 1 grain extra "for the pot," was effectual. After the age of 18 years the full 20 grains should be given. If young children can be induced to swallow the drug the results in their cases are just as good as in those of their elders. I believe that young persons have a great tolerance of salicin. One mother, in whose family several cases of various ages occurred, gave a girl aged 12 years the full 20-grain doses instead of her own proper allowance of 13 grains. Her recovery was extremely rapid. But I have kept to the smaller dosage as it is quite successful.

It is quite useless to attempt to treat influenza with small doses of salicin. No effect whatever is produced. The large frequently repeated dose is what is required, and it must be given and pushed with confidence and without fear. I have come across quite an appreciable number of instances in which, following my advice, practitioners have attempted to treat the illness with salicin, but have been afraid of the proper dosage. One particular case comes to my memory in which a very eminent physician, of a past generation, got particulars of the details of the treatment from me and proceeded to treat an even more distinguished surgeon who was suffering from the disease in 1891. He

came to me the next day and said it had produced no good effect. On inquiry I found that he had given 10 grains only three times a day! We saw the surgeon that morning, and after taking the proper doses he recovered at once. Therefore, give and push 20-grain doses.

The more acute the case at the commencement and the higher the temperature the more quickly does it yield to this treatment and the more quickly does the patient become convalescent. When the fever has dropped, before I let the patient out of bed, I very frequently give 60 drops of sal volatile three or four times a day, and afterwards, should any tonic be required, some strychnine and nitrohydrochloric acid. Three times I have treated myself in this way, and on each occasion with the same success, in that I was not laid up more than one day in any case.

The fact that in my first cases, treated on ordinary lines, I had about the ordinary average number of complications, and that when I started this somewhat drastic treatment I had very quick recoveries and no complications, has encouraged me to persevere.

Since 1891 I have been asked to see a large number of cases in which the disease has been in evidence for some days. I have found that if no complication be present salicin treatment, though commenced a great deal too late, will almost certainly prevent complications and sequelae. But if bronchitis or pneumonia be present it does not seem to do very much good, though I have thought in some cases it has been of use. In such cases it is the complications rather which require treatment.

I have had the great advantage that in all the cases I have treated with this drug the patients have been able to stay in bed and take care of themselves. I should not hesitate to give salicin even in unfavourable domestic circumstances, but there is no doubt but that well housed, well looked after persons are the best subjects for this treatment.

In a large number of households of my acquaintance a stock of cachets containing 20 grains of salicin is always kept in readiness, so that should a member of the family show symptoms of influenza during an epidemic I am able to give the remedy as soon as ever I see him. This is a tremendous advantage, as the table I have appended shows.

In my experience salicin not only cuts short the duration of the disease but also abolishes the numerous sequelae which were so marked a feature in all the epidemics. I have had hardly a single patient, whom I have treated in the acute stage with salicin, come back to me later complaining of one of the numerous ills which followed an acute attack. This was most marked in the 1889-90-91 epidemics, when for

months, and even years in some cases, patients suffered from various neuroses the sequelae of a severe attack. In the later epidemics, though nerve affections were observed, there were, in addition, pulmonary and cardiac mischief of a serious nature arising from the same cause. I have seen practically no such cases.

On several occasions I have been able to watch the behaviour of cases of influenza, the results of the same infection, in a household when I have given some of the inmates salicin and the others have been treated on other lines. In every instance those who took salicin were well, out and about before the others were out of bed. In several instances the latter suffered from severe pulmonary complications, in one instance resulting in death.—*B. M. J. July 16, 1927.*

TROPICAL TYPHUS AND BRILL'S DISEASE

William Fletcher and J. E. Lesslar, writing in the *Journal of Tropical Medicine and Hygiene*, November 15, 1926, xxix, 22, point out that the epidemic typhus fever of Eastern Europe has its feebleness in tropical typhus. Epidemic typhus is essentially a disease of cold and temperate climates; when it breaks out in subtropical countries it flares up in winter and dies down in the spring, while tropical typhus appears in spring and dies down in winter. The symptoms of epidemic typhus and tropical typhus are the same, both diseases run the same course, and in both the Weil-Felix reaction is positive; but the two diseases are totally different from the standpoint of the sanitarian and the public.

Tropical typhus does not spread from man to man, does not give rise to epidemics, is not carried by lice, special precautions to avoid infection are unnecessary, and the mortality rate is low. In tropical typhus, as shown by Von Loghem, two groups of *B. proteus* are concerned: (1) The *indologenes*, which produces indol in peptone water, and (2) the *nonindologenes* group which does not react thus. The authors have employed in the Weil-Felix reaction, a nonindologenic strain of *B. proteus* x19 (Kingsbury) and a number of indologenic strains, and in this way have demonstrated the two groups of tropical typhus. One group, which they call K, agglutinates an anindologenic strain (Kingsbury) but does not agglutinate the indologenic strains, such as Warsaw and No. 67 from the National Collection of Type Cultures. The second group, W, agglutinates the indologenic strains, but does not agglutinate the nonindologenic strains. These two groups seem to be equally common in the Malay States; they differ but little in their course and symptoms. In neither group is there evidence of transmission by lice, but there is reason to suspect that the disease is

conveyed by an ectoparasite of the rat or the mouse, as the disease has a tendency to attack cattle keepers and agricultural workers. The authors point out the similarity of tropical typhus and Brill's disease, which, as described by Brill, resembles typhus fever more than does any other disease, but, unlike typhus, is not communicable, not a grave and fatal malady, and epidemics do not arise, though it is constantly present in the community. These mild forms of typhus-like fever are widespread, having been reported from every quarter of the globe. It is important in using the Weil-Felix reaction to make two cultures of *B. proteus* x 19, one indologenic and the other nonindologenic, in every case.—*Jour. of N.Y. State of Med. January 15 1925.*

POTASSIUM PERMANGANATE IN PNEUMONIA

Spectacular, if not extravagant, claims are made by Nott for the potassium permanganate treatment of lobar pneumonia. Two grains of the pure chemical are dissolved in one and one-half pints of warm water and this is given slowly per rectum in three or four ounce quantities every two and one-half to four hours for the first twenty-four to thirty-six hours. After this it is administered twice daily for three days, then once a day for three days. The course of the illness naturally determines the frequency and length of administration. Forty cases have been so treated with a 5 per cent mortality. Nott claims for this method a remarkable sedative action, the clearing up of blood from the sputum within a few hours after its first administration, and a rapid temperature fall by lysis. He makes no attempt to explain the phenomenon. If the results are as good as the author believes, they are deserving of substantiation with more carefully controlled clinical observation. He also administers thyroid extract by mouth but doubts whether this is a factor in the good results.—*Jour. of Lab. and Clin. Med. June, 1927.*

DISCUSSION ON FOOD DEFICIENCY CONDITIONS IN RELATION TO PREVENTABLE ILLNESS

STUART J. COWELL, M.B., B. CHIR. CANTAB., M.R.C.P. Lond.,
Sheffield.

The Scientific Point of View

To sum up: it would appear possible at the present moment practically to eliminate rickets, to improve enormously the condition of the teeth of our people, to lessen the infant mortality from malnutrition, diarrhoea, and respiratory infections, and in general to raise the

standard of physique and health. The measures that are recommended to bring about this result are quite simple. Ensure an adequate supply of fat-soluble vitamin in the diet: begin with the pregnant and lactating mother and continue with the child from the earliest days of his independent existence. When the child is weaned, the less milk, eggs, and butter that can be included in his dietary, and the less opportunity he has for being exposed to natural ultra-violet rays, the more important is it that he should be given cod-liver oil or one of its reliable preparations, and that foodstuffs such as oatmeal, which have a rickets-producing effect, should be excluded from his diet.

HELEN M. M. MACKAY, M.D., M.R.C.P. Lond.,
Physician to the Queen's Hospital for Children, Hackney.

The Clinical Point of View

To sum up. Of the three dietetic deficiencies in children which I have asked you to consider—those of vitamin D, vitamin C, and iron—the diseases associated with the first two are well recognized and we are already steadily diminishing their incidence; but the fall in their incidence, in my opinion, could be greatly accelerated by our consistently advocating the prophylactic use of cod-liver oil and of orange or tomato juice for all artificially fed infants and many breast-fed infants. These rich sources of vitamins D and C are within the reach of practically all sections of the community. The prophylaxis of alimentary anaemia is a much more difficult question. But iron deficiency is very widespread, at any rate during the first one to one and a half years of life, and the resultant ill health should be preventable. Much more information of a practical kind as to how this can best be achieved is urgently needed.

JAMES WHEATLEY, M.D.,
County Medical Officer of Health, Shropshire

The Public Health Point of View

It will be useful to state concisely the *supposed* effects upon health of food deficiencies that have so far been investigated.

Deficiencies of fat-soluble vitamins A, D, and E (?)—in mothers' food causing stillbirths and premature births, marasmus, and general feebleness of infants, resulting possibly in a considerable proportion of

deaths during the first month of life; defective growth of infant and child; infections of lungs, intestines, and eyes; rickets, and defective structure of teeth predisposing to caries; possible predisposition to enlarged tonsils and adenoids; and the train of symptoms associated with the catarrhal child.

Deficiency of vitamin B—loss of appetite; subnormal temperature, lowered function of the gastro-intestinal mucous membranes, resulting in inflammatory changes, constipation, and intestinal infections directly or indirectly causing a very considerable proportion of the illness after middle life; colitis, appendicitis, and gastric ulcers; lowered bactericidal power of the blood, and consequent lessened resistance to accidental infection; interference with growth.

Deficiency in vitamin C—infantile scurvy, greater susceptibility to infection, possibly interference with growth.

Deficiency in calcium, in addition to being an important factor in the production of rickets and defective teeth, produces certain important blood changes.

Deficiency in iron—anaemia; evidence of anaemia due to food shortage is not very obvious, except in persons kept on milk diet for long periods.

Deficiency in iodine is probably the basal factor in the causation of endemic goitre, and a cause of lowered general metabolism.

Deficiency in roughage has been assumed to be the important factor in causing intestinal stasis and the infections that follow from it. These results are now attributed largely to the shortage of vitamin B. Roughage probably has a value apart from the vitamins it contains—certainly as a compeller of mastication and probably by fulfilling a mechanical and perhaps an absorbent function in the intestines. *B. M. J.* July 31, 1927.

Book Reviews

An Illustrated key to the Identification of the Anopheline Larvae of India, Ceylon, and Malaya, west of Wallace's Line, with Practical Notes on their Collection; C. Strickland, M. A., B. C. (Cantab), and K. L. Choudhury, M. B., D. P. H. (Cal). With a foreword by Sir. Ronald Ross, K.C.B., K.C.M.G., F.R.S. Tacker, Spink and Company, Calcutta and Simla. 1927. 67 pp., 12 plates. Cost rupees 4/8.

This little book from the Calcutta School of Tropical Medicine is a sequel to a similar work by the senior author on the adult anophelines of the same region.

Chapters 1 and 2 are devoted to the collecting and handling of anopheline larvae. Valuable details are given which are indispensable to the amateur collector, not only with regard to the specimens collected but also as to his own habits and clothing while doing field work in the tropics.

The key itself differs in type from the dichotomous key now in general use for zoological identifications. It is more descriptive than eliminative, presenting the specific differences in columns, and grouping closely related species on the same page. Opposite each page is a plate of very clear single-line drawings which add greatly to the value of the key. In fact one wonders whether this type of key would be very useful without figures to interpret the minute differences in structure as given in the key itself.

In the five Appendices following the key, further instructions and suggestions are given for mosquito collecting and for organizing an antimalaria survey. The geographical distribution and type of breeding place of the anopheline mosquitoes of the region are also given.

This book meets an important need in making possible the identification of mosquitoes without the necessity of breeding them out, thus saving much time, labor and equipment, and avoiding the danger of failure of hatching. It should prove a valuable addition to the equipment of those interested in the study of the mosquitoes of China.

H. E. M.

NEWS AND COMMENTS

**Postoperative
Massive Atelectasis**

The Editor greatly regrets that certain mistakes in figures were allowed to slip through in the final proof reading of this paper which appeared in the August issue of the Journal. Readers are asked to make the necessary changes in their copies on page 716.

9/2 to read 9½

1 1/2 ,, 1½

White count 51,000 to read 21,000

7 1/2 on page 717 to read 7½

Dr. Cochran

Dr. Samuel Cochran assumed the post of Medical Director of Lawrenceville School at Lawrenceville to-day. He had been appointed last spring. Dr. Cochran, who served for almost twenty years as head of a hospital in China, received the degree of Doctor of Philanthropy from Princeton last June.

N. Y. Times, Sept. 2nd, 1927.

Nurses Association of China

Will doctors kindly note, that the Kwang Hsueh Publishing House, 44 Peking Road, Shanghai, is the official publishing house of all the books of the N. A. C.

To members of the N. A. C. and Schools of Nursing registered under the N. A. C. a ten per cent discount is given on all books purchased. This can only be given when books are ordered directly from the N. A. C. Publishers and not when ordered through some other organization or publisher.

Remember to order all nursing books directly from the N. A. C. publishers and get ten percent discount. Doctors will find at the end of the year that they have saved quite a considerable sum in this way.

Mortality in Tuberculosis

In 1875 the mortality from all forms of tuberculosis in Scotland was 361 per 100,000, while in 1925 it was 110. In 1875 the mortality from pulmonary tuberculosis in Scotland was 252 per 100,000, while in 1925 it was 76. In other words, during the fifty years there has occurred in each case a total drop in mortality of over two-thirds. This is something more than part-expression of the reduction of the general death rate of the country, in which the fall during the same period amounted to less than one-half. The relative fall is illustrated by the fact that, while in 1875 deaths from pulmonary tuberculosis constituted 10.6 per cent. of deaths from all causes, in 1925 they constituted only 5.7 per cent.

B. M. J. July 23, 1927.

NEW MEMBER PROPOSED

Shih, Ching Jen.

M. B. Tsinan

R. C. A.

Kulangsu, Amoy.

Proposers: C. H. Holleman

T. Bosch.