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NEOSTIBOSAN IN THE TREATMENT OF KALA-AZAR

Notes on the Treatment of 87 Cases

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Since Dr. Hans Schmidt in 1911 successfully prepared Stibenyl, an organic preparation of antimony, a number of much more effective organic compounds of antimony have been produced.

In the autumn of 1928, the firm of I. G. Farbenindustrie Aktiengesellschaft, of Leverkusen, Germany, kindly sent us a generous supply of Neostibosan. We immediately began to use it on all Kala-azar patients as they were admitted. During the past two years, September 1928 to the end of September 1930, the number of Kala-azar patients admitted was 91, 87 of whom were treated with Neostibosan. These cases, which represented all types, both severe and mild, have been used as a basis for this report. The diagnosis of Kala-azar was confirmed in every case by finding Leishman-Donovan bodies, by liver or spleen puncture.

Owing to civil war in the province, still continuing, the suspension of railway traffic and the danger from bandits to overland travellers, the number of those who have returned for re-examination has been less than we had hoped. One is not, however, surprised that patients who have recovered and who are perhaps very poor fail to make a return journey of a hundred miles or more.

One father wrote that his boy was well, but that he was unable to keep his promise and bring him back because of bandits.
One patient, who took away with him a questionnaire in a stamped addressed envelope, did not return the letter but sent four other Kala-azar patients from the same district. One of these reported that the patient we had discharged was quite well.

We sent a registered letter to each patient treated and in many cases the letters were returned undelivered. It is not, however, unreasonable to suppose that the number of cases cured is probably as large in the group of which we have lost trace as in the group which has replied to the questionnaire. We do, however, consider that a patient should remain well for at least six months following treatment before he may be described as cured.

Description of the Drug. In his article "The Pentavalent Antimony Compounds in Tropical Medicine," Dr. Schmidt states that the pentavalent antimony compounds which have so far been prepared can all be regarded as derivatives of p. aminophenyl-stibinic acid. He divides them into three groups:

1. Salts of p. aminophenyl-stibinic acid:
   Sodium p. aminophenyl-stibinate (stibamine).

2. Derivatives obtained by substitutions in the amino group of p. aminophenyl-stibinic acid:
   Stibenyl, Urea-stibamine, stibamine glucoside "Neostam," amino-stiburea.

3. Derivatives obtained by substitutions in the benzol nucleus of p. aminophenyl-stibinic acid or p. acetyl-aminophenyl-stibinic acid:
   Stibosan (sodium-m-chlor-p-acetylaminophenyl-stibinate).

The reasons why the preparations in group 1 have not hitherto been used therapeutically is because the only known salt of p. aminophenyl-stibinic acid, the sodium salt, will not keep. When the stable diethylamine salt of this basal substance, p. aminophenyl-stibinic acid, had been prepared (Compound 693), Napier found it to be of value in the treatment of Kala-azar patients.
By varying the method of preparation, Schmidt was able to obtain a modification of the diethylamine salt of p. anino-phenyl-stibinic acid which had definite chemical properties. This compound, 693 B, is the one which has been placed on the market under the name of Neostibosan. The toxicity of the compound is very low, as shown by the fact that mice weighing 20 grams tolerated doses of 40 milligrams Neostibosan (42% Sb.), as compared with 15 milligrams of Stibosan (31% Sb.), and 0.4 milligrams of tartar emetic (36.6% Sb.).

**Dosage**

**Adults**

The initial adult dose was 0.1 intravenously and subsequent doses 0.2 gm. to 0.3 gm., depending upon the weight and condition of the patient. In some cases injections were given daily and in others every second day. If a patient complained of any symptom following an injection which might have been caused by the drug, the interval between the injections was increased and the next dose decreased by 0.1 gm. We considered it advisable to give from 2.6 gm. to 3 gm. as an average total dose for an adult of from 100 to 120 lbs. in weight. Of the 9 adults known to be cured the averages are as follows:

Average age 25 yrs.

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<tr>
<td>weight</td>
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<tr>
<td>total dose</td>
<td>2.63 gm.</td>
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<tr>
<td>time under treatment</td>
<td>23.3 days</td>
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</table>

**Children**

In children, both intravenous and intramuscular injections were given. Dr. Annie V. Scott who treated the children says that in no case has she found any local reaction from intramuscular injections. The initial dose was 0.05 gm., followed by 0.2 gm. on alternate days. Total dose 1.6 gm. to 2 gm. In cases with noma the above quantities were given daily, without any noticeable ill effects. This is true for all ages and regardless of the condition of the patient. The cases with lung signs never showed any increase in lung findings which Dr. Scott felt justified in attributing to the injections of Neostibosan. The 14 children who were cured were from 3 to 11 years of age.
Average of children's ages 8 yrs.

" weight 43 lbs.
" total dose 2.10 gm.
" time under treatment 32 days

(The average for 10 of these patients was 22 days.)

**Adjuvant Treatment**

A liberal diet rich in iron bearing foods and vitamins is advisable, even when patients are suffering from dysentery. Liver and meat are included in the diet. Iron is prescribed, usually in the form of Blaud's pills. Transfusions are done when required. Although these additional forms of treatment are of value, it is only antimony in a suitable non-toxic form that can be relied upon to cure Kala-azar.

**General Results**

Treatment with Neostibosan usually causes a rapid amelioration of all symptoms. The temperature often falls after the second or third injection; there is a decrease in the size of the liver and spleen; an increase in hemoglobin, in the white and red blood cells; general improvement in strength and an increase in weight (see table). When, however, patients are under treatment for only two or three weeks, the time is too short to note the ultimate effect of the drug. It has been customary to do a spleen puncture before a patient is discharged, and if sufficient time has elapsed since the completion of treatment this may help one to decide whether further injections are desirable. The finding of L. D. bodies at this stage does not, however, necessarily mean that the patient is in need of further treatment, as he may proceed to an ultimate cure without anything more being done for him.

Of the first 30 cases in which spleen puncture was done on discharge, parasites were present in 6. Three of these are known to have been well after 11, 7, and 7 months respectively. It should also be remembered that the absence of parasites from spleen puncture does not necessarily indicate that the patient may not suffer a relapse. This is illustrated by one case in this series whose spleen puncture for L. D. bodies was negative on discharge; he nevertheless returned later with manifest signs of the disease and an enlarged spleen from which L. D. bodies could easily be recovered.
Results in 87 cases

Result known

| Well, 6 or more months after treatment | 28* |
| " 4 " | 10 |
| " 2 " | 5 |
| " 1 " | 4 |
| Died | 3 |

Result not yet known

| Discharged presumably cured but not traced | 37 |

(Some of these patients have been discharged only a few days so the result of treatment cannot be known for some months. 45 were discharged at least 6 months ago.)

Intensive Treatment

In India Napier treated successfully a series of patients with daily injections of 0.3 gm. of Neostibosan. Our experience, however, with this and other antimony preparations would seem to indicate that the Chinese patient does not tolerate them quite so well as does the Indian. As our patients have all been treated in the hospital, and since there is a constant demand for beds, we have tried to speed up treatment in most cases to the limit of what we thought possible without risk to the patient. We were able in this way to complete the course of treatment in a number of patients in less than 16 days. We might have given daily injections of 0.3 gm. to a larger number of cases, but from our experience with a number of patients who exhibited mild reactions it is our opinion that 0.3 gm. is too large a single dose to be given continuously to any but adults in fairly good condition. We also consider that it is better not to push the drug until toxic symptoms appear, but to give doses well within the tolerance of the patient, even though it may require a week or two longer to effect a cure.

Deaths

There have been three deaths in 87 cases. The first was a man 20 years of age who gained 7½ lbs. and was making satisfactory progress, but left the hospital contrary to advice when he had received only 2 grams of the drug. He returned to the Out-patient department on injection days and altogether

*This includes 2 cases which relapsed after the first treatment.
received 2.4 grams. The extra exertion in very hot weather evidently helped to lower his resistance. He was admitted 8 days later with tonsillitis due to a hemolytic streptococcus. Necrotic patches appeared on both tonsils. The gums became exquisitely painful and before death were necrotic in a number of places. (Autopsy not obtained)

The second (K. A. 468) was a child 9 years of age who complained of fever, a mass in the abdomen for 14 months and diarrhoea with mucus for 10 days. He had two to seven stools a day passed involuntarily. The child was very emaciated. Rales were present in the upper lobe of the right lung.

Blood transfusions, subcutaneous and intravenous saline and glucose was given. Twenty days after admission cancrum oris began in the left cheek. The stools contained many red blood cells and white blood cells. Leishman-Donovan bodies quite normal in character were found by spleen puncture at this time which was 3 days before death. Altogether 1.7 gm. Neostibosan had been given.

Dr. P. C. Hou who performed the autopsy reports the anatomical diagnosis as follows:

- Splenomegaly (due to Leishmaniasis, L. D. bodies found.)
- Multiple ulcers of transverse, descending colon and rectum. Less severe in ascending colon. B. dysenteriae, type Hiss, found in culture. Multiple minute haemorrhages in the mucosa of jejunum near the caecal valve.
- Bronchopneumonia of left lower lobe.
- Brown induration of lungs.
- Acute dilatation of the right ventricle, parenchymatous degeneration of myocardium. Ascites 1000 c.cm.
- Cancrum oris, left upper gum and right lower lip. Ulcers of larynx. Hyperaemia of liver and kidneys.
- Hydrothorax, 500 c.cm. left side, and 200 c.cm. right side.
- Malnutrition and general anaemia.
- Ascariasis.

Ulcers of skin at right nipple line between 4th and 5th ribs and of sacral region.

The third was a middle-aged woman with advanced pulmonary tuberculosis, who was very ill on admission. She was
given 3 injection of 0.1 gm., 0.2 gm., and 0.3 gm. Neostibosan at one and two days intervals. It is possible that her death was accelerated by the drug. (Autopsy not permitted.)

REATIONS

Reactions have been remarkably few, almost negligible as compared with the days when we used sodium antimony tartrate. However, reactions sometimes occur. Every case must be watched and treated accordingly.

Coughing, which was so often encountered after the injection of sodium antimony tartrate, has not occurred after injections of Neostibosan.

Lymphadenitis. Five and a half hours after the first injection of 0.1 gm. of Neostibosan, one of our patients (K. A. 466) complained of pain in one of the anterior cervical glands. The gland, which was enlarged, remained tender for a week. At the same time the white blood count fell from 4,350 to 1,600. Treatment was suspended as long as the gland was tender, but resumed and completed with Neostam without any untoward reactions. Lymphadenitis has at times been encountered when patients have been treated with antimony preparations, such as potassium or sodium antimony tartrate, sodium antimony thioglycollate, or stibosan. It appears to be caused by some toxic action of the antimony in the cells of the lymph gland.

Fever.

K. A. 508, Serial No. 79, a man 24 years of age, weighing 113 lbs. did not react well to antimony. After 3 injections of Neostibosan or a total of 0.5 gm. he had pain and tenderness in the submaxillary and cervical glands. Injections were continued every second day, instead of daily, and 0.2 gm. was given instead of 0.3 gm. After he had had 2.3 gm. his temperature ran up to 39.8 degrees C. He developed gingivitis with very painful gums and a few necrotic areas in the lower jaw. No further injections were given. The temperature fell after 5 days and the condition cleared up. Presumably this was a toxic condition due to an accumulation of antimony in the body.

A boy weighing 57 lbs. was admitted with a temperature of 38.4 degrees C. Before injections were commenced the temperature had become normal. After 5 daily injections, (an
initial injection of 0.1 gm. followed by 4 injections of 0.2 gm.)
his temperature went up to 40.1 degrees C. This was accom­
panied by rales and bronchial breath sounds in the bases of both
lungs; an increase in the size of both liver and spleen; an
increase in the total white blood count of from 1,400 to 12,400
with a relative decrease in neutrophiles of from 50 to 25 per­
cent, the large mononuclears remaining approximately the same.
A differential count done by Dr. Chang Hui Ch’uan by the
supra-vital staining method of Sabin & Cunningham showed
polymorphonuclear leucocytes 20%, lymphocytes 46%, large
mononuclears 22%, non-motile 12%.

After an interval of 6 days a further injection of 0.2 gm.
was given and was followed by a rise in temperature on suc­
ceeding days to 39, 39.4 39.8, 40 degrees C. His temperature
persisted for two and a half weeks before becoming normal.
Five weeks after the last injection of Neostibosan had been
given treatment was begun again, using Neostam instead of
Neostibosan. The injections were given on alternate days until
a total dose of 1.5 gm. of Neostam had been given. His spleen
had become somewhat smaller, the blood picture had shown
some improvement and there was considerable improvement in
his general condition.

He returned a few days ago, a month after discharge,
his spleen measurement was 7 cm. less than on discharge. The
rales in the lungs have cleared up. The water test for globulin
is negative. His general condition is good, and the presumption
is that he is cured.

Oedema and Bronchitis

In June 1930 we had in the hospital a patient, K. A. 503,
who developed oedema of the face and legs, and bronchitis,
following injections of Neostam. His condition became pro­
gressively worse and finally Neostibosan was substituted and no
further untoward effects were noted. This was a very severe
case, with a white blood cell count of only 1,700, hemoglobin
37%, red blood cells 1,900,000, temperature 38 to 38.8 degrees C.
He would probably have died if sodium antimony tartrate had
been used. He received altogether 0.8 gm. Neostam and
1.65 gm. Neostibosan. After Neostibosan was begun he made
satisfactory progress and left the hospital considerably im­
proved. He returned September 19th two and a half months
Neostibosan in Kala-azar

after discharge, having walked a distance of 80 miles in 4 days. When discharged his spleen was almost as large as on admission. Then it was 18 cm. now it is 4 cm. from the rib margin. He has evidently recovered. As this patient was given two drugs he has not been included in the series. (Photo)

Decrease in White Blood Cells and Increase in the Size of the Spleen

In March, a man 26 years of age (K. A. 486), was admitted with slight jaundice. His condition was fair. Temperature 39 degrees C. After the first injection of Neostibosan the urine, which had been normal on admission, showed numerous red blood cells and white blood cells, and some albumin. After 4 injections had been given the white count had fallen from 4,000 to 1,000. The spleen and liver both became appreciably larger and the general condition of the patient less satisfactory. Injections were resumed after a rest of 9 days and given as before every second day. The patient was making satisfactory progress, but left the hospital against advice, having had a total dose of only 1.35 grams of the drug.

Relapses. In the first 40 cases there have been 2 relapses. Sufficient time has not elapsed to tell how many there will be in the second forty.

The first, K. A. 432, a girl 8 years of age, admitted November 28th, 1928, weight 52 lbs. She was given 8 injections of 0.2 gm. at two or three days intervals, making a total dose of 1.6 gm. The spleen decreased from 9 cm. to 2 cm. from the rib margin and a spleen puncture on discharge was negative for L. D. bodies.

She returned March 23, 1929, ten weeks after discharge. The water and formalin tests for globulin were negative, no L. D. bodies were found on spleen puncture. She was considered probably cured.

She was readmitted December 13, 1929, eleven months after discharge, complaining of having had fever for the previous twenty days, with loss of appetite. The spleen was 15 cm. from the rib margin. The blood showed the usual increase in globulin, characteristic of Kala-azar. On spleen puncture L. D. bodies were found.
She was again treated with Neostibosan. This time 13 injections of 0.2 gm. each were given during 21 days. The spleen receded to 5½ cm. from the rib margin. After the second course of treatment she has remained well for over 6 months. Although a reinfection in this case is a possibility, this is probably a case which relapsed.

The second case to relapse was K. A. 435, a man 36 years of age, admitted February 20th, 1929.

The patient (weight 123 lbs.) was given in 15 days 2.8 gms. There were no reactions. The spleen decreased in size; his strength and general condition improved. He returned a month later, showing a continuance of the improvement with a further reduction in the spleen of 5 cm. and an increase in weight of 9 lbs.

On October 1, after an interval of 7 months, he was readmitted. Recurrence had begun 5 months after discharge. He responded rapidly to treatment, received 3.1 gm. and in May 1930, seven months after the second course, was quite well.

Complications

Albumin and Casts. Serial No. 22, K. A. 448. On admission, albumin and casts were present in the urine. After treatment was begun, the albumin increased in quantity, and red cells appeared in the urine. Treatment was discontinued for a few days and then resumed and completed. The urinary signs, instead of getting worse, tended to improve.

Two other patients showed red cells in the urine after beginning treatment, but in both cases treatment was continued without any untoward result.

Cancrum Oris. There were 5 patients with cancrum oris. The gangrenous area usually improved rapidly after injections with Neostibosan had been begun. In one of these patients the noma began while the treatment was in progress and cleared up soon after treatment had been completed. The chief local treatment employed was to keep the area clean. For this purpose hydrogen peroxide is very useful. Four of the five patients with noma recovered.

Dysentery. Serial No. 12, K. A. 438. Male, age 22. This patient on admission was passing 17 stools a day with blood and mucus. The third injection given, which was 0.25 gm. caused

Healing very well. Still attending the O.P.D. for dressings.


The gangrenous area improved rapidly after treatment was begun. About 3 months after treatment had been completed the child was brought back to the O.P.D.

The spleen was not palpable and the liver was not enlarged.

The child was able to eat well but was unable to open the mouth to the full extent.
Serial No. 19, K.A. 445 Age 18

Photo taken 10 days after admission
Admitted May 6th, 1929,
Spleen 36 cm. from the rib margin
Liver 5 cm. below the rib in mid-clavicular line
Discharged June 12th. (6 weeks later)
Spleen 9 cm. from the rib margin
Liver not enlarged
10 injections over 19 days. Total dose 2.1 gm.
Has not been heard from since discharge

Serial No. 74, Ch'en Kiang Ch'ing
Showing reduction in size of the spleen in 7 weeks

During the same period
W.B.C. increased from 3,800 to 6,800
R.B.C. increased from 3,421,000 to 5,000,000
Hb. increased from 55% to 80%
Weight on admission 60 lbs.
Present weight 80 lbs.
This patient returned with K.A. 568 for re-examination on Sept. 20th, 1930

Ch'en Ping Hau Age 17
On admission a very severe case.
Photo taken 11 weeks after discharge
Showing a reduction in size of the spleen from 18 to 4 cm. from the rib margin
This patient walked a distance of 50 miles to hospital for re-examination.
Refer to in the text under Reactions, Oedema and Bronchitis.
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nausea 2 hrs. after the injection. The following day 0.2 gm. also caused some nausea. This dosage, 0.2 gm. was continued on alternate days and the patient made an uninterrupted recovery. Total period of treatment 29 days.

The spleen, which on admission was 14.5 cm. from the rib margin, was just palpable on discharge. He was discharged in good condition, though still passing 5 stools a day. Neither amoebae nor dysentery bacilli had been found in the stool at any time.

Two months later he returned to the hospital on foot, two and a half days' journey from his home, which was 240 li away. He had gained 13 lbs. He said he had 3 normal colored stools a day. He felt and looked very well.

Frost-bite. Serial No. 8, K. A. 436. Came to the hospital because of frost-bite of both feet. Had also gangrene of toes, bed sores, bronchitis, malnutrition. Was found to have Kala-azar. Well 6 months after discharge.

Malaria. Serial No. 9, K. A. 434. Fever occurring during the course of treatment was proved by finding the parasite in the blood to be due to Tertian Malaria. Other complications: Hookworm disease, Ascariasis.

K. A. 499 was supposed to have a recurrence and was readmitted. The fever was caused by malaria. Malarial parasites were found.

Streptococcic Infection. Serial No. 13, K. A. 439. Male, age 21, weight 123.5 lbs. After 3 injections of 0.3 gm. Neostibosan, he developed a streptococcic abscess of the scrotum, accompanied by a temperature up to 40.5 degrees C. After the abscess was opened and the temperature had fallen, he developed erysipelas of the face. His condition was critical for 2 days but he finally recovered. Altogether he had received 1.6 gm. of the drug. No further injections were given. Six weeks after discharge, he returned on foot, with the patient mentioned above, a distance of 80 miles. His general condition was good and his strength had increased. The spleen was at the rib margin.
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Pulmonary Tuberculosis and Hookworm Disease. Serial No. 17, K. A. 443. Although he had hookworms, the eosinophiles were only 1%. After treatment for Kala-azar only, the eosinophiles rose to 8%. He was in hospital 32 days, gained 8 lbs. and was discharged in good condition. The spleen was considerably reduced in size.

Three patients out of the 87 had pulmonary tuberculosis.

Kala-azar patients who have also had tuberculosis of the lungs have, as a rule, improved when treated with antimony, whether in the form of sodium antimony tartrate or an organic preparation.

Additional Notes

Scanty L. D. Bodies. Serial No. 6, K. A. 433. Leishman-Donovan bodies were difficult to find. On admission, two liver punctures were negative, and from a spleen puncture, after the prolonged examination of 3 slides, only 3 parasites could be found. Half an hour after each of 5 injections, the patient complained of epigastric pain. No complaints were made after further injections. He was given 2.95 gm.

Conclusions

1. 2.8 to 3 grams of Neostibosan was found to be an adequate dose for most patients.

2. For Chinese patients we find that a daily injection of 0.3 gm. (as used by Napier in India) is too high a dosage for routine use.

3. By careful treatment with Neostibosan, if there are no serious complications, a cure rate of from 95 to 98% is to be expected.

4. When a reaction occurs with one drug, it is well to try another organic preparation.

5. It has not been possible to forecast which patient is likely to suffer a relapse.
<table>
<thead>
<tr>
<th>Serial Number</th>
<th>Kala-azar Number</th>
<th>Date of Admission</th>
<th>Duration of Symptoms in months</th>
<th>Sex</th>
<th>Age</th>
<th>C.2</th>
<th>O</th>
<th>D</th>
<th>Wt. in Lbs. Before Treatment</th>
<th>No. of days under Treatment</th>
<th>Max. Dose</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>L.D. Bodies</th>
<th>Condition on Discharge</th>
<th>No. of months after treatment known to be well</th>
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<td>48</td>
<td>89</td>
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<td>11</td>
<td>27</td>
<td>0.3</td>
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<td>45</td>
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<td>+</td>
<td>+</td>
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<tr>
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Neostibosan in Kala-azar
<table>
<thead>
<tr>
<th>Serial Number</th>
<th>Kalazar Number</th>
<th>Date of Admission</th>
<th>Kalazar Number</th>
<th>Age</th>
<th>Duration of Symptoms in Months</th>
<th>Wt. in Lbs. Before Treatment</th>
<th>No. of Infections</th>
<th>Max Dose</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>L.D. Bodies</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>Condition on Discharge</th>
<th>Remarks (Complications)</th>
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<tbody>
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<td>7</td>
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<tr>
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<td>6</td>
<td>6</td>
<td>119.5</td>
<td>135.5</td>
<td>7</td>
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<td>14</td>
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<td>6</td>
<td>6</td>
<td>06</td>
<td>125.5</td>
<td>12</td>
<td>32</td>
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<td>8</td>
<td>46</td>
<td>2150</td>
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<td>-</td>
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<tr>
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<td>18</td>
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<tr>
<td>16</td>
<td>422</td>
<td>39,080</td>
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<tr>
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<td>15</td>
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<td>42</td>
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<tr>
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<td>12</td>
<td>06</td>
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<td>+</td>
<td>-</td>
</tr>
<tr>
<td>21</td>
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<td>12</td>
<td>06</td>
<td>125.5</td>
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<td>13</td>
<td>42</td>
<td>2750</td>
<td>2,784,000</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Remarks:
- "Cured" indicates recovery after treatment.
- "Died" indicates death within 10 days after discharge.
- "Improve" indicates improved general condition.
- "Spleen just palpable" indicates the spleen was just palpable.
- "Spleen not palpable" indicates the spleen was not palpable.

Additional notes:
- Macular eruption after treatment.
- Severe Dysentery gained 13 lbs in Wt. Since discharge, spleen just palpable.
- Otis media, double.
- Palms, B. Hookworm disease.
- Hookworm disease.
- Splen just palpable 15 days after discharge.
- General condition improved.

The China Medical Journal
<table>
<thead>
<tr>
<th>Serial Number</th>
<th>Kala-azar Number</th>
<th>Age</th>
<th>Duration of Symptoms in months</th>
<th>Sex</th>
<th>No. of Injections</th>
<th>No. of days under Treatment</th>
<th>Liver before Treatment</th>
<th>Spleen before Treatment</th>
<th>W.B.C.</th>
<th>R.B.C.</th>
<th>Liver before Treatment</th>
<th>Spleen before Treatment</th>
<th>Condition on Discharge</th>
<th>No. of months after treatment known to be well</th>
<th>Remarks (Complications)</th>
</tr>
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<tbody>
<tr>
<td>33</td>
<td>430</td>
<td>16</td>
<td>43</td>
<td>M.</td>
<td>8</td>
<td>20</td>
<td>0.8</td>
<td>1.8</td>
<td>60</td>
<td>62</td>
<td>4000</td>
<td>3800</td>
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<td>+</td>
<td>Cured</td>
</tr>
<tr>
<td>34</td>
<td>400</td>
<td>6</td>
<td>22</td>
<td>F.</td>
<td>10</td>
<td>21</td>
<td>0.9</td>
<td>1.05</td>
<td>6</td>
<td>16</td>
<td>4200</td>
<td>3800</td>
<td>+</td>
<td>-</td>
<td>Otitis media, double</td>
</tr>
<tr>
<td>35</td>
<td>401</td>
<td>8</td>
<td>22</td>
<td>M.</td>
<td>10</td>
<td>21</td>
<td>0.8</td>
<td>1.8</td>
<td>17</td>
<td>17</td>
<td>4000</td>
<td>3800</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>402</td>
<td>8</td>
<td>29</td>
<td>M.</td>
<td>12</td>
<td>22</td>
<td>0.8</td>
<td>1.05</td>
<td>11</td>
<td>17</td>
<td>4000</td>
<td>3800</td>
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<td></td>
</tr>
<tr>
<td>37</td>
<td>403</td>
<td>5</td>
<td>27</td>
<td>M.</td>
<td>6</td>
<td>14</td>
<td>0.2</td>
<td>1.05</td>
<td>4</td>
<td>8</td>
<td>6800</td>
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<td></td>
</tr>
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<td>38</td>
<td>404</td>
<td>13</td>
<td>24</td>
<td>M.</td>
<td>10</td>
<td>13</td>
<td>0.8</td>
<td>1.15</td>
<td>12</td>
<td>10</td>
<td>5200</td>
<td>4000</td>
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</tr>
<tr>
<td>39</td>
<td>405</td>
<td>8</td>
<td>36</td>
<td>M.</td>
<td>9</td>
<td>10</td>
<td>0.85</td>
<td>1</td>
<td>10</td>
<td>8</td>
<td>2160</td>
<td>2100</td>
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<td>Died</td>
</tr>
<tr>
<td>40</td>
<td>406</td>
<td>9</td>
<td>47</td>
<td>M.</td>
<td>14</td>
<td>17</td>
<td>0.2</td>
<td>1.7</td>
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<td>28</td>
<td>1400</td>
<td>6400</td>
<td>+</td>
<td>+</td>
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</tr>
</tbody>
</table>
ACKNOWLEDGEMENTS

We are grateful to the manufacturers and their agent in Shanghai, Mr. Kornatz, who sent us a supply of the drug sufficient for the majority of the patients treated.

I am indebted to the other members of the medical service, Drs. Scott, Morgan, Mosse and Smyly, for help and permission to report cases which were treated on their service; and to the hospital residents and internes who did most of the work, especially the histories and laboratory examinations. Questionnaires were sent out by Drs. Wang T'ung An and Lin Lien Ch'ing. Dr. Wang also assisted in preparing data for the table.

REFERENCES

Napier, L. E., and Mulick M. N. (1928)

The Intensive Treatment of Kala-azar by Neostibosan.

Schmidt, H. (1928).

The Pentavalent Antimony Compounds in Tropical Medicine.

KALA-azar TREATED WITH NEOSTIBOSAN

Report of a Series of Cases
S. E. Bethell M.D. Choutsun, Shantung.

The cases included in this series have not been selected. They are the first cases treated with this preparation, and have been taken in sequence. A sufficient time has elapsed since the completion of treatment for us to form an opinion as to the value of the preparation.

The main details of the courses, and results of treatment are given in tabular form. In each case the lower line gives the result of an examination carried out from 4-6 weeks after the completion of the injections. It will be seen that no fewer than seven of the cases had complications so that from one point of view they were not ideal cases on which to test the efficiency of a drug.
Reaction

A marked feature has been the almost entire absence of reaction after injection. It was noted in two cases only. In one it took the form of an urticarial rash, and the other of a number of petechiae on the legs. In neither case did it interfere with the treatment. There has been no marked rise of temperature, and no vomiting. No case of albumuria has been traced to the drug. This absence of reaction has been one of the most characteristic features of the drug.

Condition of the Patient

Most of the patients were in very poor condition on arrival, but an improvement was quickly noticed on commencing treatment.

Course of Treatment

In nine cases the injections were given daily, and this method has proved very satisfactory, chiefly because of the rapidity with which the course of treatment could be completed. We have not noticed any difference in the results of treatment by this method as compared with alternate day dosage. This observation also applies to other cases not included in this report which have been treated with other preparations. Most of the injections have been given intravenously, but the intramuscular method has been used, and this seems to be equally satisfactory, and does not give rise to pain at the site of injection.

Results of Second Examination

The table shows these clearly. In the column “L. D. Body” the plus or minus sign indicates the presence or absence of this body in the Spleen (S) or Liver (L) as tested by puncture. In only one case was it found in the Liver, and in this case the condition of the patient continued to improve after discharge from hospital. In every case the Spleen had diminished markedly in size, but the Liver in every case but one had returned to normal size.

The blood picture showed an improvement, but a return to normal was not to be expected.

All the patients with the exception of No. 11 were in good condition. This patient improved rapidly after two transfusions of blood, and was eventually discharged in good condition.
Complications

These do not call for any comment. They did not cause any interruption in treatment. In case No. 11 Pneumonia developed after completion of treatment. It was thought at the onset that the temperature might have been due to a recrudescence of Kala Azar, and an injection of 0.05 gram of 693 b. was given. Although the patient was in a critical state no adverse effect was noted.

Several of the patients had albuminuria. The injections were continued at the usual dosage. Not only was there no increase in the amount of albumen, but on the contrary it disappeared as the treatment progressed.

The Glycosuria in case No. 10 cleared up without any other form of treatment.

Results

No death has occurred in this series. Four patients have been re-examined at periods of from two to four months, and they were apparently cured. Of one other case we have had several reports to the effect that the patient was in good health. There have not been any return cases and we think that it is likely that the cases, not seen since discharge, are also cured.

Having had considerable experience in the use of various antimony compounds in the treatment of Kala Azar we regard 693 b. as the most valuable both in use and in after results.

I am indebted to Dr. L. H. Feng of this hospital for considerable help in the drawing up of this report. All the laboratory examinations, and the injections have been undertaken by him.

We have to thank the makers for a generous supply of the above drug through their agents The China Export Import & Bank Co. Shanghai.
<table>
<thead>
<tr>
<th>Reactions</th>
<th>Liver</th>
<th>Splen</th>
<th>% R.H.</th>
<th>% R.G.</th>
<th>L. D. Body</th>
<th>Body Weight</th>
<th>Before and After Treatment</th>
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<tbody>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
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</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perforated ulceration</td>
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</tr>
<tr>
<td>Cheek Cervical Adenities</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrops Jaw</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

### General Condition
- Ray's Test: _
- L.D. Body: _
- Complications: _

### Body Weight
- Before: _
- After: _

---

*The China Medical Journal*
In a covering letter Dr. Turner writes:

We are much pleased with the results of treatment with Neostibosan and the only definite reactions we have seen from its use have been a moderate fever, or fever and chill beginning about an hour after injection and lasting one or two hours when the largest doses 0.3 gm. were given. This occurred in from 1/2 to 1/3 of the cases.

In the two cases that died, in No. 242 the temperature rose two days after injection and the patient died the next day. On admission he gave the picture of a severe typhoid somewhat delirious. It is impossible to say whether or not the treatment hastened his death. In Case 303 it is believed the treatment played no part. I am sure that in both these cases treatment should have been delayed until further observation.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Date of admission</th>
<th>Sex</th>
<th>Duration of Inv. in months</th>
<th>No. of Inj.</th>
<th>No. of cases under treatment</th>
<th>4x</th>
<th>Before Treatment</th>
<th>After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>X. in Inj. before treatment</td>
<td></td>
<td></td>
<td>4X</td>
<td>Before Treatment</td>
<td>After Treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>L. D. Bodies</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>REMARKS</td>
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<table>
<thead>
<tr>
<th>L. D.</th>
<th>Apparently cured</th>
<th>Died</th>
</tr>
</thead>
</table>

1. **Uncinariasis.**
2. **Ascariasis Whooping Cough.**
3. **Unspecified Ascariasis.**
4. **Bronchitis Influenza? Typhoid fever?**
5. **Uncinariasis Two admisions Interval of 43 days between infection 9 and 10.**
6. **Uncinariasis.**
7. **Pneumonia, lobar. Malaria.**
8. **Uncinariasis.**
9. **Uncinariasis.**
10. **Ascariasis.**
11. **Malaria, tertian.**
12. **Uncinariasis.**
13. **Bronchitis.**
14. **Uncinariasis.**
15. **Ascariasis.**
16. **Uncinariasis.**
17. **Malaria.**
NEOSTIBOSAN IN THE TREATMENT OF KALA-AZAR.

L. S. MORGAN, M.D.

Ellen Lavine Graham Hospital, Haichow, Kiangsu

The present report grew out of a suggestion from Mr. W. Kornatz of the pharmaceutical department of the China Export-Import & Bank Co. which company donated to this hospital sixty grams of neostibosan for the purpose.

We have, at this hospital, from one hundred to one hundred and sixty kala azar patients under treatment all the time. The greater part of these, of course, stay in one of our two kala azar hostels or with friends or at inns in the city. But we also constantly have a certain number in the hospital wards, these being taken in because of some special complications or of the extreme severity of the disease itself. Most of the cases reported here are from our wards, those from the hostels being chosen partly because of the severity of their sickness and partly because more complete data was available in these particular cases.

With such a number of kala azar patients (which is constantly increasing) and with a limited staff, it is not possible to do more in the way of diagnosis than is indicated in the accompanying tables. This, however, seems quite sufficient. With a clear precipitation test, enlarged spleen and, in many cases, enlarged left lobe of the liver, anemia of a more or less pronounced grade and poor nutrition, kala azar speaks loudly for itself as soon as it appears in the clinic room. There are, it is true, early cases, where the diagnosis is not easy. These require special observation and care in diagnosing.

We chose, then, for this series, the most advanced ten cases of kala azar we could find. We treated them just as we do all our kala azar patients. A fair and square trial of neostibosan. The charts show the results. Comment is almost unnecessary. This remedy is far less toxic, more effective by far and much speedier than any we have had the opportunity of using.

Several months ago, following the lead of Dr. J. B. Woods and Dr. L. N. Bell of Tsingkiangpu, we discarded all other
remedies for kala azar and confined ourselves to neostibosan alone. Since then several hundred of these patients have passed through our hands and we are ready to proclaim the change a great improvement. The accompanying tables could be duplicated from our records many times over with just as favorable results.

I cannot think of a more depressing sight than a crowd of kala azar patients as we used to have them when we treated them the old way. How very, very slowly they improved, how many and serious were the complications, how miserable they looked, how many, all too many, passed out before the treatment could do them any good. A hundred and fifty of these people with their friends and attendants in the dispensary courtyard waiting for their injections formed a spectacle which would make a convention of the world's worst pessimists look like a bacchanalian festival. In the words of a discouraged missionary friend they were "looking up to scratch bottom."

But the present neostibosan crowd is a far happier lot. Why not? Are they not getting well? Cannot everybody see plainly that they are rapidly improving? Why not be happy then? And they are.

As to complications. As everyone who has had anything to do with kala azar knows, its complications are terrible. Cough, extremely distressing, stomatitis and noma so often fatal, intractable epistaxis, pneumonia, all these directly due to the disease. Then the other serious diseases that group themselves around kala azar. Amoebic dysentery especially, the most intractable malarial infections, nephritis, streptococcic infections, diphtheria and anemia of severe type. All these we find are largely absent under the neostibosan and we are saved much hard, unsatisfactory work and much expensive medicine.

It is true that neostibosan is more expensive, to begin with, than antimony tartrate. Our patients complained of this at first. But it did not take them long to find that the new remedy cured so much more quickly and saved so many of the complications, that the extra initial expense was much more than compensated for in the long run.
### Kala Azar, History and Diagnosis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Resides</th>
<th>Nutrition</th>
<th>Color</th>
<th>Tem.</th>
<th>Pulse</th>
<th>Spleen</th>
<th>Liver</th>
<th>Precip test</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>12</td>
<td>M</td>
<td>Village</td>
<td>Poor</td>
<td>Anemic</td>
<td>100</td>
<td>90</td>
<td>Below umb.</td>
<td>Left 1. large</td>
<td>+</td>
</tr>
<tr>
<td>II</td>
<td>40</td>
<td>M</td>
<td>Town</td>
<td>&quot;</td>
<td>&quot;</td>
<td>102</td>
<td>90</td>
<td>Just above umb.</td>
<td>Normal</td>
<td>+</td>
</tr>
<tr>
<td>III</td>
<td>32</td>
<td>M</td>
<td>Village</td>
<td>&quot;</td>
<td>&quot;</td>
<td>98.5</td>
<td>72</td>
<td>Well below umb.</td>
<td>&quot;</td>
<td>++</td>
</tr>
<tr>
<td>IV</td>
<td>11</td>
<td>M</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>104</td>
<td>125</td>
<td>&quot;</td>
<td>&quot;</td>
<td>?</td>
</tr>
<tr>
<td>V</td>
<td>30</td>
<td>M</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>-</td>
<td>-</td>
<td>&quot;</td>
<td>Left 1. large</td>
<td>+</td>
</tr>
<tr>
<td>VI</td>
<td>13</td>
<td>M</td>
<td>Village</td>
<td>&quot;</td>
<td>&quot;</td>
<td>-</td>
<td>-</td>
<td>Below umb.</td>
<td>Both 1. large</td>
<td>++</td>
</tr>
<tr>
<td>VII</td>
<td>16</td>
<td>M</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>-</td>
<td>-</td>
<td>Well below umb.</td>
<td>Left 1. large</td>
<td>++</td>
</tr>
<tr>
<td>VIII</td>
<td>18</td>
<td>M</td>
<td>&quot;</td>
<td>Poor</td>
<td>Anemic</td>
<td>104</td>
<td>120</td>
<td>Level umb.</td>
<td>Both 1. large</td>
<td>+</td>
</tr>
<tr>
<td>IX</td>
<td>27</td>
<td>M</td>
<td>&quot;</td>
<td>Poor</td>
<td>&quot;</td>
<td>101.5</td>
<td>90</td>
<td>Well below umb.</td>
<td>R. 1. large</td>
<td>++</td>
</tr>
<tr>
<td>X</td>
<td>17</td>
<td>M</td>
<td>Town</td>
<td>&quot;</td>
<td>Poor anemic</td>
<td>100.5</td>
<td>110</td>
<td>&quot;</td>
<td>Normal</td>
<td>++</td>
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</tbody>
</table>

Note—Cases V, VI, VII treated in hostel. All others in Hospital Wards.

### Kala Azar, Neostibosan Treatment

<table>
<thead>
<tr>
<th>Case</th>
<th>Initial dose</th>
<th>Increase every 3rd or 4th dose</th>
<th>Final dose</th>
<th>Total No. injections</th>
<th>Total am't. injected</th>
<th>Total No. days treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>.05 gm</td>
<td>.05 gm</td>
<td>.3 gm</td>
<td>15</td>
<td>3.05 gm</td>
<td>38</td>
</tr>
<tr>
<td>II</td>
<td>.1 gm</td>
<td>&quot;</td>
<td>&quot;</td>
<td>22</td>
<td>5.7 gm</td>
<td>56</td>
</tr>
<tr>
<td>III</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>25</td>
<td>7.55 gm</td>
<td>47</td>
</tr>
<tr>
<td>IV</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>18</td>
<td>9 gm</td>
<td>42</td>
</tr>
<tr>
<td>V</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>24</td>
<td>6.4 gm</td>
<td>56</td>
</tr>
<tr>
<td>VI</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>21</td>
<td>5.7 gm</td>
<td>49</td>
</tr>
<tr>
<td>VII</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>23</td>
<td>6.8 gm</td>
<td>52</td>
</tr>
<tr>
<td>VIII</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>21</td>
<td>5.25 gm</td>
<td>49</td>
</tr>
<tr>
<td>XI</td>
<td>&quot;</td>
<td>.35 gm</td>
<td></td>
<td>29</td>
<td>6.85 gm</td>
<td>63</td>
</tr>
<tr>
<td>X</td>
<td>.3 gm*</td>
<td>.4 gm</td>
<td></td>
<td>32</td>
<td>8.7 gm</td>
<td>49</td>
</tr>
</tbody>
</table>

*Case X transferred from Antimony Tartrate treatment.  

Note—Average total dosage 6.5 grams.  
Average duration of treatment 49.9 days.  
Average number of injections 22.4.
KALA AZAR, Results of Neostibosan Treatment

<table>
<thead>
<tr>
<th>Case</th>
<th>Spleen</th>
<th>Liver</th>
<th>Precip. Test</th>
<th>General Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Barely palpable</td>
<td>Normal</td>
<td>Neg.</td>
<td>Good</td>
</tr>
<tr>
<td>II</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>III</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>IV</td>
<td>Not palpable</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>V</td>
<td>Barely palpable</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>VI</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>VII</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>VIII</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>IX</td>
<td>&quot;</td>
<td>&quot;</td>
<td>Slightly positive</td>
<td>&quot;</td>
</tr>
<tr>
<td>X</td>
<td>&quot;</td>
<td>&quot;</td>
<td>Slightly positive</td>
<td>&quot;</td>
</tr>
</tbody>
</table>

Note—Cases IX and X went home before the precipitation test was quite negative. Both went on account of serious situations at their homes.

KALA AZAR WORK IN THE TSINGKIANGPU GENERAL HOSPITAL

Preliminary Report

JAMES B. WOODS, SR., M.D. and L. NELSON BELL, M.D.

That Kala Azar has been prevalent in this section for many years there is little doubt, but due to lack of understanding of the disease and its treatment, few patients found encouragement to come, and it is only during the last two years that an attempt has been made to adequately care for them.

History of the Work—In January 1929, through the generosity of a friend, we were able to offer to treat all Kala Azar patients with the new “quick” medicine, rather than the old, slow, tartar emetic treatment. At that time we had only about fifteen patients under treatment, but as the news spread, and the greatly improved results were evident, the number of
patients increased tremendously until for September of this year alone, we admitted a total of 680 new patients to this department.

**Basis of Report**—This report is based on a total of 2539 patients admitted for the first eleven months of 1930—January to November inclusive—and of this number 1097 were treated as in-patients, cared for and observed as any regular hospital in-patient. The remainder, 1442, were quartered in inns outside of the hospital and came to the special morning Kala Azar Clinic for their injections.

As indicated in the heading of this article, this is simply a preliminary report of this work, the enormous mass of records and material available being entirely too formidable for us to seek to analyze now, with our limited staff and the pressure of our regular work.

**Facilities Available**—The in-patients have been quartered in the Boys' School buildings which are immediately adjacent to the hospital compound and the outside cases in numerous inns outside the hospital gate. The largest number of patients under treatment at any one time was 767. Much of the time of three doctors and an interne, and all of the time of six pupil nurses has been taken. There have been also two injection teams of three nurses each, giving injections at the same time. The head nurse for each team being one of much experience and proven dependability.

**Drug Used**—After experimenting with various products we have settled on *Neostibosan* as being the least toxic and giving the best results, and except for a few cases treated at the first of the year, all of the patients in this report have received that preparation.

**Dose**—With an adult in good condition, weighing an average of 120 lbs. the first dose is *Neostibosan* grm. .10, while a patient whose condition is not so good will receive grm. .075. This dose is increased by grm. .05 until a maximum dose of grm. .30 is given to in-patients and grm. .25 to ambulatory patients outside of the hospital. The dosage for children is worked out on a corresponding basis.

In connection with the dose to be given it has been our experience that the large doses reported as being given in India
and elsewhere cannot be tolerated by the Chinese in this section. However, we may have been too conservative as to the dose given in the past and the present tendency of our work is to increase its size. As would be expected, young adults, say from 18 to 30 years of age, are best able to stand the heavier doses.

**Frequency**—At present we give an injection on alternate days, but we are experimenting with a few favorable cases, giving daily doses, and are keeping the patient quiet and under constant observation.

**Amount Used**—The total amount of *Neostibosan* given for the average adult is 3. grms. but some receive as much as 3.25 grms.

Adjuvants of specific treatment are tonics, and when necessary, anthelmintics and cod liver oil.

**Symptoms of Primary Overdosage**—Vomiting, chill, high fever. Urticaria and cough sometimes begin immediately after an injection, but this does not necessarily mean an overdose, as much as too rapid injection of the drug, or an idiosyncracy for it.

**Symptoms of Cumulative Overdosage**—Nausea and vomiting, extreme weakness, hemorrhage from the bowels, high and violently fluctuating temperature.

It is our experience that after four or five injections the patient usually begins to show improvement, appetite returning, and a desire for meat and eggs, which many claim had been absent before, making itself felt. If, after four or five injections, the patient shows no improvement, careful search should be made for some concomitant disease such as Tuberculosis, Intestinal Infection, or Nephritis.

**Contraindications**—When a patient presents himself for treatment, and at the same time has his case complicated by nephritis, diarrhea, heart disease, or pulmonary tuberculosis, he should not receive injections until these conditions have been materially improved.

**Complications**—All who have had experience with Kala Azar patients know how low their resistance is, and how easily they contract other diseases. The complications we have been
faced with have been diarrhea, dysentery, nephritis, bronchitis, septic throat, diphtheria, and pneumonia, probably in about the order named. Noma, or ulcerated gums, are also not infrequently noted and in these conditions Neosalvarsan has been found most helpful, given intravenously and also applied locally to the noma, or ulcerating gums. The complications are sometimes fatal and always require heroic methods of treatment. For instance, a case developing diphtheria will usually require more antitoxin than an otherwise normal patient would.

**Instruction for Patients**—We have found very helpful short talks given to the patients gathered at the injection clinics. These stress care of the mouth and teeth, diet and internal hygiene, the avoidance of chilling and over exertion, the free drinking of water or tea, and instruction in some of the other elementary rules of cleanliness and care of the body.

**Results Obtained**—Many of the cases we have treated have been very late in presenting themselves and these are always the worst risks, but including these, with a total of over 2500 patients, the results are as given below. By picking the cases, as one would for surgical work, rejecting cases with small hope of recovery, this percentage of cures could be raised to possibly 95% but even the lower percentage including the worst cases justifies the relief which it affords some.

<table>
<thead>
<tr>
<th>Cured</th>
<th>1,914</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment not completed*</td>
<td>109</td>
</tr>
<tr>
<td>Deaths</td>
<td>43</td>
</tr>
<tr>
<td>Under treatment now</td>
<td>473</td>
</tr>
</tbody>
</table>

**Total** | 2,539 |

**Conclusion**—It is our hope, with the clinical material available, to work out a comprehensive report and set of statistics in the future. It is a great privilege to share in a work which holds out hope to such a large proportion of those poor people suffering with a disease which is, without treatment, almost certainly fatal.

*Patients left before receiving full treatment, some for financial reasons, some due to their serious condition.
DIAGNOSIS OF VISCERAL LEISHMANIASIS

T. M. YATES, M.D. Hwai Yuen, Anhwei

In regions where the disease is endemic the diagnosis of kala azar presents no special difficulties, except in very early cases and when masked by other conditions.

The first thing noted when viewing a patient ill for any length of time with kala azar is the severity of the condition. The "rearing back posture" of the patient, due to the weight of the enlarged spleen (and to a less extent, the liver) is usually very marked. With some individuals the pigmentation of the skin of the face, a black masklike discoloration extending over both cheeks and nose, is quite striking. There is generally some anemia, sometimes to the extent of a 30-40 haemoglobin; aggravated by the almost universal ankylostomiasis. The patient is often quite emaciated and this serves to accentuate the enlargement of the abdomen. The spleen outline is sometimes visible, extending even past the midline and down into the pelvis. Many of these patients have ulcerated gums, and noma is not uncommon.

There may be no fever present at time of examination. We have cases which come into the hospital, receive treatment and leave at the end of a month without once having had an elevation of temperature. These are more likely to be cases with a two or three year history. If present the fever is inclined to be irregular in type, depending to some extent on secondary infection. Extreme hyperpyrexia is common with such complications as pneumonia and dysentery.

There is a leucopenia present in almost every case. This is very marked generally and the blood count may be below a thousand. The average white blood count of thirty-six cases was 3,275. The increase under treatment is very rapid:—One patient who came in with a count of 2800 left four weeks afterwards with a count of 4800. This leucopenia is so consistently met with that if the pulp secured by the first liver puncture fails to show Leishman-Donovan bodies and there is a leucopenia present we feel justified in doing a liver puncture again with a fair assurance that the pulp will then show Leishman-Donovan bodies.
The spleen is extremely enlarged. The greatly stretched capsule can be conceived as being so tense as to continually threaten to split open. A blow or any trauma producing a slight crack in its capsule might therefore promptly prove fatal. With this view of conditions we approach spleen punctures with great trepidation. In a case which is clinically kala azar, and where we repeatedly fail to find Leishman-Donovan bodies in the liver pulp, we give a course of calcium lactate, watching the clotting time, and then following a day or so of this preparation, we have done spleen punctures. So far we have had no fatalities following these, but have had patients complain of abdominal pain for several days thereafter. The past year or two we have done very few spleen punctures, as we have had such a high proportion of positive liver punctures.

A diagnostic procedure which we consider much less dangerous to the patient and one which gives a high proportion of positive findings in cases clinically kala azar, is the examination of liver pulp secured by puncture of the liver by hypodermic needle.

The examination is as follows:—The needle used is a very fine one long enough to reach the liver. The syringe, (an ordinary Luer) and needle must be perfectly dry. Patient is prepared with iodine and puncture is made in the right lower costal region, in the anterior axillary line. Needle is inserted through the skin, fascia and muscle, patient is instructed to hold his breath and then as quickly as possible the needle is pushed into the liver, suction applied and needle withdrawn. The point of the needle is laid on a slide and the plunger pushed in repeatedly, forcing a fine spray or possibly a drop or two of fluid out over the slide.

Often there are only a few specks of spray forced out and yet examination will promptly disclose Leishman-Donovan bodies. If the fluid withdrawn is opalescent with no large proportion of blood, the chance of getting a positive smear is much greater than when fluid resembling blood is obtained. Occasionally there is nothing in the needle but after disconnecting the needle and the syringe a small drop of fluid may be found in the neck of the syringe. The slide is fixed and stained according to the Wright method, using eosin-azure or Leishman stain. When examined it should show liver cells. In searching through this, large numbers of Leishman-Donovan bodies may
Diagnosis of Visceral Leishmaniasis

be found, sometimes in clumps of ten or more, but more often scattered over the slide. Frequently the whole slide must be gone over carefully to find the two or more necessary for diagnosis. A very definite finding must be made before the slide is called positive.

In one hundred of our most recently discharged cases of kala azar, ninety-five gave a positive examination on the first liver puncture. The other five were positive on the second attempt, which was made a day or two later.

In our hands examination of blood smear has not proved a useful method. It is time consuming and not as fruitful in positive findings as the examination of the liver pulp.

Dr. C. B. Ray in the Indian Medical Gazette, vol. lvi, (1921) describes a test as follows:—Two drops of blood are mixed with twenty drops of distilled water. "Instead of a clear transparent solution, the blood of kala azar will show itself by its turbidity. On keeping the solution for some time a white flocculent precipitate will appear all through the blood, which on further keeping will form a marked deposit." In another paper Dr. Ray shows that the serum-globulin and especially the euglobulin are markedly increased in kala azar.

We have been using this Ray's test the past seven years on all cases suspected of having kala azar. Our routine is as follows:—When the patient is seen in the O. P. D. about two c.c. of distilled water is put in a small test tube such as the ones used in the Kahn test, or smaller. The blood is allowed to drip from a puncture hole in the ear of the patient until the solution is faintly pink. The test tube is inverted several times and then allowed to rest a few minutes, while the history of the patient is being dictated. (It was found that extreme cold interferes with the test, so the solution is kept somewhere near blood temperature.) After a minute or so the blood-tinged fluid can be seen to be forming a suspension, the particles of which increase in size until they become in some cases almost one mm. in diameter. These gradually settle to the bottom of the tube, forming a column of precipitate of variable height.

In an earlier series of ninety cases of suspected kala azar we found this test to agree with clinical diagnosis in all except one. Unfortunately we took only one liver puncture before treatment was begun and this also was negative. Patient was
treated with organic antimony preparation, diagnosis being based on clinical findings and patient improved greatly under treatment. This case came from a region where kala azar is common and probably really was kala azar.

The persistence of this test in a patient cured of Kala azar is still problematical. Of thirty-one cases examined after cure all showed a positive test at time of discharge. Several cured cases who returned for various reasons, e.g. to bring friends for treatment, etc., were examined and all showed this precipitate, the longest time being nine months after leaving hospital.

With the idea that possibly some information could be gathered regarding prognosis, progress of treatment, etc., the height of a column of precipitate in standard size tubes cast down from a measured quantity of blood into a fixed quantity of water was measured after the lapse of a constant interval of time. The quantity of water was two c.c. in a test tube of seven mm. diameter. The quantity of blood used was the amount delivered by filling the Sahli pipette twice and the reading was made one hour after mixing. Ten cases examined in this way are listed below. (See table.)

One notable case was No. 8711 who gained six pounds in weight and whose W. B. C. increased from 700 to 2800 and yet the amount of precipitate in the Ray's test was the same as at the beginning of treatment, viz 4 mm.

**Summary and Conclusions**

A brief review of some of the symptoms is given with diagnostic procedures. The spleen puncture procedure is counted too dangerous for routine use and presents apparently very little advantage, if any, over liver puncture. In one hundred cases clinically kala azar a positive liver puncture was secured in ninety-five on first puncture. The other five were positive on second puncture. The Ray's test is described. It gives a very high percentage of positive findings in cases of kala azar.
### Kala-azar as a Clinic Disease

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8679</td>
<td>1 plus yr.</td>
<td>103.6</td>
<td>2,200-7,200</td>
<td>2.5 mm.</td>
<td>4 mm.</td>
<td></td>
</tr>
<tr>
<td>8694</td>
<td>1 plus yr.</td>
<td>105</td>
<td>2,500-6,400</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>8699</td>
<td>4½ mos.</td>
<td>101.8</td>
<td>2,700-4,200</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>8674</td>
<td>3 plus yr.</td>
<td>102</td>
<td>1,600-2,400</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>8691</td>
<td>2 years</td>
<td>101.6</td>
<td>2,400-8,300</td>
<td>4</td>
<td>5</td>
<td></td>
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<tr>
<td>8651</td>
<td>1 plus yr.</td>
<td>102</td>
<td>1,800-3,200</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>8701</td>
<td>1½ yr.</td>
<td>104.6</td>
<td>4,100-6,700</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>8711</td>
<td>1 plus yr.</td>
<td>104.4</td>
<td>3,000-5,800</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>8716</td>
<td>10 mos.</td>
<td>102.2</td>
<td>6,000-</td>
<td>2.5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>8717</td>
<td>1 plus yr.</td>
<td>102.2</td>
<td>4,900-6,250</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Averages: 2,920-5,272, 3.7, 4.2

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**KALA AZAR AS A CLINIC DISEASE**

A. A. McFadyen, M.D. Suchowfu, Kiangsu

Fifteen years ago, almost as soon as we began to treat Kala Azar with Tartar Emetic, it was evident that within the limits of a fifty bed hospital the numbers seeking treatment could not be accommodated. Thus, forced by necessity, we began to treat them as outpatients, and feel that the results attained have been satisfactory.

**Diagnosis**

We do not feel justified in doing spleen or liver puncture on outpatients in order to confirm diagnosis. For diagnosis we rely mainly on the general appearance of the patient; his enlarged spleen and, or, liver; progressive anaemia, leucopenia, associated with persistent nose-bleed; this last being the symptom most often complained of by the patient. In Northern Kiangsu there is no schistosomiasis, and very little malaria, consequently we feel that the Serum Globulin test is confirmatory of Kala Azar. Quite a few cases of Splenic Leukemia present themselves for treatment, and insist that they are just like the other
big spleens. The "board-like" hardness, and, usually, excessive size of these Leukemic spleens, should put us on our guard. In the hurry of clinic work, we may fail to see that the cloudiness, caused by Leukemic corpuscles, does not settle down in the test tube, as does the excess serum globulin. However, the microscope discloses, readily, the excess of "whites," and makes clear the diagnosis.

**Age Incidence**

Kala Azar is a disease of childhood and young adolescence. In the six year period, covered by this paper, of the total of 2040 cases referred to, 1435 were under 20 years of age; a decided majority in the decade from five to fifteen, and with only one or two beyond the age of fifty.

**Treatment Tartar Emetic**

As Kala Azar is essentially a village disease, one of the great drawbacks to its cure in the O. P. D. is the lack of continuity in treatment. We have insisted on the patient paying in advance for the full course of treatment, and have thus secured fairly satisfactory attendance on "needle" days. From the first we have used Tartar Emetic, 1% solution, in dosage of \(\frac{1}{2}\) to 10 cc, according to age and physical condition of patient. It is extremely important to inject slowly, hence well to use a 20 gauge, or smaller, needle. With the best of care some will react—vomit—and to lessen the dosage does not always stop the reaction. One small boy vomited blood after each injection, yet went on to a good recovery. Tartar Emetic has proven fairly satisfactory for warm weather work, but decidedly irritating to the lungs during the winter months.

**Statistics**

A word of explanation is necessary in regard to the column marked "Uncertain" in the following statistics. It includes many whose treatment was satisfactory, but who quit without giving notice; some who received only one or two injections; and others who undoubtedly went home to die. Our estimate is that at least one-half of those in this column are still living.
Kala-azar as a Clinic Disease

Total Treated with Tartar Emetic—1934

<table>
<thead>
<tr>
<th>Age</th>
<th>No. cases</th>
<th>Cured</th>
<th>Deaths</th>
<th>Uncertain</th>
<th>Av. No. injections given</th>
<th>Average dose in cc</th>
<th>Total drug given in grammes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>568</td>
<td>258</td>
<td>87</td>
<td>223</td>
<td>43</td>
<td>3</td>
<td>1.29</td>
</tr>
<tr>
<td>10-20</td>
<td>863</td>
<td>325</td>
<td>85</td>
<td>393</td>
<td>48</td>
<td>5.1</td>
<td>2.44</td>
</tr>
<tr>
<td>20-30</td>
<td>412</td>
<td>185</td>
<td>61</td>
<td>166</td>
<td>46</td>
<td>6.9</td>
<td>3.15</td>
</tr>
<tr>
<td>30-40</td>
<td>127</td>
<td>61</td>
<td>18</td>
<td>48</td>
<td>46</td>
<td>7.2</td>
<td>3.32</td>
</tr>
<tr>
<td>40-60</td>
<td>24</td>
<td>9</td>
<td>3</td>
<td>12</td>
<td>40</td>
<td>6.8</td>
<td>3.35</td>
</tr>
</tbody>
</table>

Neo-stibosan

Tartar Emetic has so many obvious dangers that, despite the advantage of its cheapness, we welcome any better drug. Stibosan and Neo-stibosan, when first introduced, were practically prohibitive, on account of price. By a very limited use of both we were convinced of the lessened toxicity of the new drugs and their power to cure in a much shorter time. Now, since quantity production has put Neo-stibosan on the market, at a price within the reach of our smaller hospitals, we are shifting from the “slow” to the “quick” cure, and no longer offer Tartar Emetic as an alternative course. When Neo-stibosan was first introduced, following the Indian practice, daily doses of from .1 gramme to .3 grammes were given, for ten days. Some very severe reactions followed, with one or two deaths,
that were directly due to the medicine, or rather, its method of administration. Complete loss of appetite, with severe hemorrhages from bowel and stomach were the usual symptoms. A change was made to one injection every other day for ten injections. As it is extremely hard to convince a Chinese, whose spleen “lump” remains practically unchanged, that he is cured, we adopted the expedient, following the tenth injection, of sending them home for a month. At the end of that time they return and are re-examined. If the spleen has retracted satisfactorily, excess serum globulin disappeared, and general appearance good, we discharge as cured. If spleen is still large and serum globulin persists in excess amounts, we give an additional course of five injections. As yet, no one has returned after the second course of treatment. Aside from the rapidity of cure, the most striking fact in regard to Neo-stibosan is the lessened number of lung complications. This alone should result in the saving of an additional ten percent of the run of cases.

Results of Treatment According to Age of Patients

<table>
<thead>
<tr>
<th>Age: 1-10</th>
<th>Av. No. injections</th>
<th>Av. dose in cc</th>
<th>Total amt. used</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. cases</td>
<td>81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>30</td>
<td>13</td>
<td>.14</td>
</tr>
<tr>
<td>Deaths</td>
<td>1</td>
<td>2</td>
<td>.1</td>
</tr>
<tr>
<td>Age: 10-20</td>
<td>No. cases</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>31</td>
<td>15</td>
<td>.27</td>
</tr>
<tr>
<td>Deaths</td>
<td>2</td>
<td>8</td>
<td>.25</td>
</tr>
<tr>
<td>Age: 20-30</td>
<td>No. cases</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>21</td>
<td>13</td>
<td>.29</td>
</tr>
<tr>
<td>Deaths</td>
<td>5</td>
<td>7.6</td>
<td>.28</td>
</tr>
<tr>
<td>Age: 30-60</td>
<td>No. cases</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>12</td>
<td>17</td>
<td>.29</td>
</tr>
<tr>
<td>Deaths</td>
<td>4</td>
<td>7.7</td>
<td>.27</td>
</tr>
</tbody>
</table>

The distinctly higher death rate among the older patients is directly attributed to the attempt, on them, to bring about a quicker cure. We thought them safer risks than the younger children.
Complications

Pneumonia is the most frequent, as well as most dangerous complication. Sometimes it is frankly lobular, and some recover. More often it is bronchial, and nearly all die. Dysentery is a fairly common, and sometimes fatal complication. Canerum Oris, while rightly classed as an intercurrent disease, is so frequent in occurrence, and so distressing in results,—whether the patient lives or dies—that it should rank as one of the major complications of Kala Azar in China. Foul smelling ulcers, especially on the inner aspect of the leg, just above the ankle, are often met with. They persist even after the disease is cured. The above, with an occasional heart decompensation, are the usual causes of death in Kala Azar. It is rare that an uncomplicated case dies under treatment. Nearly all are the result of some violation of one of the prime requisites to success in treatment, a warm body, kept free from sudden chilling, a clean mouth, and a stomach full of easily digested food.

Advantages of Clinic Treatment

1st. From patient’s point of view, cheapness.

2nd. Does away with “herding.” They do not pick up diseases from each other.

3rd. Kala Azar is a walking disease, and they get a maximum of sunlight outside.

4th. Children are with their parents. After the first few needles, they are a happy and hopeful lot.

Disadvantages of Clinic Treatment

1st. Economy pushed too far. Parents apt to go to the cheapest inns, often sleeping on a mat on the ground. One cold March day I was called to see four children, and found them on the ground with only one comfort as cover, and all with pneumonia. Poor economy it turned out to be in their cases.


3rd. Diet. Not apt to be given enough of really appetizing food.
Hostel treatment would seem to be a real solution, in that sanitary conditions could be cared for, food and bedding attended to, without the necessary restrictions of hospital life. Our unoccupied school buildings may thus be utilized to advantage. The unheated dormitories are ideal for sleeping quarters, and class rooms can be fitted out as wards, in case of need.

Kala Azar patients do not need coddling, only the bare essentials are necessary. Disturb the routine of their lives as little as possible, but see that they sleep warm, brush their teeth, and are well fed. Under such conditions, with Nostibosan injections, from 80% to 90% of the run of cases should be cured.

A FEW FACTS ABOUT THE DISTRIBUTION OF KALA AZAR IN MANCHURIA
H. W. Y. Taylor, M.B., Ch.B., Moukden

In 1917 Leishman Donovan bodies were found by spleen puncture in an in-patient in Moukden Mens Hospital. Unfortunately, it is not known whether he was a native of the province or not. From that year until the present a small but persistent stream of cases, clinically Kala Azar, has trickled into the hospital wards. Most of these are children or young adults who come with striking regularity from the Liaoyang district, which lies south of Moukden. The number of cases has gradually increased from four or five to nine or ten a year.

Dr. W. Phillips of Newchwang reports a similar state of affairs from the area lying south of Liaoyang, namely Kaiping Hsien. He sees from ten to fifteen cases a year.

The following list of place names is not to be regarded as a complete survey of the distribution of Kala Azar in Manchuria, but only as a beginning in the attempt to collect exact information. From these places during the last ten years children or young adults, born and brought up in Manchuria, have gone to hospitals where spleen puncture diagnosis of Kala Azar has been made.

Along the Moukden—Dairen Railway
1. Moukden City 澎江城 2 cases in 10 years
2. Liaoyang Hsien 遼陽縣
A Typical History

Wang Wen Ho, age 9, from Min Chia Tien near Kuang Ning, a girl. Her mother noticed a lump on her left side 9 months ago. The lump gradually grew until it reached beyond the mid line of the abdomen. There has been no pain, no fever and no diarrhoea. Although the appetite remained good, the child became thinner and weaker.

She was brought to the hospital because her sister had had a lump of the same kind for one and a half years and then died. At least eight children in the same village were known to the mother to have similar lumps in their abdomens.

Temperature swung daily between 99.2 and 97.4. Pulse 90—105, Blood count. W.B.C. 3125; R.B.C. 2,900,000 Hb. 57%. Spleen puncture:—L. D. Bodies about 2 per microscopic field.
Urine:—Acid reaction, 1010—1015 specific gravity, shewed an occasional trace of albumen.

CONCLUSION

It is certain that Kala Azar is widely scattered over the South West part of Southern Manchuria. In this area two centres are known to be fairly heavily infected.

All the native cases treated at Moukden Hospital have come from the districts fed either by the Liao River or by the smaller adjacent streams all of which flow into the Gulf of Liao Tung 進東 濱。
PARAGONIMIASIS IN CHINA

A Preliminary Report

JAMES L. MAXWELL, M.D.
Department of Field Research, Henry Lester Institute, Shanghai

Owing to his frequent opportunities of seeing the disease in Formosa, paragonimiasis has always been a subject of special interest to the writer and since 1914 when, as noted below, his attention was first called to its presence in China, he has been constantly endeavouring to verify this claim but for various reasons he was prevented from succeeding in this until very recently. It is with special interest therefore that he is able to report here the final establishment of this claim.

HISTORICAL

The Paragonimus as a human infection was first identified by Manson in Amoy from a specimen of Ringer's obtained from an autopsy on a Portuguese patient in North Formosa where paragonimiasis is endemic.

The full account of this is given in the Imperial Customs Medical Reports No. 20, page 10, of the year 1880.

The specimen was sent to Cobbold who named it Distoma ringeri.

In a later number of the Reports, No. 22 page 55, Manson gives a very full account of the myracidium stage of development of the ovum.

For the next 30 years no mention was made of paragonimiasis in China as far as we have been able to ascertain until a claim was put forward in the report of the Inghok hospital near Foochow in 1913 that the disease was frequently met there (C.M.J. XXVII p. 263). Repeated enquiries for confirmation of this statement failed to elicit any definite evidence on the point, and Dr. Lewis who has been working at this station in recent years informed us a little while back that he had failed to find cases of paragonimiasis. In view of the constant communication between Foochow and Formosa where the disease is
endemic, it is possible that the cases referred to in the hospital report may have been imported from that island, though it must be confessed that considering the nature of the country round Inghok it would not be surprising if paragonimiasis were found there. Without definite confirmation, however, the verdict on the Inghok cases must be one of non-proven.

In 1914 Dr. Mabel Pantin of Dongkau, Fukien, some days' journey northwest of Foochow, was on a visit to Formosa and saw some cases of paragonimiasis at our hospital in Tainan. She then told us that she had seen similar cases in Dongkau and on her return to her station she wrote us as follows:

April 24th 1914.

Dear Dr. Maxwell,

I have got the *Paragonimus westermani* eggs quite proved to my own satisfaction at last. Since I returned from Formosa, I have been hunting up old cases and new and doing my best to prove I had been mistaken.

* * * * * * * * *

I am still finding new cases. One patient can expectorate blood almost at pleasure—always when angry—as I found in one of the text-books.

* * * * * * * * *

Your sincerely,

Mabel Pantin

The report here is perfectly definite but lacks full confirmation and this it has been impossible to obtain. Dr. Pantin fell ill shortly after and had to leave Dongkau and never returned there. The writer was away on war service for some years and by the time he returned to Formosa there was no doctor stationed at Dongkau. It is only of very recent years that a doctor has again been stationed there and the fighting and brigandage of recent years have made travelling in that district impracticable and have of recent months made even residence there impossible.
As regards the Dongkau patients all that we can say is that the evidence is very strongly in favour of their being definitely indigenous cases but full confirmation of this is not yet forthcoming.

The next report of value was one from, we believe, Dr. George Hadden of a single case in southern Hunan. We cannot at the moment give any further reference to this. It was not absolutely certain that the case was not an imported one, though this seems unlikely, and it is evidently impossible to trace it now. As regards this Hunan case then the probabilities are in favour of it being a native case of the disease but it certainly must be put in the doubtful list till further evidence is forthcoming from this region.

A few months ago Dr. Borthwick of I'chang mentioned a definite case in that region in which it seemed practically impossible for the patient to have been an imported case. Dr. Borthwick has however failed to get in touch with the patient again as he lives some distance away from the city. Here again the probabilities of the patient being a genuine Chinese case of the disease are very great but absolute confirmation is still lacking.

Finally Dr. Ying of Shaohing reported a couple of cases from the neighbourhood of that city which he had seen two years ago. The report was made in the *National Medical Journal* of October 1930 and through the kindness of the Editor we received a copy of the account of these cases before they were actually published.

Personal enquiries in connection with these patients have enabled us to confirm fully the indigenous nature of paragonimiasis in this region and a brief account of these investigations will now be given.

The foregoing summary includes all the cases known to the writer in which claims have been put forward that the disease occurred in China proper. In addition to the patients referred to above many individual cases have been reported from hospitals near the coast but apparently all such patients had resided...
and acquired the disease in Formosa, Korea, Japan or the Philippine Islands, in all of which countries the infection is more or less widespread.

The Essential Factors in Indigenous Infection

As it is hoped that the publishing of this paper will stir up a wide interest in the subject of paragonimiasis, it is well here to deal briefly with the factors on which an indigenous infection depends.

The ova-containing sputum having been expectorated into fresh water a myracidium develops, escapes from the ovum and enters the first intermediate host. This host is a small black-shelled snail, Melania, very common in streams in China. After further development a cercaria escapes from the snail and enters the second intermediate host, a crab or crayfish. It would appear that the crab Potamon is the most probable host in this country and is found commonly in fresh flowing mountain streams. The crab is then eaten raw and the infection thus conveyed to man.

The essentials for the spread of infection in any area may be summarised thus:—

1. Hilly country
2. A fresh flowing stream in immediate proximity to a village
3. The presence of melania snails in the stream
4. The presence of crabs or crayfish—most probably Potamon in the stream
5. The habit of eating raw crabs by the villagers. This is a popular habit we believe through China, the shell fish being merely dipped into hot wine and eaten raw.

The Shaohing District

The area in which we found the Paragonimus comprises a hilly district south east of Shaohing. Shaohing itself, famous as the centre of the Fasciolopsis buski area, is a large city some
Village of Tongwu

in which cases of Paragonimiasis were found.

Note: Stream running through centre of village in which were Melania and Polumon.
Paragonimus Eggs in Sputum
Woman aged 32

× 80

× 375
Paragonimiasis in China

thirty miles east and a little south of Hangchow. From the ferry across the river a fine motor road runs to the place.

Leaving Shaohing by one of the canals a sail of 15 li takes one to Le-kong from which place a road enters a pass through the low hills. A mountain stream, evidently quite a river in the rainy season, flows down this valley. A walk of some three to four miles takes one to Lan-din, the low hills gradually closing in as one ascends.

Lan-din is famous for the lily pavilion built in honour of the Emperor Kang-hsi and in which a huge stone tablet commemorates the visit of the Emperor to this spot. Beyond the pavilion is a large village where lime kilns abound and near which is a great quarry where limestone rock is blasted for the kilns. The village looks very prosperous and a mountain stream flows through the principal street. It was here that one of the cases reported by Dr. Ying lived.

A couple of miles further on and in a side branch of the main valley is the little village of Tong-wu where the second of Dr. Ying's cases came from.

Tongwu is a pretty little farming village also with a stream running through it. The stream abounded with snails, among them being many of the Melania species, crabs were also to be found in the stream, one of which has been identified as Potamon.

The Investigation and its Results

Dr. Sturton of the C. M. S. Hangchow Hospital very kindly accompanied the writer to Shaohing and on arrival there we visited the Baptist Mission Hospital where Dr. Ying had seen the two cases of paragonimiasis referred to. Owing to the absence of records of these cases from the hospital files and the fact that both of them had died in the interval of two years since he had seen them, the difficulties of the investigation were considerably increased. However Mr. Wong, the hospital technician, remembered the patients and knew the district from which they came. With the permission of the hospital authorities Mr. Wong very kindly accompanied us next day on our expedition and his services were of great value in locating our places and in assisting with the investigation.
Rev. J. G. Bird who knew the neighbourhood well also went with us and gave very material assistance.

With very limited time at our command owing to distance and our ignorance of the exact locality we were only able to deal, and that very cursorily, with the village of Tong-wu. This however appeared to be an ideal spot for such an investigation as the stream passing through the village street contained the intermediate hosts, the place was secluded and though the inhabitants were very friendly a foreigner had apparently never visited the village before and the intercourse with the outside world was evidently very limited. On questioning we got an immediate reply that crabs from the stream were freely eaten and eaten raw.

Dr. Sturton had brought some drugs with him and, when we had located the place from which one of Dr. Ying's patients had come, he started a little general dispensary work and there was no difficulty in securing patients. From these he selected one or two likely patients who complained of cough and gave slight indefinite physical signs in the chest and from them Mr. Wong obtained sputum and prepared smears for examination. The writer had brought with him a travelling microscope and established himself in the courtyard with such light as a curious crowd would allow him.

Of five sputa examined two showed paragonimus ova, one in small numbers, the other in very large numbers. Both of these cases were women, the former between 50 and 60, the latter 32 years of age. It was especially satisfactory to establish the diagnosis in women rather than men as there was little likelihood of the women having travelled much and as a matter of fact it was doubtful whether either of them had been far outside the village limits.

It was not our purpose at this time to attempt to gauge the extent of the infection but only to establish its presence as an indigenous disease, and this had been fully accomplished, so nothing more was done beyond collecting specimens of the sputum of these cases and snails and crabs for more careful examination at home.

It is planned to have a further and more complete survey at a later date when we hope it may be possible to determine the
relative incidence and the geographical extent of paragonimus infection in this region.

We believe that the findings here, combined with the very suggestive evidence brought forward in the earlier part of this paper, hint at least at a widespread paragonimus infection in China in such areas where the factors favouring the spread of the disease are to be found, and we hope that physicians in such regions will keep this possibility in mind and be on the outlook for cases of paragonimiasis. We shall be glad to render any help we can in such a search.

It only remains to the writer to express his very hearty thanks to all the members of his little party for the help they gave, one and all, in this investigation; without it the results here recorded could not have been attained.

CONTINUOUS INTRAVENOUS INFUSION

A. H. SKINNER M.D. Hankow.

Dr. R. H. Cox described an ingenious apparatus in the China Medical Journal Vol. XI, page 109 for the administration of salt solution into the veins in patients drained of water and salt by cholera.

Dr. J. A. Thomson, my former senior partner, employed the apparatus with good effect and was enthusiastic as to its value and described it in detail in a paper read at the last meeting of the C. M. A. at Hankow, (1909) (C. M. J. XXIV. 181).

Since that date we have used it on many occasions, not merely for cases of cholera, but also in any cases where by vomiting the patient is dehydrated,—especially in treatment of shock, ileus etc.

I venture to send you a description of the apparatus as we use it for the benefit of those who may not be familiar with it. I have seen in various medical journals accounts of continuous saline infusion systems that are inferior in many ways.
The accompanying two photographs should be referred to in the following:

**Figure I.** Shews the outfit in detail. The primary unit is formed by a filter-candle rubber-tube and intravenous cannula,—this is the essential part.

A is the cannula of glass, brass, or silver to tie into the vein,—it should be polished internally or dipped in hot paraffin wax just before use.

B is the glass inspection cannula.

C is a glass connection containing a short-stem thermometer (made by J. & J. Hicks, Hatton Garden, London) reading from 100° Fahr to 150° Fahr (38° Cent to 66° Cent) (Hicks Pattern No. 20334).

D: Drop-regulator (Canny-Ryall pattern: Allen & Hanburys New Catalogue No. 1759). As used in this scheme it contains air almost to lower end so that drops can be counted (it can thus be set to deliver so many hundred cubic centimetres per hour). Also it serves as a bubble trap. It can further if required be unscrewed into two parts and the upper part used as an intravenous cannula. The washer should be tested to make sure there is no leak. The tubing C to D should be about 2 to 3 feet long so as to permit the patient to change posture and to allow this part to be kept warm by a rubber bottle if needful. See that the stopcock of the Dropper works smoothly and that it is polished clean inside (old salt deposit removed).

E: Glass Y-connection. This we have introduced with a useful extra-opening (F) with spring-clip so that at any time additional remedies may be run into the vein, either accompanying the saline or replacing the saline.

For example, extra glucose, extra salt, citrated blood etc. may be run in, but for the last-named use a syringe barrel with a plug of glass-wool to hold back clots. Also drugs such as pituitary extract, eserine, caffeine, sparteine, strophanthin, calcium gluconate can be added to the saline by this route. The patient is thus relieved of extra punctures, and the drugs can be given as slowly as necessary.
Continuous Intravenous Infusion

G is the upper spring clip to shut off the saline (if so desired) while giving fluid medicaments at F.

H: The Filter-Candle with its nickle outlet-tube bent as a siphon. Two of these are kept ready, and autoclaved wrapped in a towel or paper. They are put into the boiling saline when the outfit is prepared so that they come to the patient saturated with fluid and free of contained air. After use they should be scrubbed with a hard brush and washed free of salt.

I: The support for J, the water-jacket which holds the copper can (K) containing the saline solution. J should be kept full.

The support (I), originally, I believe, a form of opium lamp, contains the lamp (P) burning alcohol (hot flame) in winter, and bean oil in summer. The size of the flame, if so desired, can be regulated by light collars of metal or porcelain with a light wire handle placed round the wick—or a lamp can be used that has an arrangement for raising and lowering the wick. The bath-thermometer (O) indicates how much lamp heat is needed. (Dr. Cox worked out an ingenious system of controlling the flame automatically by means of a rising and falling collar,—a see-saw controlled by sucking oil from a reservoir at the opposite end of the beam and connected by a rubber tube to an air-cell in the saline in K. This extra fitting we do not use, as attention to the lamp by a nurse of ordinary intelligence suffices).

L is the siphon which feeds the can K from the six-pint reservoir M. There are two of these large square cans (of nickelled copper) and they serve to boil the whole apparatus and extra saline. The siphon is formed by two glass upright tubes, a connecting rubber tube and a screw-stopcock.

N is a rubber ball-syringe, boiled with the rest of the apparatus, used to draw the saline through the siphon, delivery tube, etc.

Figure II which shows the whole apparatus set up for actual use is self-explanatory.

The patient’s appearance, the amount and the consistence of the urine are the best criteria of the rate at which the fluids
are to be given. Rather than remove the cannula from the vein too soon, let it remain an extra day flowing at minimal rate until it is certain that the patient is well out of danger.

In conclusion: The advantages of the filter are obvious. No saline can be prepared from any water containing a trace of lime without insoluble particles separating out. Furthermore powdered glucose can be thrown into the container \((K)\) and stirred to dissolve and safely given thus into the vein,—thereby dispensing with the expensive ampules of the sterilised glucose solution.

Dr. Maxwell kindly referred me to Dr. Cox's full account in the *Customs Medical Reports*, No. 55, of Oct.-March 1897-98, wherein he gives notes of the history of the method, his technique as modified from Dr. Little's original instructions, and the reasons for insisting on treating the cholera patient from the first by this method and seeing him through not only the collapse stage but also any return of collapse by this effective treatment. He gives notes of eleven severe cases treated with only four deaths. The later history of this method in cholera confirms his views, and now both in Shanghai and here the mortality in patients who receive the treatment in the first few hours (assuming they are otherwise healthy) is very low. Apart from Cholera, the *Indications for Continuous Intravenous Infusion* are conditions of dehydration resulting from vomiting or purging or both, whatever be the cause. Salt has to be made up also, and if the patient is shrivelled and shrunk, then extra salt has to be given in the first hour. Haden & Orr (*B. M. Journal*, Epitome No. 419:1929, Vol. I) state that a patient of 11 stone (say 70 kilogramme) can use per hour 250 cub cm water and 4.4 gramme salt and 60 gramme glucose. We prefer to use half this amount of glucose as it is less irritating to the vein, and no insulin need be given.

Once the loss of fluid and salt has been made up, then the fluid can be left to run in at a rate of three litres per day (normal saline only) until the patient is out of danger or until operative measures (e.g. relief of intestinal obstruction) are undertaken. And here it may be pointed out, that if one assistant carries the can holding the filter, the patient can easily be moved to the operation table and the infusion continued throughout.
Continuous Intravenous Infusion

In a prolonged infusion I do not see the need of exceeding 1% of glucose once the patient has rallied, and any amount between 0.1 and 1.0% is not likely to irritate the vein.

Following Locke's Formula, it may be stated that the following can be given continuously:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Grams</th>
<th>Per Litre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Chloride</td>
<td>9.0</td>
<td>per litre</td>
</tr>
<tr>
<td>Calcium Chloride</td>
<td>0.2—0.24</td>
<td></td>
</tr>
<tr>
<td>Potass Chloride</td>
<td>0.4—0.42</td>
<td></td>
</tr>
<tr>
<td>Sodii Bicarb</td>
<td>0.1—0.3</td>
<td></td>
</tr>
<tr>
<td>Glucose Puriss</td>
<td>0.1—2.0</td>
<td></td>
</tr>
</tbody>
</table>

The first and the last substances may be doubled in amount for a time if required.

Throughout the treatment (and certainly every hour while percentages greater than those just named are being administered), the urine should be recorded hourly as to (1) amount, (2) reaction, i.e. pH to an Indicator showing range from 4 to 9, (3) Specific Gravity, (4) Sugar, qualitative only, and (5) Chlorides, rough quantitative test.

The solution devised by Bayliss to meet cases of haemorrhage, we have not given through a filter candle, but we see no reason why it should not be used, allowing a little extra height to make up for the slower filtration.

It is:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Grams</th>
<th>Per Litre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Chloride</td>
<td>20</td>
<td>per litre</td>
</tr>
<tr>
<td>Potass Chloride</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Calcium Chloride</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Powdered Gum Acacia</td>
<td>50.0</td>
<td></td>
</tr>
</tbody>
</table>

And this would be especially useful in cases of shock and haemorrhage at the commencement of the infusion.

At the minimal rate (one litre per eight hours) there cannot be the slightest risk of embarrassing the heart.

If for any reason the cannula has to be removed and the vein is still patent and can be used again, do not tie the vein itself (i.e. the proximal end in which the cannula has been tied), but pass a straight needle with a linen thread transversely through the skin and under the vein, tie a slip knot and put on a compress of citrate solution. (Surgery, Gyn & Obstetrics, Vol. XLIX, page 208).
Postscript:

In "Lancet" of November 1st, page 952, Mr. Chas. Donald suggests that the chief factor in lowering the mortality due to Scalds and Burns is the treatment of the Toxic state by general (as much as by local) methods, and of general methods, the chief is free administration of fluid with salt and glucose.

Finally it may be said that a patient resents the vein route far less than the subcutaneous, and that alone makes it worth while using the vein when dosage, temperature and filtration are easily controlled.

(See Lancet: 1930, ii, p. 952, and the references there given to treatment of toxaemia from burns by fluids).

A CASE OF PANCREATIC STONE*

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Pancreatic lithiasis is of very rare occurrence both clinically and at autopsy. Since the first report made by Graffe in 1667, Osier was able to collect previous records of only 70 cases up to 1900. Later a few more reports were made by various authors and the grand total of cases discovered either by operation or by autopsies up to the end of 1925 is only 104 cases.

Opie reported only two cases of pancreatic stone among 1500 autopsies performed by him. Seeger in 1925 collected 22 operation cases, added his own case and analysed the symptoms, while at the end of the same year Hartman reported four more cases from the Mayo Clinic and the present description of symptoms is largely cited from the information given by these two authors. The present report is the first of its kind in Korea and the authors’ effort to find a report of a similar case in Japanese literature has so far failed.

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The pathogenesis of pancreatic stone is far more obscure than that of gall stone. Biliary stasis, cholelithiasis and inflammation of the biliary tract leading to the formation of gall stone may each have its counterpart as possible factors in the pancreatic stone formation. Cholesterinaemia and a disturbance of calcium metabolism, probably due to dietetic error offers an additional hypothesis. However, the occurrence of a comparatively large number of cases of choletheliasis and such a small incidence of pancreatic stones and the very rare occurrence of these two together indicates that local factors play a more important role in the formation of stones both in pancreas and in gall bladder.

In regard to the symptoms of this disease, so varied and ununiform are the descriptions that none of the following points are at all pathognomic.

According to Seeger and Hartman in their analysis of symptoms, we may say that the age variation is great, extending from 20 to 63 years with an average of 43 years. Sex variation is found to be in the ratio of 8 males to 16 females. Pain especially in the epigastric region is a common feature and was described in 19 cases out of 27. Slight tenderness was present in 2 cases and was altogether absent in 8 cases. The nature of the epigastric pain also varies greatly; sometimes it is paroxysmal or colicky, while at other times it is dull and radiates to the lumbar or dorsal region, or even more commonly downward to the pelvis thus reminding one of renal calculi. Ordinarily it occurs 2 or 3 hours after meals, while sometimes it has no relation to the taking of food. Jaundice was observed in only 7 cases and was absent in 20 cases. Gall stone was found in only 2 cases in the whole series. Glycosuria either early or late in the disease was discovered only twice. Other signs such as loss of weight were noted in 6 cases, enlarged liver was present in 2 cases, tumor was palpable in that region in 2 cases. Two cases had fever. Greasy frothy stools were noted in 5 cases. A long standing history of duodenal ulcer was found in 2 cases. Summing up these facts it is seen that the diagnosis of this disease is very difficult and only two cases of preoperative diagnoses were made. In others duodenal ulcer or gall stones were diagnosed and in others laparotomy for cholecystitis or for trouble in an ovary revealed pancreatic lithiasis.
Case Report

Our patient named Kim was a woman aged 20 who was admitted to the medical service on August 25, 1930 and died September 23, 1930.

The chief complaints were dyspnoea, retention of urine and dyspepsia. Her present illness began about 5 months ago when she first noted oedema of limbs and indigestion.

Her husband and two children are all alive and well. Her past history was negative.

Physical examination showed anemia and oedema of the whole body. The heart showed slight palpitation while the pulse was weak, irregular and rapid. The lungs were normal. There was a slight abdominal tenderness in the epigastrium.

Laboratory findings. Urinalysis: scanty reddish alkaline urine showed albumin and sediment; output of urine rarely exceeded more than 150 cc per 24 hours. The blood report was: hemoglobin 55% T., white cells 7,800. A diagnosis of Chronic Nephritis was made.

Bedside notes. The temperature was 37.4°C on admission and fluctuated between 37° to 38°C but became subnormal for 7 days previous to her death. The pulse was 90 at the time of admission, ran between 80 and 100 and a few days before death dropped a little.

Prostration was marked and she passed many sleepless nights. She died on September 23rd at 6 a.m.

Post Mortem Findings

Autopsy was made on September 25th, 52 hours after death.

General description. The body was that of a young female poorly developed. The breasts and external genitals were imperfectly developed. Rigor mortis was absent in the limbs. Post mortem staining was present on the back between the scapulae in the form of two erythematous patches at the centre of which were found multiple dark spots. The body measured 145 c.m. in length. The cornea was glazed and the pupils were equal, 0.6 c.m. in diameter. The abdomen was slightly sunken and dark blue in color. Oedema especially of the lower limbs was marked. Conjunctival and oral mucosa showed a little jaundice. Teeth were normal in size and shape but extensive pyorrhea was present. The cartilage of the alanasi was missing.
On opening the abdomen the intestines were pale and moderately distended and contained about 100 cc of reddish yellow turbid fluid in the pelvis. The appendix was 6.5 c.m. in length and no adhesion was found. The general shape and position of the viscera were normal.

The left kidney weighed 100 gms and measured $10 \times 5 \times 2.5$ c.m. It was slightly swollen. Embryonic lobulation was marked. The capsule peeled easily and was smooth and dark red in color. The cut surface showed a yellowish cortex and the boundary between cortex and medulla was not clear. The renal pelvic mucosa was thin and anemic. The right kidney weighed 80 gms. and measured $9 \times 5.8 \times 2$ c.m. This also was swollen in appearance while the capsule peeled readily and the general appearance was similar to that found in the other kidney.

Microscopically there was a marked atrophy of the glomeruli throughout but Bowman's capsules were distended and partially filled with albuminous coagulum. The convoluted tubules were swollen and the lining cells had already lost their nuclei and clumped together after desquamation. Small amounts of haematoxylin pigments were found within the lining cells of the collecting tubules. Blood vessels were few in number and empty.

The liver was considerably enlarged weighing 1564 gms. and measuring $30 \times 15 \times 9$ c.m. The surface was brownish yellow in color and smooth. The cut surface showed yellow dots surrounded by deep brown rings and was smooth and glistening like yellowish lard in appearance. The biliary passages were thickened and contained small elongated flat worms within their lumen. These were found to be \textit{clonorchis sinensis}. Microscopically these yellow dots are lobules consisting of liver cells showing extreme fatty degeneration; each cell was loaded with fatty globules thus distorting the radial arrangement of cords and occasionally obliterating the central vein. Cells at the periphery of each lobule were not affected by this fatty infiltration. The interstitial fibrous tissue was not increased but a mild degree of lymphocytic infiltration was present.

The gall bladder was rather shrunken and contained about 10 cc of yellow tenacious fluid and at the bottom was found a clump of black flat worms (\textit{clonorchis}).

The spleen was slightly enlarged and weighed 112 gms. It measured $10.5 \times 7.8 \times 3$ c.m. The organ was deep red in color, roughly triangular in shape with upper tip rather sharp. It was swollen and the surface was smooth and glistening. Many dark red patches were found scattered especially along the anterior margin. The cut surface showed dark red in color, rather firm in texture and the dark spots were slightly elevated from the surface. A small amount of serous fluid oozed from the cut surface. Neither nodules nor necrosis were noted microscopically. It showed extensive hemorrhage and acute inflammation. The fibrous tissue was not increased.

The pancreas weighed 147 grams and measured $20 \times 3.5$ c.m. It was completely enveloped in a greenish yellow fatty substance and showed the so called pseudo-hypertrophy of this organ. On palpation there were many
hard nodules within the organ. On a section the pancreatic tissue showed only as a thin membrane forming many pockets or cysts and the pancreatic duct was dilated and contained many calculi of varying sizes. The largest one was found in the duct near the head of the pancreas and was the size of a pigeon egg measuring 3×1.3×0.8 cc and weighed 5 gms. Two others were only half this size; many were found as small as sand. They were all hard and rough on the surface covered with a greenish grey tenacious fluid. The stone was too hard to break with the fingers and a metallic sound was heard when it was touched with the edge of a knife.

The intestine was oedematous and petechial spotty hemorrhage was noted. Adrenals and thyroid showed nothing in particular. The thymus showed atrophy. Genital organs also showed no noteworthy abnormality.

The heart showed marked brown atrophy and oedema. Fatty degeneration was present and some of the muscle nuclei were large and stained sharply (compensatory hypertrophy).

The lung showed congestion and oedema was marked. Microscopically bronchopneumonia and collapse of a portion of the lung were noted.

The chemical analysis of our pancreatic calculi was done through the kindness of Dr. Miller of the Chosen Christian College and the report was that it consisted mainly of calcium carbonate with a little organic matter on the surface. No phosphates were found.

Thus this pancreatic stone is, like almost every case as hitherto reported, composed mainly of calcium carbonate in this way differing from the ordinary gall stone.

The microscopical section of the pancreas showed areas of parenchymatous tissue with traces of islands still recognizable inside of a thick fibrous capsule.

REFERENCES


JOTTINGS FROM THE CONGRESS OF DERMATOLOGY

Copenhagen, 5-8 August, 1930

F. REISS, M.D.

The Congress was devoted to three main topics; first, the etiology and pathogenesis of eczema, second, immunity, reinfection and superinfection of syphilis and finally the treatment of tuberculosis of the skin. These subjects were discussed by leading authorities in 23 lectures, and in addition to this 176 lectures were given on other various topics. The greatest interest was shown in the discussion on eczema. Darier represented the French school, Jadessohn the German, Whitfield the British and Pusey the American school.

Great interest was aroused in connection with the discussion of Darier on etiology and pathology of eczema. He still adheres to the morphological classification and he is one of those who wishes to keep the eczema nomenclature. According to his opinion it is not important whether we regard eczema as a separate individual disease or whether we put it in the group of syndromes. What he considers as most important is the histological change, especially the reaction of the epidermis which can be produced either by exogenous or endogenous causes. In his conclusion he says that eczema is subject to certain manifestations of intolerance of the organism against substances which are or could be harmful. This manifestation, which can be due to an infinite number of causes, is especially characterized by a pathological lesion called spongiosis. Whether we regard eczema as a disease or as a syndrome it makes very little difference because he regards eczema as a special reaction of intolerance of the skin towards substances which are or could become harmful. He goes on further to say that intolerance is a sort of sensitiveness, which sensitiveness is one of the most characteristic features of life. As life is an ensemble of conditions which resist death, consequently all living organisms are sensitive (or one may call it sensitized) to intolerance. One could also say that as allergy is a manifestation of sensitiveness it is life itself, consequently he believes that we are all allergic and consequently prospective subjects to eczema.

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Jadessohn comes to a more definite conclusion and he proposes that from the group of eczemas should be excluded firstly, the pyodermias even of eczematoid nature, eczematoid diphtheria of the skin and the so-called seborrheic eczemas, mycotic and microbial dermatitis and the so-called lichens (Lichen Vidal, Prurigo Besnier). On the other hand he proposes that we classify amongst eczemas; first of all all acute dermatitis of chemical and physical origin with the characteristic histological changes which have been produced by one single first contact or by sensitization, and naturally all chronic or relapsing conditions of the same nature.

Bruno Bloch defines eczema as a reaction of the skin of a hyper-sensitive individual against a substance introduced into the organism either in a cutaneous or hematogenous way, which in a normal person would not produce any pathologic changes, or if so, only in a much higher dose. These cases of eczema he defines as allergic eczemas, whereas in the second group of eczemas he could not give any etiological cause, although he believes that in the long run most probably some allergical reaction will be detected. In cases where the eczematogenous cause could not be detected, the etiological researcher on eczema has for the time being to rely much on the disturbances of metabolism. The most important practical steps that have been taken in the direction of etiology are the eczema tests, which should never be omitted, with careful consideration of the occupation, of the surroundings and the mode of living of the patient. He emphasises the importance of eczema tests inasmuch as the success of our treatment depends on the discovery of the respective allergens.

Oppenheim (Vienna) gave a very detailed description of occupational eczemas and he emphasised that besides constitutional genesis the role of heat, cold, light, dust and water has an important part in the production of eczema. In a series of cases he showed that the skin tests are not constant, for example a painter who at a certain time showed reaction to carbol and iodine changed, and became sensitized to petrol-ether, etc., therefore he believes that specific sensitization cannot be successfully applied as in other cases of eczema, whereas he advocates that in cases of occupational eczema a non-specific desensitization should be preferred.
Pusey of Chicago does not believe in the justification of the use of the word eczema and he believes that modern usages denote simply a certain form of dermatitis. In spite of intensive study of modern methods for at least two generations we are not able, according to his opinion, to produce any criterion which would establish an essential distinction between eczema and dermatitis. The fuller our knowledge is the more significant is the fact that we find no distinction between these two artificially separated diseases. He points out that there are eczemas in normal skins from excess simply of external factors or prolonged, intense or excessive exposure to irritants that go beyond the point of normal resistance of the skin. We must concede that the disturbance of balance on the side of undue exposure represents the pathogenesis of eczema in a considerable number of cases. On the other hand, a very large number of cases frankly excited by external causes present a situation where the disturbance of balance is upon the side of internal factors—lowered resistance of the skin—so that substances that are harmless to normal skin cause a reaction in these. It is in cases in which we see a disturbance in balance through lowered resistance in the skin or, expressed in another way, increased sensitiveness which is behind the etiology of eczemas due to external irritants. Therefore he believes that when speaking of allergy as an explanation of eczema we are simply juggling with words and substituting for the old word hyper-sensitiveness a new word allergy which means no more and gives us no clearer conception of what we are dealing with. The word allergy involves naturally a new conception of the mechanism of the reaction of inflammation, that is definite, and it greatly enlarges our understanding of the reaction that we call eczema and the mechanism by which it is produced. He believes that Bloch attaches a far-reaching importance to allergy in clearing our knowledge of the pathogenesis of eczema as well as many other specific dermatoses.

Whitfield demonstrated with a few remarkable examples the question of auto-sensitization in eczema. He believes that there is a possibility that persons like physicians and nurses may become sensitized to eczema from repeated contact with a patient's serum.

In connection with the discussion of eczema, two lectures seemed to me of quite considerable importance. Barber of
London investigated allergic eczema and the urticarias, as well as the asthmas and migraine, and he found that the urine and blood showed certain biological and chemical changes. He termed this reaction an ether-reaction, by which he could separate in a number of cases from the urine of such patients a complex of nitrogenous substance which showed all the chemical properties of proteose. In acute and allergic cases he could prove that it contained a specific antigenic substance upon which the symptom or symptoms depended. Injections of minute doses of it either intradermally or subcutaneously produced exacerbations of the symptoms and in repeated doses at suitable intervals it has been used successfully in the treatment of allergic conditions.

Urbach demonstrated a similar substance which he calls pro-peptan and which he produced from the respective proteins in relation to allergic conditions. This pro-peptan can be given orally and has not only a diagnostic value but seems to have a far-reaching importance in the treatment of allergic conditions. The advantage of this method is that it can be prepared beforehand and it is not necessary to isolate it from each individual patient.

In connection with eczema, Kissmeyer gave a report of his experiences with "border" rays and he found that amongst forty two cases of chronic cases the majority could be cured with the help of border rays. I would like to dwell on this subject a little longer as this is a new field of modern therapy in dermatology.

As you know, the ray treatment in dermatology has taken an important place. I do not consider it necessary to speak about X-ray, radium, and ultra-violet rays. We always made use of well filtered X-rays and took special precautions not to work with unfiltered rays, that is, soft rays. The so-called border rays are just the contrary. They are super-soft X-rays with a special long wave length which are situated in the spectrum between the soft X-rays and the ultra violet rays. The therapeutical use of border rays has been recommended by Bucky and his idea of their action was explained through absorption in the superficial layers of the epidermis. The superiority of the border rays gains an important place especially in connection with eczema, where we are dealing with relapses
and where repeated application of border rays is entirely harmless. To give a detailed description of the biological and physical properties of the border rays would require too much time, and I would therefore only emphasize here that the border rays have already an established place in the treatment of eczemas and various other skin diseases.

The second topic concerns the immunity, reinfection and super-infection of Syphilis.

Truffi, relying on his tremendous clinical material, states that since the intensive treatment with arsenical preparations the cases of re-infection were more frequent than before.

Wade Brown (Rockefeller Institute, New York), had studied the question of syphilitic immunity in animals and he concluded that syphillis immunity in truth does not exist because the clinical and pathological manifestations of this disease differ from other infectious diseases so much that it is a logical expectation that there will also be a fundamental difference in their protective reactions. Syphilis is a disease entity, and there is no reason according to his opinion that a protection acquired in syphilis should conform to the conditions presented by other diseases.

Professor Arzt of Vienna came to the same practical conclusion by studying 540 syphilitics who had been treated with an abortive treatment and whom he could follow up to date. In his conclusion he states that the tendency to meta-syphilitic diseases after an abortive treatment is not in any way increased. On the contrary, cerebro-spinal syphilis, tabes and paralysis, all showed far lower figures than he expected. A successful abortive treatment in the sero-negative stage prevented to a great extent any further attack of the disease on the central nervous system. The sero-positive stage is not so hopeful as the results are less favourable regarding meta-syphilitic diseases, as here he could trace four per cent of cases. Finally, he concludes that we should not blame the abortive treatment for any disturbances in the natural production of immunity, which he proved by the fact that none of these cases which went through an energetic treatment with neo-salvarsan and mercury ever showed any signs of neuro-syphilis, whereas he believes that serious after-effects of syphilis are only due to lack of treatment.
The third topic was the question of the treatment of tuberculosis of the skin. Adamson gave an interesting division and explanation of the tuberculides. In his account of the treatment he lays more stress on the use of iodides than the present day trend with the gold treatment, which gave him no encouragement whatsoever. He emphasizes the importance of hygienic conditions, open-air life and good nourishment. Tuberculin treatment he believes has an effect even in minute doses, but he believes that we are apt to disturb the already favourable balance of immunity reaction in a patient who is already hypersensitized to tuberculosis.

Reyn of Copenhagen gave a critical description of various treatments in tuberculosis of the skin and came to the conclusion that gold did not effect a natural cure, although a slight improvement was noticed in several of those treated. Copper was without noticeable effect. Most important in the treatment were rays, especially Finsen rays, which gave him not only absolute anatomic but the best cosmetic results, compared with X-ray treatment especially. He did not give any definite opinion about the results of the salt-free diet, as his experiences have not been long enough.

Bruusgard of Norway pointed out the increase of skin tuberculosis in children, in spite of the fact that in most of the provinces in Norway there is no bovine tuberculosis at all. Consequently he believes that the infection is due to human T. B. bacilli, and the port of infection in most of these cases is the lung. He also recognised the well known fact that the older the children the less can be traced a lung lesion, but this does not exclude primary infection of the lung which could always be traced in X-ray pictures.

While Jesionek says that the most important and remarkable factor is the salt-free diet, Wichman of Hamburg came to a quite different conclusion. Wichman concludes that the salt-free diet is not a harmless method and it may do damage—the question as to which factors are the most important in this diet could not be decided by him. The salt-free diet, according to his experience, could not be given the credit for the success. He observed cases in which a rigid salt-free diet was followed by a complete cure of the patient, but he also observed cases where an addition of salt improved conditions.
A very remarkable contribution was the work of Professor Lowenstein and Kren, who succeeded in cultivating T. B. bacilli from the circulating blood. It has always been a puzzle in dermatology whether tuberculides are the results of T. B. toxins or T. B. bacilli. Although a few authors have succeeded in cultivating the bacilli in skins of tuberculides and, furthermore, although a few animal experiments have been successful in producing real tuberculosis from tuberculides, still there has been no satisfactory proof until recently. Professor Lowenstein and Kren succeeded in proving in 100 per cent of cases that the tuberculides were of the nature of tuberculosis. Consequently the theory of toxin etiology had to be dropped, and also our belief that the circulating T. B. bacilli is always a sign of miliary T.B. had to be changed. It seems to be possible with T.B. bacilli, as with Spirochaeta pallida, that these can circulate in the blood without causing the slightest symptoms, not even in a mild form. The skin seems to be the most practical observation field for the deposition of T.B. bacilli. In these cases critical points are the vessels, either capillaries or arteries or bigger vessels which are always damaged and where the bacilli remain deposited, penetrating afterwards through the walls of the vessels, reaching the tissues and producing various manifestations. Thus we explain the frequency of erythema induratum on the legs of younger girls where the blood circulation is found very faulty, and also explain tuberculides occurring so frequently on the hands and feet previously affected by chilblains.

The question now justly arises as to why do not the circulating T. B. bacilli give a manifestation of miliary T. B. in adults. The answer is given in the super-infection and in a higher degree of immunity.

A further interesting statement but not exactly belonging to dermatology was made by Professor Lowenstein that he also succeeded in cultivating T. B. bacilli in the blood of acute rheumatics (in 100 per cent).

This is a short review of the most important lectures which I thought would interest you. It is really impossible for me to review the 176 lectures in such a short time as has been at my disposal.
Clinical Notes

MASSIVE ATELECTASIS OF LUNG

Horace E. Campbell, M.D., Foochow, Fukien.

Since reporting a case of postoperative atelectasis in the China Medical Journal in August 1927, the writer has recognized five cases of this affection. Two of these followed chloroform anaesthesia, one spinal combined with chloroform, one with spinal alone, and one occurred prior to operation. Under the circumstances only three of these cases could be photographed and x-rayed.

Case 2 had definite clinical signs and the displacement of the heart was confirmed by several medical observers. By the time that we obtained the x-ray, however, the displacement was not confirmed by the x-ray and on physical examination the heart was found to be almost normal. Evidently the prolonged examination by the several doctors permitted the lung to re-expand.

Case 3 is remarkable in that the collapse occurred prior to operation apparently within twelve hours after the severe pain that betokened perforation of the appendix. The condition soon after admission, about fifteen hours after the onset of the collapse of the lung, is shown in figures 1 and 2. Together with several consultants, we decided to defer operation since the patient seemed totally unable to withstand the procedure. He improved somewhat for a day or so, and there was evidence of localization. He then became worse and we operated, intending merely to drain. There was such poor localization that it seemed best to find the appendix. This was difficult, but a greatly distended appendix oozing pus from a small perforation near the base was removed after some difficulties. The patient died three hours after operation, the temperature rising to 104 soon after leaving the table. At the beginning of the operation the collapse of the lung had mitigated somewhat, but was still present and the heart was still greatly displaced. This was not increased after operation. In retrospect, it seems that the
obvious illness of the patient on admission was probably fifty per cent due to the atelectasis and that after a preliminary infusion, he should have been operated on promptly, regardless of the lung condition.

Case 4 is one in which collapse occurred after appendectomy under spinal anaesthesia plus twenty minutes of chloroform. The condition recurred twenty-one days after the first attack, with all the clinical signs, but of much less severity. Unfortunately, in the writer’s absence, a roentgenogram was not taken at the height of this second attack.

Henderson, in the J.A.M.A. for August 23rd, states that atelectasis occurs in some degree in one case after each five operations. Inhalation of carbon dioxide is evidently to be recommended after every general anaesthesia, and since the evidence does not incriminate general anaesthesia in particular, it is reasonable to believe that carbon dioxide should be administered regardless of the type of anaesthesia.

LEGENDS

Fig. 1. Case 3. Note great depression and contraction of right chest. (Photograph by Dr. S. Y. Li)

Fig. 2. Case 3. Note displacement of heart into right chest with great deviation of trachea.

Fig. 3. Case 4. The depression of chest is not so apparent here, but can be detected by noting the lower position of the nipple on the left side. The infraclavicular space on the right is obscured by the pectoral eminence, whereas on the left it is entirely visible. (Photograph by Dr. S. Y. Li)

Fig. 4. Case 4. X-ray about twelve hours after onset of dyspnea and cough, which began about 48 hours after operation. Even though the right border of the heart is visible to the right of the spine, percussion revealed a resonant note over the lower sternum.

Fig. 5. Case 4. Four days later showing diffuse pneumonia(?) of both lungs. Patient clinically much better but still had tenacious sputum and displacement of heart.
Fig. 6. Case 4. Two weeks later than Fig. 5. The heart is still displaced somewhat and is also displaced upward by the persistently high diaphragm. On the next day collapse recurred, but an x-ray was not taken.

Fig. 7. Case 4. Nineteen days later than Fig. 6. The trachea and mediastinum have returned to normal position. The left diaphragm is well shown, and is still very high, even higher than the right.

TETANUS
Report of a Case
K. H. Li, Soochow Hospital

C. F. S., Hospital No. 13044, a farmer of 37 came to hospital on September 5th, 1930, complaining of painful muscular spasms of the back. He gave as history that he was entirely well up to about 4 weeks ago when he first noticed a slight difficulty in swallowing. One week later painful spasms of the muscles of the back, neck, abdomen and lower extremities began. These spasms occurred at first only once or twice a day, but gradually became more frequent so that on admission he was having them every few minutes and they were more severe in character.

Family and past history irrelevant except for a mild injury to his left knee while working in the field about two months ago. This was treated by the ashes of soap tree leaves and healed.

On examination he was found to be a robust and muscular man with normal mentality. His entire body was rigid and he was able to walk only when supported. During the spasm which lasted only a couple of seconds, he showed a sardonic facie with head and back jerking backward. He could open his mouth only halfway. Pupillary reactions were normal and no ocular palsy was found. His neck was a little stiff especially
Clinical Notes

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during the spasm. His chest was barrel-shaped with hyperresonant note to percussion due to chronic emphysema. Heart and lung were negative. Muscles of abdomen were very rigid and the recti stood out prominently. No tenderness nor mass could be made out. Lower extremities were held in strong extension and could be flexed only with difficulty and all superficial and deep tendon reflexes were exaggerated. There were many old scars over the skin of both lower legs. Varicose veins were noted on both sides but no evidence of any recently healed wound was detected.

Laboratory examination showed nothing abnormal except for ova of ascaris. Kahn and Wasserman tests were negative.

A diagnosis of Tetanus was made and patient was admitted to a ward for treatment. He was given a dose of Tetanus antitoxin 1500 units, Magnesium sulphate, 25% solution 5 cc. well diluted was injected subcutaneously every 12 hours for three doses. It had a decided relaxing effect on the spasms so that they were less severe and less frequent. But patient was unable to sleep. He could open his mouth a little wider.

September 7th, 7 a.m., 4 cc. of fluid Avertin (Bayer) dissolved in 150 cc. of distilled water was given per rectum. A drowsy state came on in half an hour. His pulse and respiration were unchanged and he seemed to be in a normal sleep. When pricked over his skin, he would only occasionally make defensive movements with his hand. He could be aroused to open his eyes and nod his head but made no effort to answer questions when asked. His abdominal muscles and legs were stiff. He remained in this state until about noon when he was wakened up for his lunch. He slept again after lunch. However his abdominal muscles were not entirely relaxed. His legs were not quite so rigid. He was able to walk slightly better than on admission. His mouth could open wider. The relaxing effect of Avertin lasted about 12 hours after which attacks of tetanic spasm recurred frequently.

September 8th, 9 a.m., 2nd dose of Avertin was given. Patient again fell asleep in 12 minutes. No tetanic spasm noted for 6 hours. Then a few occurred. Abdominal muscles were not relaxed.
From September 8th to 11th, four more doses of Avertin were given. Their effect on the spasms was quite definite. Avertin always induced a state of normal sleep from which he could be aroused to answer questions and open eyes. Pin pricks were readily appreciated no matter where over the skin the patient was pricked but the abdominal muscles were never fully relaxed.

On September 12th, 2 p.m., Dr. Snell was called for consultation and it was decided to give him Sodium Amytal 1 gram in 10 cc. of distilled water. This was given intravenously at the rate of 1 cc. per minute. Patient began to close his eyes when 4 cc. was injected. After 7 cc. he went to sleep and did not respond to questions. Altogether 9 cc. was given. Pin pricks to his face, elicited slight response. All muscles were relaxed and reflexes abolished. Pupils were contracted, while respiration, pulse and blood pressure were not changed. When examined 10 minutes after injection, he was entirely unconscious with perfect relaxation of all muscles of the body. Three hours after injection, he was seen scratching his legs violently as if itching. He pulled off the bandages from his neck. When asked he answered correctly but sluggishly. At supper time he was called to take his meal and he took it as if well and awake. No excitement or tetanic spasm was noted throughout the entire period after the injection of Sodium Amytal. No dizziness, headache or other uncomfortable symptoms were noted upon his awakening. However his abdominal muscles became rigid again after 3 hours and 10 minutes. Six hours later patient was still in a more or less stupor. But he got out of his own bed and crawled into one some 6 feet away and slept there. When told to come back he did accordingly. Ten hours later he was found still sleeping quietly.

September 13th, the next morning when he was greeted, patient said that he slept very well and had been free from tetanic spasms. He did not know anything of what had happened the day before as to eating his supper and getting out of bed. He claimed that he waked up from his sound sleep about daybreak feeling weaker but free from any ill symptoms.
Mouth could be opened to the normal extent. However tetanic spasms returned about 30 hours later. Magnesium sulphate solution was given subcutaneously.

September 4th to 16th—3 more doses of Avertin were used. While their effects were quite similar to those given before, the duration of sleep and relaxation of muscles was definitely lessened.

September 16th, tetanic spasms returned after the effects of Avertin had worn off. At 4 p.m. a lumbar puncture was done, and 25 cc. of clear fluid was withdrawn under slight pressure, 4 cc. of 25% Magnesium sulphate solution was slowly injected into the spinal canal. Throughout this operation and afterward patient's bed was raised at the head end. Blood pressure taken 5 minutes after L.P. was 130/74. Soon afterward he complained of numbness in the lower extremities but when tested no impairment of sensation was noted. Knee jerk was much more exaggerated than before lumbar puncture and abdominal muscles were still tight. At 6 p.m. patient vomited his supper. His mental condition was rather dull while the pulse showed no change. At 7 p.m. the interne noted that patient was unable to talk normally. At 8 p.m. when the writer visited him, his abdominal muscles were completely flaccid. Extremities were cold. He was conscious but not able to speak readily. His pupils were contracted but reacted to light promptly. Eyeballs were not able to follow finger and vertical nystagmus was noted when looking down. There was much salivation in the mouth. Complete motor paralysis with total loss of knee jerk was present, but only partial anesthesia to pain. There was no visual disturbance nor incontinence of urine and feces. Respiration was a little slow. These manifestations following intraspinal treatment with Magnesium sulphate solution immediately suggested ascending paralysis due to the mounting of the drug toward the vital centers. So at once 15 cc. of 5% Calcium chloride was given intravenously. The result was quite marvellous because patient’s speech promptly improved so that at 10 p.m. his mental condition changed to normal and he could talk normally. Both the legs and abdominal muscles were still flaccid, but there was partial
return of motor power in the legs although knee jerks were still absent.

September 17th, 9 a.m., there was a rise of temperature to 102°F with severe headache which lasted some 24 hours. Complete restoration of motor power of both legs as noted about 12 hours later, with a return of normal knee jerks:

There was no occurrence of tetanic spasms following the intraspinal treatment with Magnesium sulphate solution. On September 20 patient was discharged in good condition. Four days later he sent us a patient to hospital for treatment and she reported that he was still in good condition.

**COMMENT**

The above Tetanus case is of interest because it was cured by apparently symptomatic treatment. It also afforded opportunity to observe and compare the action of newer remedies—Avertin (Bayer) and Sodium Amytal (Lilly) which have decided value in relieving tetanic spasms. Magnesium sulphate seems also to have a relaxing effect when given subcutaneously but very much milder. However when given intraspinally it has a strong anti-spasmodic effect which in this case even caused temporarily motor paralysis of the legs. It also has a dangerous untoward action of affecting the vital centers of respiration and speech which requires close watching. To counteract this we have in Calcium chloride a physiological antidote. The fact that there was no return of tetanic spasms following its intraspinal use is rather suggestive that magnesium sulphate may possess curative value in Tetanus.
Editorials

1931

This year opens with better hopes and prospects than have been possible for many past years New Years. Despite wars and brigandage the hospitals through China have managed on the whole to carry on in a marvellous way during the last twelve months. To this there have been unfortunate exceptions in one or two of the provinces but for the most part the work has been well sustained.

If there can be freedom from war and a serious tackling of the brigand problem, which seems likely just now, the future will be brighter than it has been for many a day. We trust that this favourable opportunity will be seized for consolidating and extending the hospital work.

Unfortunately the authorities seem likely to adopt the very retrograde step of abolishing the Ministry of Health and subordinating the department under another Ministry. This is its position in a few other countries, especially Japan, but with disastrous consequences as regards the initiation of public health measures and we trust that a more progressive policy will be adopted in China.

The position of medical men in this country is still very unsatisfactory and the past year has seen some very unfortunate occurrences, such as the scandal of Dr. Teng's imprisonment about which a notice sent us by the National Medical Association appeared in our last issue. We believe that this is only a temporary phase which an enlightened Government will remedy before long. More serious are the added difficulties to the performance of post-mortem examinations which are greatly hampering medical progress in China. Unfortunately there are no signs of this being remedied and to our mind it is the most serious handicap there is to the advance of China in medicine to her proper place in the scientific world.

In the course of this year our own position as an Association will have to be very carefully considered and definite
steps taken at the joint Conferences in 1932 to decide the future of our organisation. In this connection it has to be remembered that the National Medical Association which continues to make remarkable progress has now opened the door to union when the right time for this has arrived.

The union of Journals has already been long under discussion and great advance has been made towards this end. Further reference to this is made in another Editorial.

We have already mentioned the Conference of next year. This it will be remembered is to be a joint conference of our own and the National Medical Association and it is planned to hold it in Nanking in February 1932. This ought to be the largest and the best medical conference ever held in China, and we trust that our own members will do their full share to ensure this being the case, both on account of the really essential value that such a conference has in stimulating our own medical work and as a compliment to the National Medical Association which has issued the invitation to us. By a full and enthusiastic attendance we can not only help ourselves but we can also help the National Association to that predominant position in Chinese medical affairs which is the right and proper place for that Association in whose beginnings we are proud to have had our share.

Will all our Members, as far as they possibly can, plan to be present at the 1932 Conference and take their part in its proceedings?

PARAGONIMIASIS

Special attention is called to the paper on Paragonimiasis in China in this issue of the Journal. It has long been suspected that the lung fluke was to be found in China, although many of the cases reported have been imported ones from neighbouring countries. It is now certain that the infection is actually native to China and is possibly wide spread. If this should be correct the question arises as to why this has not been earlier recognised.
The answer is that the disease is seldom a very serious one and can hardly be said to threaten life. A little chronic cough with occasionally a little blood tinged sputum is often the only evidence of the complaint and this does not hinder the host of the fluke from doing a full day's work, or from looking the picture of health. Hence he or she seldom comes to the clinic for this condition alone.

Yet another reason for failure in diagnosis is that should the presence of blood suggest an examination of the sputum this will almost certainly be made for the presence of tubercle bacilli and the process of staining for T. B. will destroy the eggs and make them unrecognizable.

The possible presence of the disease should however be borne in mind wherever patients come from hilly districts, especially where mountain streams run through or in close proximity to villages.

Nothing could be easier than the recognition of the ova in fresh sputum, they are as quickly found as ascaris eggs in the stool and are quite unmistakable.

KALA- AZAR

Two facts, which many of us have probably failed to realise are brought out in the papers on Kala-azar which we publish in this issue. First, that the disease is far more prevalent in the endemic areas than we had believed, and, second, that its treatment has been almost completely revolutionised by modern methods.

The first of these is strikingly exemplified by the fact that one hospital alone has treated over two thousand five hundred cases in a single year. This raises the further question as to whether the increase in numbers treated is due to the newer methods employed or whether there is a rapid spread of the disease as has been the case in parts of India. We are not ourselves in a position to answer this question, but we feel that it
is a matter that requires very serious consideration and a reply should be forthcoming from those who can speak with authority. For it is only too evident that if kala-azar is rapidly spreading, those interested in the health problems of China ought to know and ought to take steps to combat the spread.

The second fact is also one of no little importance. Formerly when tartar emetic was the drug in general use the treatment was risky and hospitalization for comparatively long periods almost essential. Now safe treatment in outpatient clinics can be given and the number of patients that it is possible for one hospital to deal with is thus enormously increased. Further the loss of working days to the patient is greatly lessened. Unfortunately the cost of treatment is not thereby correspondingly decreased for the newer drugs are much more costly and must necessarily be so. One point in regard to this seems to us of great importance. On looking over these papers for publication we were struck with the difference in the total amount of neo-stibosan per patient used in different hospitals. This varies from 2 to 6 grams without any very evident explanation of why this should be. We suggest that this is a matter of no small moment where so costly a drug has to be employed. Will not some of the workers on the problem of Kala-azar make this point clear?

As to the best drug for treatment there appears to be little difference of opinion. From Recent Advances in Chemotherapy by G. M. Findlay, Wellcome Bureau of Scientific Research we quote the following:

While the anaphylactic-like condition is by no means uncommon with aminostiburea and urea-stibamine, it is rare with stibosan, and has not been observed with preparation 693 B or 'Neostibosan.' Jaundice also a common sequelae, is apparently rare with Preparation 693 B, while vomiting, which is so frequent a complication, is entirely absent in cases treated with 'Neostibosan.'

As regards ease of administration, 'Neostibosan' would appear to be superior to all the other pentavalent antimony compounds, for of them only 0.1 gm. can be given intramuscularly, as a maximum, while 0.3 gm. of 'Neostibosan' can be injected without pain and without any local reaction. If the results already obtained by Napier and Mullick (1928 and 1929) are confirmed, 'Neostibosan' would appear to be the most useful drug yet produced for the treatment of Kala-azar.
THE CHINA MEDICAL JOURNAL

The future of our Journal has been engaging the attention of the Executive Committee for some time and negotiations somewhat delayed by the absence of your Editor on furlough last year have been on foot for an amalgamation with the English section of the National Medical Journal. With the many important interests to be considered, such negotiations are never very easy, and the Editor wishes here to express his great appreciation of the spirit in which they have been conducted. Each difficulty as it arose has been considered and discussed, and we may say in nearly every case overcome in the most friendly fashion, and if the final objective has not been quite reached it is at least within easy view. Festina lente is a proverb which is very applicable here, and if some may think that the progress has been unnecessarily slow, we feel that it is more than worth while if an agreement can be reached which meets in the fullest way the desires and aspirations of both parties, and this we confidently believe will be the outcome.

In the mean time, may we remind our own Members that till this actually reaches fruition we are in honour bound to carry on our own Journal at as high a standard as possible, and to do this the Editor needs more support than he has been getting lately. We can boast some excellent recent numbers and we believe that the present issue with its series of papers on Kala-azar maintains our fine tradition. But at times the Editor has found his post a little difficult from lack of fuller support from contributors. The Editor's time is not his own and he can give only a limited period to this work, and the attempt to dig out contributions from those well fitted to supply them has sometimes been both strenuous and trying.

Hospital Doctors are very busy people but the Editor has also his time pretty well occupied and has to give many off-duty hours to the Journal, and he hopes that the many able and really willing medical workers in China will keep the needs of the Journal in view this year,—the year before a Conference is always the hardest time to secure papers.

Once again may he ask contributors to attend to one or two simple rules which would make the work easier for him and for our Chinese compositors. Difficult work for the latter means more work in proof reading for the former.
All papers should be type-written, *double spaced*, with ample margins on both sides of the page and not on the thinnest paper obtainable.

Paragraphs should be not too long and headings should be clear and on separate lines. Capital letters should be used with discretion and it is a good rule to omit them where not absolutely essential. Names in Latin or other foreign languages should be in italics which is indicated by underlining; the second word of a Latin name should never begin with a capital.

It would add enormously to the ease of handling papers if writers would believe that the perfect typist is rare and would therefore go over papers carefully after they have been typed and correct obvious spelling errors and transposition of letters.

Above all tables should be checked for the correctness of the figures. It would astonish the ordinary person to know how many tables which reach the Editor add up incorrectly,—e.g. three in the current issue.

THE HOLT SCHEME

Under the *China Medical Association Section* in the current issue will be found a reprint of the rules governing the Holt Scheme for sending graduate Chinese physicians to Liverpool for special courses of post-graduate work. Applications under this scheme must reach the Committee in time for full consideration by May 1st of this year. Successful candidates will be expected to leave for England during the month of August.

THE EDITOR

The Editor expects to be away from Shanghai for January and the greater part of February. He has received an invitation from the Leonard Wood Memorial Fund to attend a special conference on Leprosy in Manila and with the approval of the Trustees of the Henry Lester Institute he is accepting this invitation. He is hoping also to be able to pay some other visits in the South before returning to Shanghai. Arrangements have been made for carrying on the Journal as usual, but there will necessarily be some delay in replying to personal letters. Will correspondents kindly take note of this and excuse any delay in answering such communications?
THE Holt SCHEME

To enable Chinese Medical Graduates to Study in England

Owing to the generous offer of Mr. R. D. Holt of Messrs. Alfred Holt & Company of Liverpool, the Executive Committee of the China Medical Association are able to offer annually to a limited number of suitable Chinese medical graduates free passages to and from England for a period of study. The passages will be given on Messrs. Holts' "C" Class Blue Funnel Line boats (equivalent to 2nd class). As these boats carry male passengers only, women will not be eligible under this scheme.

The selected candidates will be expected to study in the first place at Liverpool University Medical School or Liverpool School of Tropical Medicine, but may afterwards proceed to other centres of study if sanction is obtained from the representative of the scheme in Liverpool, at present Professor Roxby (Warden of the University Students' Hostel).

The Liverpool representative of the scheme is also willing to give a general oversight to the studies and welfare of the students. Return passages will be granted upon his recommendation to Messrs. Holt & Co.

Selection of candidates will be arranged by the Executive Committee of the China Medical Association in Shanghai, who will forward the selected names to the Blue Funnel Line, asking for the grant of passages at dates to be arranged.

It should be noted that Messrs. Holt reserve the right to give notice to terminate this arrangement subject to their finding return passages for any students who have already left Shanghai.
Preliminary Regulations as Adopted by the Executive Committee of the China Medical Association

REGULATIONS

1. Candidates must be of Chinese descent and be graduates of a school of medicine in China recognized by the China Medical Association or National Medical Association or be graduates of the University of Hongkong.

2. They must produce a certificate from the authorities of their school (or other responsible person) of their ability to benefit by studying abroad. A good knowledge of English is essential, and at least two years' hospital experience after graduation is desirable.

3. They must produce two certificates of moral character from responsible persons to whom they have been personally known for at least six months.

4. They must produce satisfactory evidence of their financial ability to live in England for the required time and to pay for the proposed course of study.

5. They must obtain a passport—see notes.

6. Nominations for free passage will only be made by the China Medical Association Executive Committee in Shanghai after a full consideration of each case. Candidates must therefore send in their applications to the Secretary at the office of the C. M. A., Missions Building, 23 Yuenmingyuen Road.

NOTES

1. No money is available under this scheme, only free passages.

2. The cost of board and lodging in Liverpool in 1928 was 35/- to 40/- per week (say $35.00 per week). The fees for courses vary and may be ascertained from the Secretary in Shanghai.

3. A passport is necessary for all students proceeding to England, which must be visaed at the British Consulate before starting. There will then be no difficulty en route.
4. Particular attention is directed to regulation 4. It will be necessary for applicants to state how long they desire to stay in England and to indicate the proposed course of study. It is also desirable that they should state what they propose to do on their return to China.

5. Applications for this year must be received by the Executive not later than May 1st.

Special facilities to be granted under the Holt Scheme

The Council of the University of Liverpool has passed the following recommendations of the Medical Faculty:

(1) "That Chinese Medical Graduates, if recommended by the China Medical Association, be permitted to enter for the D. T. M. and D. T. H. Examinations."

(2) "That Chinese Medical Graduates, if recommended by the China Medical Association, be admitted to the courses of study for the Diploma in Public Health."

Notes.

Resolution (1) means that Chinese Medical Graduates whom the China Medical Association recommends will be allowed to take the courses for the Diploma in Tropical Medicine and the Diploma in Tropical Hygiene (under the same conditions as graduates holding registerable qualifications in Great Britain), and on passing the examinations, will be granted the Diplomas.

Resolution (2) means that Chinese Medical Graduates will be permitted to take the courses of study in Chemistry and Bacteriology etc. for the Diploma in Public Health and have all facilities for studying the Public Health Administration in the City of Liverpool. They cannot, however, by a ruling of the General Medical Council, be admitted to the D. P. H. Examination unless registered in Great Britain.

Graduates who do not desire to take the special courses referred to above will be admitted to the general post-graduate training of the Hospitals, or to the facilities in special subjects provided by the University and by the different hospitals recognised by the University. They will also be admitted as Research Scholars.
Graduates can also be admitted to diploma courses other than those specified, but as in the case of the D. P. H. cannot obtain the Diploma unless registered in Great Britain.

The usual regulations with regard to the admission of foreign students will not be enforced in the case of Chinese Medical graduates recommended by the China Medical Association.

Fees for Post Graduation Courses

Diploma in Public Health (D.P.H.) 1 year course .................................................. £45. 0. 0
" " Tropical Medicine (D.T.M.) 3 months course .................................................. 21. 0. 0
" " Tropical Hygiene (D.T.H.) 10 weeks course .................................................. 10.10. 0
Apparatus Fee .......................... .................................................. 1. 0. 0
Breakage deposit .................................................. 10. 0
N.B. The D.T.H. is only open to holders of D.T.M.
" " Medical Radiology & Electrology (D.M.R.E.)
6 months course limited to 6 graduates .................................................. 24. 5. 0
Research Graduates Laboratory fee per session,
Oct.—July (3 terms) .................................................. 10. 0. 0
Graduates pay in addition for special materials and apparatus.

Fees for Hospital Practice

General.

12 months .................................................. £18.18. 0
6 " .................................................. 12.12. 0
3 " .................................................. 6. 6. 0
1 " .................................................. 4. 4. 0

One Dept. only

12 months .................................................. £12.12. 0
6 " .................................................. 8. 8. 0
3 " .................................................. 4. 4. 0
1 " .................................................. 3. 3. 0

Examination Fees

Diploma in Tropical Medicine — Examination .................................................. £5. 5. 0
" " " Re-examination .................................................. 3. 3. 0
On obtaining Diploma .................................................. 1. 0. 0
Diploma in Tropical Hygiene — Examination .................................................. 5. 5. 0
" " " Re-examination .................................................. 3. 3. 0
On obtaining Diploma .................................................. 1. 0. 0
Hospital Reports

THE UNIVERSITY HOSPITAL,
SHANTUNG CHRISTIAN UNIVERSITY, TSINAN.

For the year ending 30th June, 1930
Dr L. R. F. Heimburger, Medical Director.
Inpatients 1,501 Outpatient attendances 46,486

Considerable structural changes have been made during the past year including remodelling the basement, moving the laundry and erecting a heliotherapy verandah for children.

Details are given of nurse's and workmen's strikes which so seriously threatened the existence of the hospital during the past year but which are now happily settled. The Director's report deals also with financial problems.

There are interesting reports of the various departments and full tables of diseases and operations. As a whole the report is one of the most interesting that the hospital has produced.

THE KAILAN MINING ADMINISTRATION

Report of Medical Services, 1st July, 1929 to 30th June, 1930
Dr J. G. B. Muir, Principal Medical Officer
Hospital Inpatients 4,301 Outpatient Attendances 233,185

The report contains a general survey of the work of the medical services. It begins with details of the medical organisation with its extensions and developments followed by particulars of hospital work and comments on public health conditions.

It is encouraging to note here what a large amount of charity work is done by the medical services of the Administration, including in the hospitals 1,016 charity inpatients and 32,033 outpatient attendances.

Details are given of such groups of cases as Communicable diseases, Exanthemata, Tuberculosis, Influenza, Venereal diseases, Anthrax and Ancylostomiasis,
A very interesting section is given to Injuries due to Industrial Trauma. Valuable tables of Diseases and Operations are found towards the end of the report.

SHOKWA MISSION HOSPITAL, FORMOSA, E.P.M. 1929
Staff: Dr D. Landsborough
Nurses: Foreign one, Formosan 3. Pupils 12
Inpatients 1,182 Outpatient Attendances 17,042

This report is addressed entirely to supporters of the hospital at home and contains practically no medical details, unfortunately not even a list of diseases or operations.

TAINAN MISSION HOSPITAL, FORMOSA, E.P.M. 1929
Staff: Drs P. Cheal, 1 Formosan
Nurses: 4 Formosan, 8 Pupils
Inpatients 1,185 Outpatient Attendances 8,165

The report is in two parts, one a general account of the hospital work and the other a short separate medical report. Both of them are very interesting.

Patients in Formosa as in China still suffer many things at the hands of many physicians, but few could beat one recorded here,—a young woman who had been for three months in a small private hospital where she had received 150 hypodermic injections of some sort; then a further course of 35 larger ones at home, and finally 12 injections of port wine. Apparently the case was cured in hospital with a course of salicylates.

An interesting table of diseases finds a place in the medical part of the report, and we notice a high incidence of typhoid among the inpatients, considerably higher than the reviewer found in earlier days. It would be interesting to know if this implies a real increase of the disease in the island. We note also that decapsulation of the kidneys still figures fairly prominently in the operation list, and we wish that Dr. Cheal would give us the benefit of his experience on the use of this much disputed procedure.
THE CLINICAL VALUE OF TESTS OF LIVER FUNCTION

GEORGE MORRIS PIERSOL, M.D.

CONCLUSIONS

We are led to conclude from our experience with liver function tests, as applied to a considerable group of patients suffering from various disorders, that the three most practical and clinically useful tests, are (1) the retention of the dye bromosulphalein; (2) the estimation of the serum bilirubin, particularly, the determination of the icterus index; and (3) the occurrence of urobilinogen in the urine.

The retention of bromosulphalein is not an early indication of liver dysfunction. The degree of retention is a helpful indication of the extent of liver damage. When dye retention occurs other liver functional tests are also positive, but we have not observed any noteworthy degree of bromosulphalein retention when the ordinary clinical evidences of liver disease were not present.

The estimation of the serum bilirubin is a more useful test of liver function, since it frequently indicates the presence of a latent icterus before liver disorders can be recognised by clinical signs, and the persistence of bilirubin in the blood after all other evidences of liver disease have disappeared.

In our hands an increase in the urobilinogen is the most delicate test of impaired function. Urobilinogen is increased even when damage to the liver parenchyma is exceedingly slight. It is persistently increased so long as any residual hepatitis remains, and it is the one test which has been positive in a certain number of cases in which liver disease was suspected but could not be proved clinically.

Because of the liver's multiple functions and because of its extraordinary compensatory capacity and remarkable ability to regenerate, it must be admitted that from the standpoint of the clinician who is seeking some means whereby impaired liver
function can be recognised, before gross clinical evidences of liver disturbance appear, the tests for liver function that are available at present have hardly justified our earlier expectations. This is the more true because in all focal lesions of the liver, especially those without biliary obstruction, functional tests yield no useful information. They are, however, of some help in differentiating the various types of jaundice and in the diffuse disturbances of the liver, in which by means of them we are enabled to estimate with some degree of accuracy, the extent and duration of the liver damage, so that they are undoubtedly of prognostic value.


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**THE INCREASE OF APPENDICITIS**

Popular opinion tends to incriminate diet, and this view has received some medical support. Mr. Rendle Short found that during the time that there has been a great increase of appendicitis, there has been a great diminution in the consumption of the cellulose-containing foods. He suggests that the increased mass of indigestible material encouraged the more regular emptying of the bowel.

A gigantic experiment in dieting followed the revolution in Russia in 1917. Owing to economic disorganization, the nation was literally reduced to starvation. Half to one pound of poor bread, a little coarse and, to the ordinary person, disgusting soup, and sometimes a little potato, was the daily allowance. This effect on the variety and course of disease in Russia was remarkable. Nearly all infective diseases were greatly increased. Surgical diseases assumed a new character. Ordinary trivial complaints became chronic and serious, and diseases formerly rare appeared suddenly as epidemics. Thus there was an epidemic of purulent infection, of hernias, abdominal ptôses, varices, peptic ulcers, flat foot, and neuroses. On the other hand, appendicitis underwent a great decrease, though enteritis and every variety of deficiency disease was rife. Appendicitis is very common amongst the civilized nations, with a full and
varied diet, and is rare amongst Hindus and the Chinese, who have a diet less varied, smaller in quantity and mainly vegetable. The disease attacks commonly, if not usually, the young and vigorous, the well-fed and otherwise healthy. The fact that a starvation diet, which encourages other infections of almost every kind, leads to almost extinction of appendicitis shows that it is not a deficiency disease, but a disease of excess. The experiments of Wilkie suggest that excess of meat diet is deleterious.

*Clinical Journal, October 8, 1930.*

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**TREATMENT OF RELAPSING FEVER**

**JOHN TODD**

The writer, from Nyasaland, recommends the use of intramuscular injections of sodium potassium bismuth tartrate for the treatment of tick fever, instead of the usual novarsenobenzol. The latter is much more expensive and must be administered intravenously; in addition, although it brings down the fever rather more quickly than the tartrate, relapses are not uncommon and two or three injections are generally necessary before the symptoms disappear. Sodium potassium bismuth tartrate brings down the temperature in 36 hours and relapses are almost unknown. The dosage for an adult is two intramuscular injections on two consecutive days, each of 0.2 gm. of the drug dissolved in 2cc. sterile water; for a child 2 to 10 years old, the drug is halved; and for a baby under 2 years old, a single injection of 0.1 gm. is sufficient.


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**SPRUE**

Its Applied Pathology, Biochemistry and Treatment

**N. HAMILTON FAIRLEY, O.B.E., M.D., D.Sc., F.R.C.P.**

We are only able here to give the summary and conclusions of this very valuable paper.
SUMMARY.

The views expressed in this paper are based on the conception that sprue is essentially an alimentary disease, and the clinical features and the pathological, haematological and biochemical findings are explained in terms of the resulting dysfunction of the gastro-intestine. Theoretical conceptions have of necessity formed an integral part of the paper, and the evidence on which certain views have been formulated is admittedly incomplete. Biochemical investigations are however being continued, and it is hoped at a later date to present fresh data having a material bearing on both the theoretical and practical issues involved. The pathological lesions which are primarily inflammatory and secondarily atrophic have a notoriously patchy distribution, and, in the later stages, implicate the whole tract. At times, however, the main brunt of the attack may fall on the ileum, the jejunum, the stomach or the tongue with corresponding modification of the clinical picture. It is suggested that derangement of the ileum specially underlies defective fat, vitamin D and calcium absorption, and that jejunal involvement, leading to an inevitable decrease in the secretion of succus entericus, prevents normal splitting of cane sugar, lactose and maltose. Abnormal fermentation of the resulting disaccharide residue is largely responsible for abdominal distension, and the acid, gaseous stools so characteristic of sprue, while their increased fat content contributes largely to their bulkiness.

Involvement of the stomach is indicated by the frequency of defective acid secretion, and, as in pernicious anaemia, deranged gastric secretion probably underlies the megaloblastic hyperplasia of the marrow and the megalocytic anaemia so characteristic of sprue. No essential relationship, however, exists between megalocytic anaemia and achylia gastrica, for several of the present series showed anaemia of this type associated with a free secretion of HCl.

It is suggested that the aplasia which the megaloblastic marrow undergoes in sprue results from malnutrition, being analogous to the corresponding changes produced in the normal megaloblastic marrow of pigeons undergoing starvation. That grave nutritional disturbance exists in sprue is indicated by the great loss of weight, the practical disappearance of all subcutaneous fat and the extreme grade of atrophy of the viscera noted at autopsy. Hyper-bilirubinaemia is much less marked
in sprue than in pernicious anaemia, and in doubtful cases both the indirect Van den Bergh reaction and gastric analysis, especially after histamine injections, afford information of considerable value. The acid response to histamine may also be used for estimating rejuvenescence of the oxyntic cells in cases of achylia gastrica. The first indication of improvement is the reappearance of acid under such a stimulus; later free acid appears in the ordinary fractional test meal.

Investigations on the blood chemistry of sprue show that total as well as the ionic serum calcium is frequently reduced, and also that this reduction is not accompanied by an increase in the inorganic phosphorus. These findings indicate that tetany is due to a calcium deficiency caused by defective intestinal absorption in which the sterols (vitamin D) probably participate. Marked lowering of the serum cholesterol was a characteristic finding in the severer cases of sprue. Its return to normal closely followed clinical improvement and recovery from the anaemia.

The essential principles in the treatment of sprue may be summarised as follows:—

(1) Alimentary rest.

(2) Restoration of the blood to a normal condition.

(3) Reinforcing demonstrable deficiencies such as lowered blood calcium and defective HCl secretion.

Emphasis is placed on the fact that in sprue starchy foods and the disaccharides in the gut give rise to acid fermentation, while fat is poorly absorbed. Of the fundamental foodstuffs protein, especially in the form of minced underdone red meat, is well tolerated, leaving little residue, and it is submitted that the most rational method of obtaining alimentary rest under such conditions is by the administration of a high protein, low-fat, low carbohydrate, adequate vitamin diet along the lines outlined in this paper. Glucose and milk are the best initial means of reinforcing the carbohydrate and fat moiety of the diet. The effects of a high protein diet are very obvious clinically since the stools show a fall in their fat content, become neutral or alkaline in reaction, rapidly decrease in bulk and number, while abdominal distension and intestinal flatulence disappear. During the first two or three weeks weight may be
lost or little gained, but once the bowel has been adequately rested and the anaemia rectified, higher calorie diets are well tolerated without the reappearance either of bulky stools or abdominal flatulence. Where patients are specially emaciated or the weight-curve fails to show the customary rise, insulin in doses of 6 to 12 units daily may be employed with striking benefit.

In all cases of megalocytic anaemia liver extract in full dosage (=1 1/4 lb. daily) was administered daily. Steady improvement in the red cell counts and percentage of haemoglobin followed, and generally a reticulocyte response was elicited, its intensity being directly related to the gravity of the anaemia. Simultaneously the colour-index and the average corpuscular diameter, as shown by halometer readings, progressively decreased toward normality. Anaemias not frankly megalocytic in type also improved under this high protein and liver extract régime, but in all types of cases it has not yet been ascertained to what extent purely dietetic measures were responsible. Where the total serum calcium was below 9.0 mg. per 100 c.cm., calcium lactate or calcium and sodium lactate were administered, and in special cases irradiated ergosterol (vitamin D) was also employed. In addition, in all instances a low fat diet was instituted. Restoration to a normal blood calcium level invariably followed treatment along these lines, and generally paralleled improvement in alimentation. HCl was supplied in adequate dosage to all cases where its secretion was proved defective.

After a prolonged experience of tropical sprue I am convinced that clinical observation should always be reinforced by biochemical and haematological data whenever possible, and also that in a disease so notoriously liable to relapse every patient should from time to time report for medical examination. Nor should treatment cease with discharge from hospital. Overfatigue, extremes of temperature and cold and chill must be avoided; and for many months, or even years, the diet may need careful supervision, especially in regard to carbohydrate excess. In cases of achylia gastrica and achlorhydria continued administration of HCl and a maintenance daily dose of liver extract equal to 1/4 lb. of the fresh organ is advised until such time as normal gastric secretion be restored.
CONCLUSIONS

1. Defective gastric secretion and malnutrition are suggested as the respective factors underlying megaloblastic hypertrophy and aplasia of the red marrow in sprue.

2. In a series of twenty-two cases examined by Eve's halometer, nineteen presented an average corpuscular diameter varying between 7.8 to 8.6 microns. The mean diameter equalled 8.16 microns.

3. In eighteen out of twenty cases of sprue the indirect Van den Bergh reactions did not exceed 1.2 units or 0.6 mg. of bilirubin per 100 c.cm.

4. A megaloblastic anaemia associated with an indirect Van den Bergh reaction not exceeding 1.2 units (0.6 mg. per 100 c.cm.) is a very characteristic finding.

5. The study of the curve of acid secretion, especially after histamine injection, will frequently enable a clear-cut differentiation being made from pernicious anaemia.

6. The response to histamine affords one of the earliest indications of rejuvenescence of the oxyntic cells in the achydia occasionally observed in sprue.

7. In twenty-one cases the total serum calcium averaged 8.8 mg. per 100 c.cm. Three were complicated by tetany, and here the values equalled 5.2, 5.8 and 6.4 mg. per 100 c.cm.

8. Simultaneous observations on the inorganic serum phosphorus in fourteen instances showed normal values, the average being 3.2 mg., the minimum 2.2 mg., and the maximum 4.0 mg. per 100 c.cm.

9. Low total serum calcium unassociated with any abnormal rise in the inorganic phosphorus indicates that the tetany is arising from deficient calcium absorption.

10. The serum cholesterol in ten cases of sprue averaged only 72.8 mg. per 100 c.cm. Hypocholesteraemia was almost invariably present, but a rapid rise followed effective treatment.

11. Defective fat absorption and abnormal fermentation of disaccharide residues are regarded as underlying the chief intestinal manifestations of sprue.

12. The fundamental basis of treatment is alimentary rest; this is best attained by a high protein, low-fat, low-carbohydrate, adequate vitamin diet as detailed.
13. Simultaneously, the megalocytic anaemia should be treated by full dosage of liver extract (1¼ lb. daily).

14. Where fractional test meal analysis reveals deficient acid secretion, HCl therapy is instituted.

15. Calcium deficiency is best controlled by a low-fat diet and the administration per os of calcium salts, the absorption of which may in some cases be assisted by vitamin D administration or ultra-violet irradiation.

16. After a period of three weeks during which the intestine has been adequately rested and the blood restored, higher calorie diets are instituted (3,000 calories).

17. At this phase of treatment the administration of 6 to 12 units of insulin daily combined with glucose per os is frequently followed by a rapid rise in the weight curve and an elevation of the blood pressure.

18. In seventeen consecutive cases treated by this method, clinical cure was obtained; one case of the series relapsed, but again rapidly responded to treatment.


**SPRUE TREATED WITH INTRAVENOUS INJECTIONS OF CALCIUM CHLORIDE**

W. Gover, M.B., B.Ch.Oxon.

The following clinical details of a case of sprue are interesting in view of the fact that this disease is very rare in Costa Rica, and there do not seem to be any published reports on this system of treatment.

A coffee planter from Costa Rica, aged 69, was first seen in August, 1928, with a two months' history of loose, frothy, clay-coloured motions, associated with loss of weight and anaemia. A diagnosis of sprue was made.

During the subsequent eleven months, some portion of which was spent in hospital, he received treatment on the usual lines. He was dieted strictly; calcium was given both as the
lactate and also in a proprietary preparation; liver, subcutaneous iron and arsenic injections, strawberries, and Batavia powder were also tried. The latter controlled the diarrhoea but did not appear to affect the course of the disease, and his condition deteriorated. The weight dropped from his usual 10 st. 6 lb. to 8 st. 13 lb., and loss of appetite and weakness were marked. In February, 1920, he was admitted to hospital and put on 2 lb. in weight, but he was discharged some weeks later very little better.

In July 1929, intravenous calcium treatment was started in conjunction with parathyroid extract, but the parathyroid was omitted later, as it appeared to have no effect. The series of injections commenced with an initial dose of 1 c.cm., which was gradually increased to 3 c.cm., at intervals at first of three days, which were increased to a week or longer as the patient's condition improved. A total of twenty-five injections was given.

The general condition of the patient greatly improved. His weight has increased from 9 st. 1 lb. to 10 st. 9 lb. His appetite is better, and he has much more energy. The looseness of the bowels has not disappeared; there are still on an average one or two motions daily, as contrasted with the daily two to three before the intravenous therapy was employed.

As an experiment, for a fortnight the treatment was omitted, and he was given instead 10 grains of calcium chloride by mouth, three times daily. No effect was produced other than heartburn and loss of appetite, and the patient did not experience that sense of well-being and energy which he always noticed after the intravenous administration. There did not appear to be any drawback to the treatment. For a few moments after the injection there was a sense of constriction in the throat, but this soon passed off, and caused no inconvenience.

Lloyd reports that sino-auricular heart-block has been produced by 4 c.cm. of 10 per cent. calcium chloride solution, injected intravenously, but that, on the other hand, 50 c.cm. of 1 per cent. calcium chloride have been injected without noticeable effect. Dutton recommends an initial dose of 1 grain in intravenous calcium administration for any purpose. In the present case a 2 per cent. solution was used.

_B. M. J., July 12, 1930._
HEMORRHHOIDS. The Injection Treatment and Pruritis Ani. LAWRENCE GOLDBACHER, M.D. Published by F. A. Davis Company, Philadelphia. Price G$3.50.

This small volume is designed to bring to the notice of the medical profession the treatment of internal hemorrhoids and pruritis ani in outpatient practice by injections of phenolized oil, 5 per cent phenol in vegetable oil.

The book is clearly written and well illustrated, the subject matter being dealt with under the following headings: General Considerations; External hemorrhoids and treatment; Internal hemorrhoids and the injection treatment; Pruritis ani.

The Author claims that internal hemorrhoids can be safely treated in the surgeon's office without hospitalization of the patient by a short series of injections and with a minimum of discomfort to the patient. Further that if his methods are carefully carried out a permanent cure is secured in the large majority of cases comparing very favourably in this respect with the results of surgical treatment. Any unprejudiced reader of this little book will acknowledge that he fairly substantiates his claim.

The extent of minor invalidism caused by hemorrhoids is hardly realised even by the medical profession. The Author quotes the statement by Otis that there were 90,958 cases of hemorrhoids during the American Civil War. In the World War there were 29,176 hospital admissions for hemorrhoids in the United States army from April 1, 1917 to December 31, 1919, representing a total loss of 623,493 days.

We believe that in China hemorrhoids are the commonest surgical condition in patients coming to our hospitals, and it is evident that any simple method which while without risk to the patient avoids the necessity for his hospitalization is one of the greatest value. Past injection methods have not always commended themselves nor have they been entirely free from risk.

It should be noted here, however, that the Author of this book points out that a careful and exact technic is essential if successful results are to be obtained, and the few special instruments designed for this operation ought to be obtained by those wishing to try this treatment.

J. L. M.

This is a difficult book to do justice to in a review as the reader is constantly irritated by the careless use of language and is therefore not quite in the mood to give full credit to an excellent book.

To get through the criticisms first. The point just noted is well exemplified in the title given above. What is a "second revised and enlarged edition?" Is it a second edition, revised and enlarged, or a third edition which is now revised and enlarged for the second time?

A title after all is not of great importance but unfortunately the same looseness of expression is found too often in the text. Terminology at times lacks exactitude. "Milk" leg is not a thrombo-phlebitis as here stated but a lymphatic thrombosis; and "ulcer cruris" is we think the most horrible hybrid that we have ever met. How potassium iodide can be given in 5 drop doses we cannot conceive.

Elephantiasis is entirely out of place in a book on varicose veins and how it can ever occur as an epidemic passes the imagination, nor do we see how the Author can be justified in condemning Kondoleon's operation for a condition which on his own showing he has seldom seen.

There is more justification for mentioning hemorrhoids in a book on varicose veins but a chapter of a page and a half only on so important a subject is worse than leaving it out altogether, and after all despite similarity in pathology, the treatment of hemorrhoids is not germaine to that of varicose veins of the extremity.

Despite these minor and very irritating faults this book is one of great value especially on the clinical side for its very careful analysis of the causes of success and failure in the injection treatment of varicose veins and the masterly description of technique. This is pre-eminently the part of the book that will appeal to the ordinary surgeon and it deserves his most careful study.

The injection treatment of varicose veins has come to stay, but there is some tendency to think that any man who can introduce a needle successfully into a vein is thereby fully qualified for this class of operation. To any such and to any who seriously think of using this form of treatment a study of this book will be most valuable.

J. L. M.

The League of Nations has recently rendered a unique service in publishing this report on the welfare of the Blind in various countries. It is the result of a questionnaire sent out to 57 countries. 26 replies were received and these replies form the basis of the report. Each country was asked to make a comprehensive statement as to the way in which it was dealing with its blind population, and the information thus obtained is set out in pamphlet form thus making a document of great value to all who are interested in the welfare of the Blind.

It deals in a very thorough and efficient manner with the whole question of the Blind, giving a comprehensive summary history of the movement starting from King Louis IX, for the betterment and education of the Blind, and following with its gradual growth until the present day when the Blind in nearly every country are taken care of in a remarkable and sympathetic manner. It explains the methods and systems employed in the education of the young Blind; of vocational and higher education; of the various occupations that are open to the Blind and the methods of remuneration. It also tells about the care of the aged and decrepit in homes and the pensions they receive. It appears that in some countries the majority of the Blind are taken care of from the time they are of pre-school age until they pass beyond the need of earthly help. Finally it deals with the causes and prevention of blindness, although this subject was not within the scope of the report. It points out "that the systematic ascertainment of the causes of blindness has hitherto only been pursued to a very limited extent in any country," but Ophthalmia Neonatorum, one of the chief causes of blindness throughout the world has been greatly reduced especially in America during the past twenty years, "but much still remains to be done before every case in which eye trouble exists can be ascertained and properly dealt with."

This report also points out the large expenditures that are involved in the care and education of the Blind. In England in 1924-1925 payments for more than £1,250,000, were made, while from other sources we understand that America has an annual economic loss of about C$36,000,000.00.

We note with great concern that China has of necessity been entirely omitted from the report, with the exception of a mention of the printing of the Braille in Shanghai and Peking. It is to be hoped that this will give this great country the necessary impetus, so that before long she may give the work among her million Blind her serious attention in order that she may be on a par with other countries.

Those who are interested in the work for the Blind have a great deal to be thankful for in the issuance of this very illuminating report and we all sincerely hope with those responsible for this report "that it may lead to a fuller knowledge of what is being done and may stimulate a pooling of experiences among administrators, to the advantage of the Blind. Much good might be done if information were collected systematically and made available."

G. B. F.

The International Association for the Prevention of Blindness was formed in September 1929 at Scheveningen. As a result this report has been published which deals with data collected as to the enormous number of blind persons and difficulties met with by governments in dealing with their precarious situation. It takes up the work of what existing organs are doing for the Prevention of Blindness which was not touched by the League of Nations' report on Welfare of the Blind.

It avers there are at least 6,000,000 blind in the world and shows how they are distributed in the various countries. The greater proportion of these could have been prevented had modern preventive methods been adopted. It considers the chief causes of blindness to be Trachoma, Venereal Disease, Ophthalmia Neonatorum, Small Pox, Congenital Defects and Glaucoma, and speaks of their causes and symptoms. It describes seriously defective vision caused by Myopia, Hyperopia, Astigmatism, Presbyopia and how those engaged in school work should be on the watch for symptoms. A summary depicting the needs of prevention work in forty-seven countries and how each is meeting the problem forms interesting reading and will be especially useful for those whose work and sympathies are along these lines. It takes as a concrete example the wonderful work done by the National Society for the Prevention of Blindness in America and tells of the magnitude and usefulness of that organization. Its annual budget runs about G$140,000.00 which is entirely raised by voluntary contributions. The services rendered by this society may be classed under the following headings. Eye infections of new born babies, eye clinics for pre-school children, saving the eye sight of children of school age, trachoma, eye hazards in industry, field service, literature and other propaganda, correspondence, publications and distribution. We may well look to America when contemplating prevention work and follow the unique example she has set the world.

"The International Association for the Blind intends in the first instance to unite the efforts of all who are willing to help in preventing accidents and disease from making new victims, in bringing about a decrease in the number of the Blind, in two words in protecting and preserving eye sight." We wish this organization every success and sincerely hope that a branch will soon be inaugurated in China.

G. B. F.
Obituary

C. Voongping Yui, M.D., D.P.H.

The "North-China Sunday News" regret to announce the death of Dr. C. Voongping Yui, one of the most distinguished Chinese medical practitioners of Shanghai, which took place at his residence at Loh's Garden, West Gate, last Thursday.

Dr. Yui was born in Shanghai in 1885 and received his medical training first at St. John's University and St. Luke's Hospital, and later at the University of Pennsylvania, Philadelphia, where he specialized in public health and obtained the degree of doctor of public health.

Returning to China in 1910, Dr. Yui soon built up a large and lucrative private practice, and his consulting rooms both in the Settlement and the city were always filled with patients. But Dr. Yui was interested also in the social problems of his people, especially in the prevention of disease. To carry out this effectively, he wrote during the past 15 years more than 20 simple tracts on health in the Chinese language, in which work he received much help from his wife, who was a very accomplished Chinese scholar.

When the National Medical Association was founded in 1914, Dr. Yui took a very conspicuous part in its organization and served for nearly 12 years as editor of the Chinese section of the "National Medical Journal." For his distinguished services Dr. Yui was elected president of the National Medical Association in 1919 and served for the term of two years.

Dr. Yui was exceedingly popular with his patients, for whose welfare he constantly imported the latest instruments and medicines, and in his consulting room could be seen the latest medical invention of the day. His death will be much felt by his colleagues both in Shanghai and elsewhere and his place will be hard to fill among the Chinese medical profession.

The executive council of the Medical Association at its special meeting on Friday passed a resolution expressing the deepest condolence with his family.

Dr. Yui leaves a widow and eight children, two of whom are married.

North China Daily News.
Dec. 7, 1930.
NEW MEMBERS PROPOSED

Proposers:—Dr. S. C. Chia,
Dr. C. C. Wang.

Proposers:—Dr. S. C. Chia,
Dr. C. C. Wang.

NEW MEMBERS ELECTED

Dr N. G. Patterson P. S. Sutsien, Ku.
Dr Doris B. Clay L. M. S. Shanghai, Ku.
Dr T. P. Tu W. M. M. S. Wusueh, Hup.
CHEELOO PHARMACY SCHOOL

Applications are invited from Mission hospitals for trained Pharmacists from the above school (attached to the Medical School of the Shantung Christian University).

A class of trained Pharmacists will be graduating in June 1931, and a few of the men are yet not fixed up to go to a hospital.

Will hospitals needing trained Pharmacists kindly apply to Mr. W. P. Pailing, Pharmacy School, Shantung Christian University, Tsinan, Shantung, and also kindly give particulars as to salary, room, board etc.

*Received too late for insertion in proper place in this issue.—Editor.