Case I.
Kala-azar
Dr. Comrie's Case. W.26.

Wightman Prize Essay, 1928.
Case I.

Kala — Azar.

During the Christmas vacation of 1927, and later in the Spring term of 1928, whilst acting as junior clinical assistant in Dr. Comrie's wards in the Royal Infirmary, I had the opportunity of studying the unique features of a case which was to prove as interesting as it was rare. Indeed Professor Ashworth once informed me that the disease under observation had only been the second of its kind in Edinburgh over a period of 20 years, the former having occurred in an Egyptian graduate from the Kassala district of Central Africa.

On the 24th December, 1927, a native seaman was sent by the harbour doctor in Leith, to the Royal Infirmary and was admitted to Ward 26.

Only a meagre history of the case could be obtained from the shipping authorities, and the patient himself knew few words of English, but it was ascertained that he was a mess-room steward named Lia Kutirn, 30 years of age, and that he had been at sea most of his life. He was a native of Goa, a Portuguese seaport in India, and the condition for which he was admitted began just after he left India on his last voyage. Apparently he had been attacked by a high fever, with rigors and vomiting after the ship weighed anchor at Bombay. Associated with this there a feeling of fulness in the abdomen and some swelling. This lasted for about a fortnight and was followed by a period of apyrexia and general improvement until they reached Madagascar, when there was a severe recurrence of his initial symptoms. Thereafter he was practically an invalid all the voyage to Hamburg in
Germany when there was a slight improvement. From Hamburg he sailed to Leith where the progressive enlargement of the abdomen and the continuation of the fever with increasing cachexia caused him to be sent to hospital. Nothing further could be elicited except that his digestion and appetite had remained unimpaired.

**State on admission.**

Patient obviously in extremis.

- Height 5 ft. 7"; Weight 7 stone 2 lbs. - Marked emaciation.
- Skin of hands and feet and around eyes deeply pigmented with an earthly grey colour.
- The eyes lustreless and sunken, showed jaundice of conjunctiva.
- There was some epistaxis.
- Lips were dry, cracked and ashen grey, and the gums lacerated and bleeding.
- The hair was dry and brittle.
- Extreme laxity of the ligaments of the joints of the fingers was present. (A feature common to many Oriental races).
- A few petechiae on arms and chest were seen. There was no rash present on the body and no evidence of oedema. A marked prominence of the abdomen on the left side, extending over the mid-line was noticed.
- The patient was bringing up copious quantities of sputum.

The blood pressure read:  
- Systolic 90  
- Diastolic 53

| Temperature | 98.4°F. |
| Pulse      | 100    |
| Respiration | 24     |

During the first few days after admission the patient was kept under careful observation, and in the meantime the physical examination was carried out.

**Alimentary system.**

**Subjective phenomena:** Appetite and digestion had remained good during patient's present illness. Otherwise there
was nothing to note.

The lips were cracked and dry, and as far as could be ascertained showed some anaemia of the mucous membrane. The front teeth were relatively healthy. The molars both upper and lower were carious. The gums were slightly lacerated and bleeding in some areas. The tongue was remarkably clean and healthy looking. There was a fairly free salivation associated with a copious green sputum.

Vomiting had occurred at the onset of the disease but had not been noticed since. No information was available as to its character.

Under the hospital regime the patient's alvine functions became regular. There was no abnormal character of the stools. The Benzidine reaction (tested later) was negative.

The Abdomen. There was a general rounding of the abdomen with a marked loss of subcutaneous fat. A definite bulging, which extended from under the left costal margin ended fairly abruptly 4" on the right side of the umbilicus. This swelling moved with respiration. There was a slight loss of tone in the abdominal wall. On palpation the most prominent feature was the swelling referred to above. No bowel lay between it and the abdominal wall. The skin over it was somewhat tender. The edges of the tumour were sharp, and a definite notch could be made out. A small space could be identified between the swelling and the erector spinae muscle. These facts showed that the bulging was due to an enlarged spleen. A dull note was obtained over it on percussion and the organ was firm and tense. A tracing of its outline was later made.

The liver was uniformly enlarged for 2" below the right costal margin as determined by percussion and palpation. It was not so tense nor tender as the spleen, and no evidence of cirrhosis was present. A tympanitic note was got over
the caecum and ascending colon and some tenderness was elicted there. There was nothing referable to the stomach. There was no ascites present.

**Haemopoietic System.**

Subjective phenomena were all referable to the splenic condition. There appeared to be no other endocrine disturbance. On the assumption that it was some splenic disease associated probably with blood changes, a careful examination of the latter was made.

The Haemoglobin was found to be 55%.
The red corpuscles 2,430,000.
White corpuscles 2,400.
The ratio between whites and reds was as 1 : 1000 (the significance of this was to be realised later).

A differential count revealed.
Polymorphs 66%. Small lymphocytes 20%.
Large hyaline mononuclears 14%.

The examination of films showed that poikilocytosis was not marked. A few microcytes and macrocytes were observed, but even on repeated examination no nucleated red cells.

The colour Index was just over 1.

**Circulatory system.**

Subjective: The marked anaemia revealed by the blood count, was not noticeable to any degree owing to the patient's natural pigmentation, but it was sufficient to cause some dyspnoea for which he was propped up in bed. There was a bad cough associated with much sputum. Otherwise nothing to note.

Pulse. 100-110 per minute. Regular in time and force but soft and weak in character. The Systolic pressure estimated by the sphygmomanometer was 90mm. Hg. The Diastolic 54mm. Hg,
Heart. Inspection, palpation and percussion showed nothing abnormal.

Auscultation: All the sounds were closed, but faintly conducted. Haemic murmurs were occasionally heard in the nutral and aortic areas.

Respiratory System.

Subjective: Slight breathlessness from the anaemia. Some epistaxis but no haemoptysis.

Breathing: Thoraco-abdominal in type: 25 Resp. per min.

Sputum. Very copious. Greenish in type and very tenacious. Loaded with pus cells, catarrhol lung cells and micro-organisms of the usual type. (Stained later every day for a fortnight by Ziehl-Neelsen method with a negative result).

Thorax. Nothing to note on inspection or palpation.

Percussion. Apices clear, also anterior, lateral and posterior surfaces.

Auscultation. A few coarse rhonchi with crepitations were heard over both bases, due to associated mild catarrh. No evidence of consolidation.

Cutaneous System.

The skin was usually dry, but when a rigor occurred was bathed in a drenching sweat. A few petechiae were seen on chest and axillae. No rash was present.

There was a marked loss of subcutaneous fat, and patient was very emaciated.

Urinary System. Nothing subjective to note.

Quantity of urine in 24 hours 30-40ozs.

Acid in reaction: Sp. Grav. 1020-1028.

No abnormal constituents.

Nervous System: Patient apparently depressed and uneasy about his condition, but sleeps fairly well. Nothing else to note.

Locomotary System. The muscles are greatly atrophied and the ligaments of the finger joints very lax. Pat. too weak to
It was at once obvious that the chief interest of the case centred around the splenic condition. It was also agreed that with this were associated the very prominent blood changes. Moreover the fairly characteristic history of rigors and sweating with progressive enlargement of the spleen, coupled with the fact that the patient had come from a tropical country seemed to point towards malaria as the disease. The relative increase of the hyaline mononuclears seemed an additional point in the favour of such a diagnosis. The temperature chart would enable us to identify the type of malaria (if present) and an examination of blood films could be made for the malarial parasite. Whilst these observations were pending, the evidence seemed sufficient to warrant the exhibition of Quinine, and this was administered to the patient in 5 grain doses T.I.D. Mist. Ammon Carb. was also given as an expectorant. As time went on it was seen that the pyrexia was of a low remittent type seldom rising above 102°F, and extremely irregular. The patient still suffered from rigors and drenching sweats. At first he asserted that he could foretell when a rigor would occur, but it was observed that his predictions did not correspond to the periodicity of the tertian or quartan malarial fevers, and in the course of a few days it was found that his forecast was seldom accurate. In the meantime despite quinine therapy, his condition grew steadily worse and he became more depressed. The temperature record now convinced us that the rigors were irregular in time and character corresponding indeed more to the malignant quotidian type. But one puzzling phenomenon of the temperature was already present, namely the double daily rise seen on December 28th and later on January 4th, a condition which seemed wholly incompatible with parasitology of the malarial fevers. One other fact of striking importance was the complete lack of response on the part of the temperature, to the exhibition of Quinine. Rigors and sweating occurred despite all efforts...
at treatment, and the climax was eventually reached, when Col. Greig announced that after repeated examination of blood films no malarial parasites could be found.

We had now to revise our table of diagnostic values. If the condition were not malaria what else might it be? The various leukaemias especially myelogenous leukaemia with its enormous spleen, were at once excluded on account of the leukopenia which was present. Trypanosomiasis was a possibility which had to be kept in mind. Egyptian splenomegaly was the rather to be excluded on account of its geographical distribution. Banti's disease bore a close clinical similarity to the disease under observation, and malignant disease of the spleen was an element in differential diagnosis.

But the case under our care recapitulated so strikingly the difficulties in diagnosis encountered by the early investigators of another tropical disease, that we revised the case history carefully for points of comparison. This other disease called Kala-Azar was long believed to be a peculiarly fatal type of chronic malaria until Sir Patrick Manson amongst others pointed out that no malarial parasites could be found in the blood; that there was no response to quinine, and lastly that there was no parallelism between the temperature in this condition and that of the known types of malaria. These observations coincided entirely with what we had found in Kutian's case. Was there any other point of resemblance? The leucopenia was extremely suggestive and then we remembered the peculiar ratio between the white and red cells in the blood, 1:1000, when normally it is 1:500. Moreover the increase of the hyaline mononuclears to 14% though less convincing was not so much as we might expect in a chronic malaria. The temperature chart was next subjected to a close scrutiny, and the significance of the double daily rise of temperature was borne in upon us. This corresponded to the
double remittent type described by Rogers as occurring in Kala-Azar. These facts taken in conjunction with the accessory points of the history seemed sufficiently convincing to indicate a search for the parasite responsible for Kala-Azar. This is the Leshman-Donovan body described separately by these two observers in 1903.

How was the parasite if present to be obtained. There were two available methods: (1) By blood culture (2) By spleen puncture. The organisms are relatively few in the peripheral blood where they occur in the leucocytes, and culture on the N.N.N. medium at 22°C. is a fairly laborious process and not always successful. On the other hand splenic puncture was not lightly undertaken. Manson states that severe haemorrhage frequently follows this seemingly trivial procedure. In Kutians case however, it was agreed that the necessity for a speedy diagnosis with a view to immediate treatment outweighed the above consideration. The parasites are distributed generally throughout the body, inhabiting the endothelial type of cell. Thus in the spleen they are found in the large macrophages or splenic cells.

On the 25th of January, Col. Greig decided that he would puncture the spleen. The skin over the part was first rendered sterile with iodine and the abdominal movements controlled by a binder. The spleen was also fixed by hand. The patient was instructed to cease breathing when the spleen was being punctured. A fine hypodermic needle, scrupulously clean and dry was used. (Water in the needle will distort or burst the organism if present, and render it unrecognisable). The spleen was then punctured and some splenic juice drawn off was transferred to slides and several films made, and stained by Leishman's method. There was no haemorrhage from the spleen. The films are so made that an abrupt edge is obtained. A localised condensation of organisms is thus secured in this area. And the method is invaluable where the organisms are suspected to be few in number.
The diagnosis of Kala-Azar was confirmed by Col. Greig who found the Leishman Donovan bodies in many of the films, examined by the oil-immersion lens.

The existence of the disease having now been established it became necessary to enquire into its pathology and complications, with a view to treatment. The organism responsible is a small oat-shaped body, 3u long by 2 u. broad with two chromatin bodies situated at the opposite poles. The macronucleus is round, whilst the micronucleus is rod-shaped. On the N.N.N., culture median at 20°C. they elongate and assume the flagellate form. It has recently been suggested that the sand-bug: Phlebotomus Argentipes - may be the vector of the disease. Kala-Azar is epidemic in Assam, especially in the Garo Hills, where in the past it has ravaged the population, but is unknown in Goa where the patient came from. Crowded quarters in squalid surroundings is however probably responsible for the spread of the disease in seaport towns. As previously indicated the organism inhabits the endothelial type of cell and thus is found in the splenic macrophages, in the myelocytes of the bone marrow, and may be found in the lungs, testicles, and other viscera, and also in the ulcers in the intestine and lymph glands draining them. It acts as an irritant, causing enlargement of liver and spleen. The latter is hard and fibrous and the capsule and septa are much thickened. In the Wellcome Bureau of Medical Research in London, where I was enabled with the permission of Dr. Dawkes the curator, to study the specimens from Kala-Azar cases many examples of subcapsular infarcts were seen in the spleen, due it was believed to stasis with thrombus formation in the subcapsular vessels; and perihepatitis (from which our patient eventually suffered) is a very common occurrence.

Before the introduction of antimony in the treatment 96% of all cases died, usually of some intercurrent disease, such as tubercle, dysentery or asthenia, whilst perforation of the in-
testinal ulcers was a frequent cause of death.

Dysenteric diarrhoea is a common sequela, and real amebic dysentery may be superadded. Congestion of the lungs and pneumonia may carry off the patient. The possibility of Phthisis caused a routine examination of the patient's sputum every day for Koch's bacillus but in the long run it proved negative. Some perihepatitis which ensued as a result of the splenic puncture was treated with hot packs and poultices. The pain was once severe enough to require Tr. Opii. m.X.

Intravenous antimony medication was begun on the 25th of January. Antimony seems to act as a real specific in these cases and has robbed the disease of many of its terrors. In Assam in 1925, 60,000 cases were treated successfully with it, and apparently the patients no longer remain infective after it has been used. It is not quite known how it acts, since the Z-D bodies may still be found in the spleen after prolonged exhibition of the drug. Its efficacy can be tested by the formal-gel reaction. In this case it was decided to use Neostan or Stibamine Glucoside intravenously beginning with 0.1 Gr. This is dissolved in 10cc. of sterile distilled water. The cubital vein of the elbow is employed for injection which is carried out slowly, after making certain that the vein has been entered by first drawing back a little blood into the syringe. Care has to be taken to prevent leaking of the compound into the tissue where it would cause sloughing. The injections were given every 2nd and 3rd day and the dose gradually increased up to 0.3 Gr. after a fortnight. Tracings of the spleen were now made and a diminution in size was observed. The initial injections were usually followed by some discomfort and general malaise sometimes accompanied by a rise in temperature, but after a week the temperature began to show a steady decrease. Its excursions were now seldom more than the daily variation and the sweatings and rigors ceased. Coincidently there was a steady depression of the pulse rate to
**Ward 26**

**Date of Admission:** 28th December 1937

**Name and Age of Patient:** Mrs. Kuttan, Age 30 yrs.

**Doctor:** Butler, Keith

**Clinical Clerk:**

<table>
<thead>
<tr>
<th>Date</th>
<th>Diet and Medicines</th>
<th>Date</th>
<th>Diet and Medicines</th>
<th>Date</th>
<th>Laboratory Examinations</th>
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<td>Milk Diet</td>
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<td>3rd Brand X-ray</td>
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<td>X-ray - Chest</td>
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<td>1/128</td>
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<td>1/128</td>
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<td>1/128</td>
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<td>7/128</td>
<td>X-ray - Chest</td>
</tr>
<tr>
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<td>Equina 5</td>
<td>1/128</td>
<td>X-ray - Chest</td>
<td>7/128</td>
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<tr>
<td>15/128</td>
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<td>16/128</td>
<td>Triple Jabs 11 p.m.</td>
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<td>3/11</td>
<td>1/128</td>
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<td>7/128</td>
<td>X-ray - Chest</td>
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**Temperature**

![Temperature Graph](image)

**Pulse**

![Pulse Graph](image)

**Respiration**

![Respiration Graph](image)

**Urine**

| Time | 4/8 | 4/4 | 3/2 | 2/8 | 1/0 | 0/4 | 6/0 | 5/4 | 5/6 | 4/8 | 2/0 |

**Bowels**

| Time | 1/0 | 2/1 | 1/0 | 0/1 | 0/0 | 1/0 | 0/0 | 1/1 | 1/0 | 2/0 | 1/0 | 1/0 | 0/1 |

**Note:** The graph shows fluctuations in temperature, pulse, and respiration over time, along with the intake of various medications and X-ray examinations.
**Ward:**

<table>
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<th>Date</th>
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<td>1st-2-28</td>
<td>Light dinner</td>
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<tr>
<td>2nd-2-28</td>
<td>W. Mel. In. Co. 3 M\rt</td>
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**Date of Admission:** 24th December

**Name and Age of Patient:** *Miss* M. Age 30.

**Diagnosis:**

**Doctor:** Butler, Luck

**Clinical Clerk:**

**Laboratory Examinations:**

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<td>24-1-28</td>
<td>N. S. 3 M\rt a m.</td>
</tr>
<tr>
<td>24-1-28</td>
<td>Mild Fever</td>
</tr>
<tr>
<td>25-1-28</td>
<td>Cold Fever</td>
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</table>

**Temperature Chart:**

- **Time:** 6-12 AM, 12-6 PM, 6-12 PM
- **Date:** 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 1, 2

**Urine:**

- **58, 34, 48, 36, 38, 38, 36, 40, 56, 48, 34, 64, 60, 54**

**Bowels:**

- 1, 2, 1, 0, 2, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1
## Date of Admission
19th December 1924

## Name and Age of Patient
Miss Section, Age 38

### Ward 2L

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<th>Date</th>
<th>Diet and Medicines</th>
<th>Date</th>
<th>Laboratory Examinations</th>
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<tr>
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<td>Light Diet</td>
<td>18-1-24</td>
<td>H.5 3:22 a.m.</td>
<td>9-1-24</td>
<td>Urine: 36, 64, 56, 48</td>
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<td>Weight 6 ft 6 in</td>
<td>20-1-24</td>
<td>H.5 3:22 a.m.</td>
<td>9-1-24</td>
<td>Bowels: 1, 1, 1, 1, 1</td>
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<td>26-1-24</td>
<td>Weight 7 st 11 lb 14 lb</td>
<td>26-1-24</td>
<td>H.5 3:22 a.m.</td>
<td>9-1-24</td>
<td>Urine: 36, 64, 56, 48</td>
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</tbody>
</table>

- **Clinical Clerk**: Dr. Section
- **Doctor**: Dr. Section

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**Note**: Medical records and diagrams are presented in a format typical of historical patient care documentation. The sheet includes sections for diet, medications, laboratory examinations, and physiological data such as pulse, respiration, and temperature. The diagrams illustrate variations in measurements over time, indicating the patient's condition and response to treatment.
between 70-30 per minute, and the respiration became normal. The copious sputum was now diminishing in amount, and the patient's mental outlook began to appear brighter. The result of the antimony medication was now observed by Napier's "aldehyde test". Napier observed that if one drop of 30% commercial formaldehyde is added to 1cc. of clear serum from a patient's blood, the serum immediately becomes solid and opaque like the white of an egg if the disease is Kala-Azar. By comparing the density of successive tests, it is obvious that under treatment if successful a diminution will be found. The rationale of this so-called "gel" reaction is not quite understood. It is believed not to be due to a specific anti-body since modified forms of the reaction are also given by syphilis, yaws etc. Col. Craig considers that it may be due to the presence of an excess of globulin. Provided the parasite has been found, it becomes thus a valuable accessory to the study of the treatment.

Napier writing in the "Indian Medical Gazette" July 1927, puts forward a test which he considers is diagnostic of the disease "The reaction", he says, "occurs with a number of pentavalent antimony compounds" and the intensity of the reaction varies according to the therapeutic efficiency of the compound used. 2 drops of 24 hour old serum to 2cc. of a 0.25% solution of Stibureo or 2 drops of freshly separated serum of 2cc. of 1% sol. Stibureo, are agitated and left for 10 mins. If Kala-Azar be present, a heavy flocculent precipitate will form, separating within 10 minutes, leaving a clear supernatent fluid". If the results claimed for this method are confirmed, it seems likely that it will obviate the necessity for spleen puncture with its associated risks.

With Antimony the parasites disappear from the peripheral blood in about three days and most of them from the spleen after 15 injections (i.e. about 4 Grammes of Neoastam). All the while the spleen is reducing in size as is shown by the drawings given. Owing to the great increase in the fibrous tissue element it
never returns, however, to its normal size. The liver is said not to diminish in size since antimony acts on it in much the same way as does Salvarsan when used in the treatment of syphilis. Probably this only holds good for certain compounds, since before the patient was discharged the liver had returned to the level of the costal margin.

I was now making a blood examination weekly and it was seen that a fortnight after treatment by Antimony was begun the red corpuscles had greatly increased in number. The whites also were more numerous. The successive steps in the progress were recorded as follows:

<table>
<thead>
<tr>
<th>Date</th>
<th>Red Blood cells</th>
<th>White cells</th>
<th>Hb</th>
<th>Ca</th>
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<tr>
<td>20.1.28</td>
<td>2,430,000</td>
<td>2400</td>
<td>55%</td>
<td>1.1</td>
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<tr>
<td>28.1.28</td>
<td>2,450,000</td>
<td>2400</td>
<td>55%</td>
<td>1.1</td>
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<td>14.2.28</td>
<td>3,200,000</td>
<td>3200</td>
<td>60%</td>
<td>1</td>
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<td>24.2.28</td>
<td>3,218,000</td>
<td>3500</td>
<td>62%</td>
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<tr>
<td>2.3.28</td>
<td>3,350,000</td>
<td>3600</td>
<td>65%</td>
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<tr>
<td>11.3.28</td>
<td>3,570,000</td>
<td>4400</td>
<td>70%</td>
<td></td>
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<tr>
<td>3.4.28</td>
<td>4,720,000</td>
<td>6600</td>
<td>85%</td>
<td></td>
</tr>
</tbody>
</table>

(a) = When Neostam was started.
(b) = When patient sent to convalescent home.

By the 1st of March, the cough had entirely stopped and the sputum and excess salivation were absent. The patient had then received 3.75 grams of Neostam and had exhibited no reaction except the slight malaise after the injection. The temperature was still somewhat irregular but never rising above 99°F. The pulse showed a somewhat corresponding irregularity, which however varied within very narrow limits. To me, it seemed that the leucopenia must be associated with an increase in the blood bacteria, and that this element was the cause of the minor elevations of temperature. I had moreover observed both in stained and wet films that the patient's blood was swarming with micro-organisms of the coccoid and diplo-coccoid type, and it seemed reasonable to conjecture that in his present state, secondary invaders of a more virulent class might carry off the patient by some intercurrent infection. To combat this I
suggested the administration of Marmite to increase the numbers of leucocytes.

On the 12th of March, Kutian had received in all 4.9 Grammes Neostigmine in a series of 20 injections over a period of 7 weeks, and it was now considered that the disease was cured. The opacity of the formol-gel reaction which had been diminishing for several weeks back now was entirely gone. It was believed that an immunity had been established, and the question of his convalescence cropped up. It was determined to send him to Corstorphine convalescent home for 3 weeks. He was now up and about a little each day, and was bright and more hopeful in his outlook. The chart showing the diminishing size of the spleen impressed him considerably. His appetite on a light diet was good and he was putting on weight. His bowels were acting regularly.

On Wednesday 28th March, I visited Kutian at Corstorphine. He was now exceedingly bright and cheerful and had obviously put on weight. He had gained 11½ lbs. during his fortnight's residence. Sister informed me that his temperature had not varied more than 1°F. from normal. There was no evidence of jaundice in the conjunctiva or sclera, and no bile in the urine; though he had been somewhat breathless especially on going upstairs before he left the Infirmary, dyspnoea was now absent and he was able to perform simple tasks about the grounds of the Institution. I took another tracing of his spleen and found a very appreciable diminution in size, it was now well within the umbilicus and in a more vertical plane, as it fell back towards the costal margin. It was now much softer in consistence and the area of perisplenitis near the lower margin was reduced in size and less tender when palpated. The edge of the organ was less easily identified than formerly.

When the patient lay down there was no localised prominence of the abdominal wall. In the erect posture a generalised swelling was still perceptible due to the displacement of the abdominal viscera by the yet enlarged spleen. The heart sounds were now
Case of Kala-Azar.  Lie. Kuthan.  Culture of spleen showing reduction in size after the exhibition of Neostam (Utranine Sulphonate).
well conducted, the lungs were clear, and the patient's general health good.

On the 3rd of April, he left Corstorphine and came to W. 26 to report for the last time.

His weight was now 9 st. 6 lbs. in a gain of over 2 stones since admission. The spleen was still further reduced in size and the blood picture was -

Reds = 4,720,000. Whites 6600  Hb. 35%.

The shipping authorities had arranged for him to get a ship back to Calcutta where he was asked to report for examination at the Hospital for Tropical diseases there.

The chart of the spleen which is reproduced here is a facsimile of that which I prepared for the Ward case.

The treatment of this case must be deemed in the highest degree satisfactory. Not merely was the actual cause found, but also a specific remedy to remove it.
Case 2.
Sub-acute Arsenical Poisoning
Dr. Goodall's Case. W.S.
Case 2.

Sub-acute arsenical poisoning.

During the Winter term of the 4th year of medical study, I was engaged in Dispensary practice at Marshall Street. The course of instruction conducted there involved district visits, as well as attendance at the out-patients cliniques. Thus it was, that I was brought face to face with a case which was to arouse considerable interest outside the immediate medical circle. Indeed, much of what follows has been taken from the official report which was prepared in the event of police proceedings.

On the morning of Wednesday, 9th November, 1927, the following note was handed in at the Dispensary.

"Dear Sir,

Will you kindly send a doctor round to see Mrs ...... as soon as possible as she is very ill.

Mr. ........
2 ........
2nd flat, left-hand lobby."

On receipt of this note, I went in company with a fellow-student, (Mr. A. Haddow) to see the case. On our arrival we found the patient in bed obviously very ill. In the house were also present her two children and a neighbour. The room was small and dirty and only meagre daylight filtered through the dusty window panes.

The patient lay in bed obviously in a very weak state. She was very emaciated, with a pale and anxious face. There was no jaundice, cyanosis nor dropsy present. The mouth was open and the thin lips drawn over the gums. The voice was very weak and husky - Hawking is a more appropriate term. The temperature was not raised. The Thyroid gland was moderately enlarged, and there was a definite exophthalmos.
The patient complained of great weakness, sleeplessness, sore tongue and throat, great thirst, impairment of voice, and general malaise.

She was fairly good witness, yet it was difficult to escape the conviction as time went on, that our questions were answered somewhat furtively. We succeeded however in eliciting the following history.

At 5 p.m. on Sunday 30th October, the patient partook of a slice of pudding sent her by her mother-in-law and brought by her husband. The pudding had no unusual taste, but the patient stated that "she did not feel sure of it". No one else partook of it. At 9.30 p.m. she went to bed with very severe symptoms...nausea, sickness, intense diarrhoea, sharp epigastric pain, loss of appetite and great thirst. At first the vomit consisted of food but later was fluid and grey with red streaks. She was not fevered however, but spent a sleepless night.

The diarrhoea, (motions fluid and flecked) continued for two days and then ceased entirely. No medical advice was sought, but the patient took a stomach powder bought from a chemist. The sleeplessness and restlessness continued, until on the 6th and 7th November the patient became worse with the development of a sore tongue and throat, with copious salivation. We then proceeded to the physical examination of the patient.

Her general features have already been noted:-

**Alimentary System:**

**Subjective:**
- No pain in the abdomen.
- Sore tongue.
- Copious salivation
- Extreme thirst.

**Objective:**
- Mouth: Most of the teeth were carious. The tongue was very red, swollen and congested, and covered with a species of membrane, which was so sticky, that a spoon used as a tongue depressor, readily adhered to it.
- Somewhat indrawn. A few striae gravidarum were seen. No tenderness in any region was elicited on examination.

**Circulatory System:**
Subjective - nothing referable to the heart.

Objective - Pulse. Rate 160, regular in time and force (9th Nov.). Irregular in time and force on 10th November. The sounds were closed, but extremely loud and booming.

Respiratory System:

Subjective - nothing to note.

Objective - Respiration not increased in number. On auscultation, moist sounds were heard at the basis of the lungs.

Urinary System:

Subjective: Patient noticed a reduction in quantity during the recent illness.

Objective: A specimen was removed on 10th November and duly examined.

Skin

Herpes was observed on the upper lip. An erythema was present on arms and chest. Mrs attributed this to the fact that she was menstruating. When we pointed out the extent and distribution of the rash however, she asserted that it was much more extensive, than she had ever before noticed it. A slight scaly desquamation on the palms and later on the brow was observed. There were no nail changes.

Nervous System:

Subjective: The patient was very nervous, anxious and restless.

Objective: a fine tremor of the fingers was probably attributable to her exophthalmic goitre.

Locomotory System:

Subjective: Patient very dizzy on attempting to walk, before taking to bed. No complaint of cramps in the limbs.

Previous History: The patient was perfectly well until 1916. After the Edinburgh air-raid of that year she developed exophthalmic goitre. She was last treated for this condition in the Royal Infirmary eight years ago. The condition has persisted since, but she has been quite able to go about her ordinary household duties. Her marriage resulted in two male children, one about 7 years of age and the younger 3 years. Both labours were exceedingly difficult, and the patient was counselled to have no more children. There have been no miscarriages.
The home conditions were extremely squalid and I enquired the nature of the husband's employment. We found he was a printer's machineman, nearing the end of a two month's spell of work. Something led me to ask if her husband treated her well. By her answer and reaction she led us to believe the reverse, and on the strength of some vague suspicious flitting through my mind I mentioned that I should like to see him. After all, I thought, our experience is very limited and Robert Hutchison has told us "that the commonest things occur most commonly". The patient described her mother-in-law as "a wicked woman". The case was obviously an unusual one, and no definite diagnosis was reached at the end of our first visit, and we masked a temporary inactivity by prescribing a pectoral stimulant.

On leaving, the neighbour accompanied us outside and confirmed the idea we had gained as to the family relations.

Haddow and I determined to discuss the possibilities of the case the same evening. He mentioned then the suspicion which had already crossed my mind, and we consulted Sydney Smith's "Forensic Medicine". The resemblance between the picture described and the phenomena we had observed in our patient was so striking when taken in conjunction with the accessory facts in the history that we agreed on the possibility of the condition being sub-acute arsenical poisoning. We decided there and then to pay another visit early next morning and collect specimens for examination.

On Thursday 10th November we called about 10.30 a.m. The patient was still in bed after a sleepless night. The condition was rather worse, especially with regard to the circulatory system. Also present were one of the children and the same neighbour. (We later discovered that the patient's father had been present in the next room). We discovered in conversation that the husband of this neighbour was ill with some condition that had not been diagnosed. On questioning Mrs. further we found that no one else had partaken of the food sent to her,
that the interval between the ingestion of the food and the onset of severe symptoms was 4½ hours, that slight nausea followed almost immediately on taking the food, that Mr. was asked to send for a doctor on 8th Nov. (i.e. 3 days after the onset of symptoms) and that the vomit was grey in colour. Retching and thirst were prominent features, and there was a definite reduction in the quantity of urine passed.

Two specimens of hair were taken - proximal and distal - and a sample of the very copious sputum. (This was later stained Zeihl-Neelsen but proved negative). We asked that all the urine passed should be kept, together with a specimen of the stools. We arranged to call for these at 1.30 p.m. the same day.

At 1.30 we again visited the house. The stools were formed, and although no blood could be made out, the patient said she had noticed it in previous specimens. A sample of urine was handed over in a lemonade bottle by the neighbour. The husband, an ex-soldier, was now present. He gave us details of his work. After we had left the house he followed us down the stairs.

He was somewhat agitated, with trembling hands, and asked if we wished to ask him anything. Haddow asked him if he associated his wife's illness with anything. He said it was due, he believed, to her goitre. He then went on to say that he would see to the bottling of the urine daily and have it wrapped up for us when we called. We then left him, rather impressed by his demeanour. We discussed the possibility of future substitution of or interference with the specimens.

The urine was taken to Marshall Street, and tested. There was a definite trace of albumen, no blood, and a strong reduction of Fehling's sol. The last observation was unexpected, but we thought it might be due to a glycosuria consequent on the exophthalmic goitre. Casts were also found.

We determined to consult Professor Barger. We heard the details and arranged to set up a test apparatus for arsenic at once on the remainder of the specimen, though the indications to
him must have seemed somewhat speculative. While with him we found that strong reduction of Fehling may be got in arsenical poisoning. Prof. Barger arranged for us to consult Prof. Murray Lyon at 4.0 p.m. Prof. Lyon heard the story and arranged for further specimens to be sent to the Bio-Chemical Laboratory. He further advised the speedy transfer of the patient to hospital, to ensure that she be removed from possible danger, and to ensure the authenticity of all specimens. A vacant bed in Ward 25 was suggested, and we arranged to meet Dr. Williams the resident there at 8.0 p.m.

In the meantime I paid a visit to the house, and collected a specimen of vomit and sputum, and prescribed a sedative stomach powder. The patient told me that her mother-in-law would be very angry if she heard that patient's illness had been associated with the pudding. As I had made no suggestion of this kind the statement was not without importance. I suggested removal to hospital; a brother of the patient, who was present was willing, but the neighbours said the husband should be consulted. The patient herself was anxious to go.

At 8.0 p.m. in Ward 25 we heard the result of the test for arsenic was positive. Prof. Barger confirmed this by phone. Prof. Murray Lyon advised us to consult Dr. Douglas Kerr, the police surgeon. Dr. Kerr advised the patient's removal to Ward 3.

We proceeded to the house. The patient was much the same but complaining of a headache. By assiduous questioning we found that there was no question of organic arsenical treatment. (As a matter of fact, the Gutzeit test had eliminated this factor as we later discovered).

The patient was removed at 9.45 p.m. to the Royal Infirmary. Dr. Gumley admitted her to Ward 3. The patient's condition on admission was as follows:

Pulse 175: temp. 99°F. Resp. 28.

About 11.30 we phoned Dr. Hamilton, of the Dispensary and ac-
quainted him with out movements.

On Friday 11th November we saw Dr. Kerr at 10 a.m. He heard the facts of the case and referred us to Lieutenant Saugster of the Police Court, who arranged a meeting between us and officers in the afternoon.

About 12 noon, we saw Prof. Barger who demonstrated the test and gave us the following details.

Cutzait's test positive.

"Two blank tests on reagents yielded no result in 15 minutes. 5cc. of urine gave yellow stain of. As Ag3 3Ag No3 when filter-paper soaked in 1:1 Ag. No3 solution was held over the outlet of Marsh's apparatus. This was obtained several times within three minutes".

We then proceeded to Ward 3, where Dr. Goodall took the history. He examined the patient and discovered absent knee-jerks and extreme flaccidity of the calf-muscles. The patients was somewhat improved, but there was a slight jaundice in the conjunctiva.

At 3 p.m. we met Mr. Stewart and Mr. Sutherland of the C.I.D. in the Royal Medical Society. They took a full account and promised to acquaint us with further developments. In the meantime Prof. Barger was arranging for Marsh mirror tests.

Dr. Kerr who was consulted on Saturday morning thought the testing of further specimens a matter for Ward 3.

The patient showed further improvement.

The following details were noted.

10th November. On admission:
Digit. mXXX
Pulse. 160-175.
Resp. 28
Temp. 99.5°F.

11th November. Digit. mlX in three doses.
H.l morphine gr. at 12.45 a.m.
H.l morphine gr. at 11.45 p.m.
Temp. morning 97°F.
evening 99.2°F.

12th November. Digit m.XV T.D.S.
With the permission of Dr. Gurnley a copy of the official case record after admission was obtained. As found that it differed from the history we had obtained in many important particulars. Thus "currant dumpling" was substituted for "pudding". Similar symptoms were described following the eating of this, but the patient goes on to state that by Saturday 7th Nov. she felt in her usual health. That night she again visited her mother-in-law who gave her some salmon, and this was followed in a few hours by the symptoms for which we were called in.

The explanation of the discrepancy may be in the fact that the patient had not associated her first condition with the taking of the dumpling and that our investigations and questionings had merely suggested the similarity of occurrences to her.

The reddish rash which we had observed now spread all over the body, being particularly marked on the chest, abdomen, back and elbows. The heart was irregular, and the apex in the midclavicular line; a systolic murmur was present in the natural area.

The bad cough persisted; rales and coarse rhouchi c. coarse creps. at the right base. Abdomen not tender but there was increased rigidity.

The tongue was reddish and showed a little disquamation. Herpetic scars present round the mouth.

On Monday 14th Nov. at 2.30p.m. we again visited Ward 3. We saw Sister Grant, who supplied us with the following report.

On specimens taken, corked and sealed and labelled in clean flasks in the presence of Sister Grant and Dr. Gurnley, an investigation was required. "Is arsenic present in either stool or urine?" The Report No. 7500 stated that arsenic was strongly positive in the urine and positive in the stool by Marsh's method. Dr. C.P. Stewart who conducted the experiment further remarks "The urine gave a definite arsenic mirror within 3 minutes. For quantitative analysis if required a 24 hr. specimen should be supplied".

The husband had paid two visits to the Ward. On the second
He brought some fruit for his wife, including one apple. These were handed to a nurse; he stated that on the occasion of his first visit his wife had particularly asked him for an apple, and that she was passionately fond of them and had recently eaten a great number. We then saw the patient. She was very much improved. There was still a slight suggestion of jaundice in the conjunctiva, and disquamation was marked on the chest.

The urine was tested with the following result.

- Albumen - definite trace.
- Fehling - reduced.
- Bile - possibly - very slight.

We were advised that the following were sent to the Bio-Chemical Laboratory. (a) 24 hour specimen of the urine, and (b) a specimen of the hair.

At 7.45 p.m. Haddow phoned Dr. Kerr regarding the new results. He was advised to communicate with Mr. Stewart C.I.D. and ordered that the apple be kept in W.3 under lock and key.

We saw Mr. Stewart at the Central Police Station the next day. He had interviewed Prof. Barger and Dr. Gumley, and promised to let us know further developments.

In Ward 3 Sister Grant informed us that the husband had been inquiring through porters and nurses as to the diagnosis of his wife's condition, but without avail.

As regards the apple the suggestion is that the husband endeavoured to convince us that the arsenic had come from the apples which his wife is said to have eaten. In any case his wife declared that she always took the skin off the apples before eating them. The rash later disappeared, and thereafter the patient progressed to a slow recovery. Her carious teeth were extracted, and methods were suggested by which she might be helped to buy an artificial set. No definite result ever accrued from the quantitative test. The excretion of arsenic in the urine becomes irregular after 13 days and eventually when tested the quantity was found to be too small for accuracy in statements. The patient was eventually discharged from hospital.
on December 30th 1927. The investigations of the police were frustrated by the fact that the source of the arsenic could not be found, at least in Edinburgh.

Our own duty in this case had now ended. Ogston states, "A medical man is deserting his true plan in Society when, leaving his duty of attending to the sick he seeks to usurp the place of the Public Prosecutor... in the collection of evidence."
Case 3.

Taucher's Splenomegaly.

Dr. Comiex's Case W.26
By a somewhat fortunate coincidence three cases exhibiting different forms of splenic disease were admitted to Dr. Comrie's wards within a short time of each other. The first case of Kala-Azar I have already described in this series, the second was a female patient suffering from Banti's disease, and the third manifested the unique condition known as Gaucher's Splenomgaly. Relatively few cases of this type have been described in the literature, probably not more than 40 in all since Gaucher first insisted on the pathological entity of the disease in 1882. I do not for one moment suggest that any additions have been to our knowledge of the subject in this brief description, yet since the clinical findings were later to be confirmed by a curious coincidence, the case may not be without interest.

The study of this disease is as much the province of the pathologist as the clinician. Probably the chief interest for both alike, lies in the fact that the widespread pathological changes should excite so little impairment of the normal health and comfort of the patient. In this respect it shows a marked contrast to Banti's disease with which it was formerly identified.

Case History.

Robert Rutherford Smith, aged 29, a painter by occupation was admitted to W. 26 in January 1928, and attended later as an out-patient for several months.

He complained of painless swelling in the left side of the abdomen which had been present for 20 years and gave rise to no symptoms except those due to its size and weight. A definite enlargement within the last year with an increasing sense of fulness in the abdomen, had interfered to some extent with his
work as a painter. Complaint was also made of an intermittent dragging pain in the upper part of the tumour area.

The history was very interesting. The patient's relations stated that he had been a healthy boy up to the age of 9 when he developed an attack of measles. Shortly after this condition subsided, they noticed a diffuse brownish yellow pigmentation appear on the patient's body. It involved the head and neck chiefly, but was noticeable on the trunk and upper extremities, though not present on the feet and ankles. Medical advice was sought and a splenic enlargement identified. The patient suffered no inconvenience in health, and apart from the bronzed discolouration was otherwise apparently a normal boy. He left school at the age of 14 and was apprenticed to a painter, which occupation he has followed since. There was no history of breathlessness, and the patient enjoyed a good appetite. With the passage of years however there was an increase in the abdominal swelling and at the age of 20 the patient came to the Infirmary for an investigation of his condition. He was admitted to Dr. Fleming's male ward and the case history was thoroughly gone into. Dr. Fleming recommended deep X-ray therapy for the splenic condition. This apparently was not too successful, and 2 years later radium was tried in its stead. There is a record that this form of treatment was followed by a definite reduction in size of the splenic tumour. There was no effect on the skin pigmentation however, and a further exhibition of radium was required a year later. Three years ago, the treatment again succeeded in diminishing the size of the spleen.

Since that time deep X-ray therapy was again tried without much success and abdominal pain recently increased. With Dr. Fleming's retirai from the Staff of the Infirmary, the case passed into the hands of Dr. Comrie. There appears to have been no other endocrine disturbance.

The onset of puberty was between 14-15 years of age, and no
history of mental or physical lassitude was admitted.

His general surroundings are those of the slum dweller, and leave much to be desired. The patient does not smoke nor drink, and his appetite and digestion have remained unaffected throughout his condition.

Family History. His mother has been twice married and claims that the patient was the child of her first husband who died without further issue. Thus a most valuable link in the differential diagnosis was broken down. The cause of death was not ascertained. The second husband's family had chiefly died in infancy. A niece of the first husband was said to be "jaundiced".

State on Examination. The intelligence was that of the average hospital patient.

Height 5 ft. 6". Weight 11 st. 7 lbs.

The patient had a well nourished appearance and the masculature was good.

The most striking phenomenon was the bronzed pigmentation of the skin especially marked on the face. It was diffuse in distribution.

A brownish yellow wedge shaped thickening of the conjunctivae was present in the nasal and temporal halves of both eyes.

The hair of the scalp was plentiful, glossy, wire like, and strikingly black in colour. There was no evidence of cyanosis or dropsy.

The temperature was normal.

The results of the physical examination of the patient were remarkably negative, apart from the splenic and hepatic condition, yet these negative factors were of value in assessing the differential diagnosis.

Alimentary System: Patient's appetite has always been good, and there has been little digestive discomfort, though recently a feeling of pressure or weight on the stomach after a full meal has been noticed. Apart from this, there was no evidence of a
gastric condition. The lips were full and fairly well formed
The teeth were uniformly carious, and evidence of pyorrhoea
alveolaris present in the lower gum. Some oozing from the
gums has been observed (perhaps from this cause) but there has
usually been an associated slight epistaxis. The tongue was
fairly clean and presented no unusual character. No history of
glands in the neck. There has been no history of vomiting,
and patient particularly insists on close questioning, that he
has not brought up blood or coloured matter's from the stomach.
The Benzidine reaction was negative as regards the stool. The
latter was fairly well formed and its contents well digested.

Abdomen. The general contour of the abdomen was rounded and no
localised bulging was observed in the erect posture. The
abdominal wall was well covered with fat and the muscles were
in good tone. The movements were gentle, uniform and regular
 corresonding with these of respiration.

On palpation a prominent rounded tumour was found extending be-
low the left costal margin in close proximity to the abdominal
wall. A fairly sharp edge with two palpable notches passed
just beyond the umbilicus and turned up towards costal margin.
The shape of the spleen was preserved, though the organ was
everously enlarged. It was firm and fairly tense on consist-
ence. No tenderness could be elicited on palpation over it.
The irregular and nodular edge of the liver could be felt descend-
ing below the R. Costal margin on palpation and percussion.
The ascending colon gave a tympanitic note; no ascites.

Haemopoetic System. The superficial lymph glands were not
enlarged. No history of tonsels or adenoids. Nothing re-
ferable to the thyroid.

Blood examination. The blood picture showed little departure from
the normal. There was some evidence of a slight secondary
anaemia.

Red cells 4,500,000
White cells 9,700 - slight leukopenia.
Spleen and liver

Anterior aspect

Spleen dullness
Posterior aspect

Enlarged liver

Enlarged spleen

Posterior aspect
Enlarged spleen
When films were made and stained it was seen that there was a slight increase relatively in the large mononuclears up to 7%.

No nucleated rods were present and only a few microcytes and macrocytes. Polikilocytosis and anisocytosis were not marked.

Circulatory System.

Subjective. Some dyspnoea had recently been present, partly from the anaemia which usually followed radiation of the spleen, and largely from the hampered movements of the diaphragm by the increased abdominal pressure.

The breathlessness had never been of such a nature however as to seriously inconvenience him. Occasionally there had been some palpitation probably from the same cause.

Otherwise nothing subjective referable to the heart.

Blood pressure 140 syst.; 95 diast.

The other systems presented no abnormal characters.

There was some huskiness of the voice and later bile in the urine but no sugar.

The Van den Bergh reaction was positive both by the direct and indirect method. The cause of this was later to be found.

The diagnosis of the splenic tumour was never in doubt, the situation, the upward extension of the splenic dulness, normally situated at the level of the 9th rib in the mid-axillary line, the notches in the anterior border and the abrupt margin of the tumour in the loin were sufficient to distinguish it from a renal condition especially since no bowel lay between it and the anterior abdominal wall. Again the fact that the enlargement was uniform and retained the exact form of the spleen caused no difficulty in differentiating it from a mesenteric mass or intestinal tumour.

The diagnosis of the condition was not however so easy. The spleen is especially prone to enlargement in disease, and
the present characteristics of its pathology were apparently sufficient only to exclude the acute fevers and the general pyogenic infections on the grounds of chronicity of its present state. Yet this very fact seemed to introduce fresh difficulties since the chronic diseases of the spleen would fill a volume. Fortunately, there existed two important factors, which were to prove invaluable in assisting us to come to a conclusion as to the true nature of the disease. These were (1) The blood picture, (2) The associated enlargement of the liver.

The fact that the patient had lived in Edinburgh all his life and the comparatively normal erythrocyte count at once excluded the possibility of the protozoal infections: malaria, Kala-Azar and Egyptian splenomegaly.

Enlargement due to mechanical obstruction (held some possibilities), but in the absence of decompensated cardiac disease, and the ascites associated with hepatic portal cirrhosis, thrombosis of the splenic vein could be ruled out on account of the long history and the very gradual nature of the increase in size.

The spleen is seldom the seat of malignant new growths such as carcinoma and sarcoma, and they were the rather to be excluded on account of the general good health of the patient over a long period of years. Further a rather severe anaemia was to be expected in their presence.

Idiopathic pernicious anaemia, the leukaemias and acholuric jaundice are associated with such characteristic blood changes that this factor alone was sufficient to indicate their lack of identity with the condition present.

At this stage the differential diagnosis had been narrowed down to the enlargement of chronic infective processes such as, Tuberculosis, syphilis and lymphadenoma and to the primary enlargement caused by splenic anaemia, splenic anaemia with hepatic cirrhosis, and splenomegalic cirrhosis. Lastly Gaucher's splenomegaly had to be considered. As regards lymphadenoma the
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points of resemblance were that it usually began in the first 3 decades of life, was progressive and associated with hepatic enlargement. Moreover, it is more common in town-dwellers. Against this had to be balanced the fact that there was no enlargement of lymphatic glands in our patient; that there was no fever and only a slight anaemia. Hodgkin's disease is fatal in 3-4 years at the most. The present condition had been present for 20 with little in the way of symptoms. Syphilis frequently causes enlargement of the spleen together with the development of a syphilitic cirrhosis of the liver in late childhood. Manifestations of the disease at a later stage may take the form of gummatus deposits in the spleen or hardaceous degeneration. There was however no evidence of syphilis before 9 years of age, and no eye troubles such as interstitial keratitis had ever been complained of, whilst the Wassermann reaction was negative.

Caseous T.B. of the spleen unassociated with tuberculosis elsewhere, in a chronic disease without emaciation or other discomfort was an unlikely explanation.

There yet remained the cryptogenetic splenomegalies. The terminology of this group of diseases is at present in a somewhat confused state. Some years ago Osler advanced a proposition, now widely accepted, "that the conditions separately described in the literature as primary splenomegaly, splenic anaemia, splenomegalic cirrhosis of the liver or Banti's disease, are stages of one and the same malady".

On this assumption primary splenomegaly and Banti's disease are regarded as initial and terminal stages respectively of splenic anaemia. Since 1907 however this classification has undergone some changes and several morbid affections previously included under splenic anaemia have been differentiated and withdrawn from this group. Thus Gaucher's splenomegaly recognised as far back as 1882 appears to constitute a definite pathological entity. The modern view is that we consider the terms Banti's
disease and Primitive splenomegaly as synonyms for Splenic anaemia. Banti considers that the disease commences as an anaemia with splenic enlargement and steadily progresses for many years to a terminal stage of hepatic cirrhosis with ascites.

Investigation has shown however that the cirrhotic stage may never be reached, and that it is advisable to regard the condition as a single disease terminating either as a fatal anaemia or equally fatal cirrhosis. When we come to consider the pathology of the condition further, we find that a blood examination shows a diminution of the erythrocytes to between 3 and 4 millions. The Haemoglobin is usually about 50% and the colour index below unity. There is a leucopenia chiefly on the part of the polymorphonuclear leucocytes.

The patients complain of increasing weakness, of anaemia breathlessness or haematemesis. The degree of emaciation varies but is seldom acute. The duration of the disease varies. Usually it is 3 years before the more fatal signs make their appearance. The patients may lead a moderately active life, but are always subject to an increase in the anaemia and likely to suffer at any time from haematemesis. The disease usually starts in the 3rd and 4th decades, and is somewhat more common in males than in females.

Was this the disease from which the patient was suffering? If it was, the prognosis was quite good since surgical interference by the operation of splenectomy has materially altered the outlook in these cases. It was essential therefore that a correct diagnosis be made. On the one hand in favour of Banti's disease we had a long history of splenic enlargement of unknown cause associated later with a semi-cirrhotic state of the liver. Further its incidence in a male subject was significant. Emaciation was not marked, and the comparative health of the patient were points of resemblance. On the other hand the chronicity was greater than we might expect in splenic anaemia without fatal symptoms. There was no history of increasing
weakness or breathlessness. Haematemesis frequently such a fatal feature of the above disease had not occurred. There was no evidence of ascites. The enlargement of the liver which here was very great is never marked in Splenic Anaemia. Moreover the anaemia usually slight (here 4,500,000) is distinctly less a feature than in Splenic Anaemia where it is between 3 and 4 millions. The leucopenia was not a prominent feature.

Could it then be possible that the disease was the rare condition of Gaucher's Splenomegaly. The clinical features of this type of splenic disease, according to Brill and Mandlebaum are usually sufficient to establish a diagnosis.

(1) Its incidence in childhood is a strong point in its favour. (2) Its frequent presence in other members of the family is important. (We have seen how evidence on this point was unobtainable, owing to a mixed family but the jaundice of the patient's cousin might be significant. (3) Most important of all is the progressive enlargement of the spleen and liver without ascites, which does not materially interfere with the normal health and comfort of their possessor. (4) The slight anaemia and leucopenia has frequently been observed. (5) No haematemesis, though oozing from the gums and epistaxis are frequent. (6) A bronzed discoloration of the patient's skin. (7) A wedge shaped thickening of the conjunctivae first on the nasal and later on the temporal halves of both eyes is said to occur in all cases.

Thus our clinical findings exactly recapitulated the picture described by those eminent authorities, Brill and Mandlebaum.

What evidence had we from the pathology of the condition to indicate lines of treatment?

Gaucher considered the disease an "Epithelioma primitive de la rate" - a primary epithelioma of the spleen. He discovered in patients who had died of the disease, masses of peculiar large mononuclear cells of an endothelial type inhabiting the spleen, liver, lymph glands and bone marrow. Iron containing pigment was present in most of these cells which possessed relatively small round, single or multiple nuclei suggesting atypical swollen endothelial cells. The splenic structure was largely replaced by dilated venous sinuses and there was a
varying amount of fibrosis. The liver was also enlarged and the connective tissue invaded by similar cells. The whole haemopoetic system was involved in this pathological change.

Thus the early investigators were inclined to view the process in the light of a new growth which was variously described as endothelioma, sarcoma etc. The modern conception is that it is not neoplastic in origin, and that the stimulus to cell formation is derived from some unknown systemic poison. The bacterial theory has found little favour, since no organism has been definitely described in connection with the disease. As regards treatment, splenectomy has been performed in 8 out of 14 proved cases, with 3 operative deaths. Of the ultimate results too little has been published to warrant any conclusion, and it was unfair to submit a patient, the exigencies of whose case did not demand it, to a somewhat speculative surgical venture.

Thus deep X-ray therapy and intensive radium treatment was persevered with, and soon there could be no question that an appreciable reduction in the size of the spleen was manifest.

In the meantime his health was good and he was attending regularly at the Radiological Department. Then one day he began to experience some abdominal discomfort which soon manifested itself as an acute epigastric pain. There was no evidence of X-ray burns, but the treatment was stopped for a week or two till the pain should wear away. It became evident however that this was assuming a serious aspect. The patient's agony became excruciating, and severe exacerbations were invariably followed by mental depression which soon passed into a mild melancholia. The unfortunate man's symptoms were a source of mystery to his relations who being accustomed to his complaints, paid no attention to his cries one night in May. To their horror next morning they discovered the unfortunate patient had poisoned himself with lysol during the night. In a comatose condition he was hurried to the Infirmary, but died in Ward 3 shortly after admission. I was present at the post-mortem and had an
opportunity of examining the specimens removed. The changes due to lysol poisoning do not concern us here but the condition of the abdomen was of unique interest. In the abdominal cavity, there was about 1 pint of blood stained fluid which had probably exuded from the bowel. There was nothing to suggest ascites. There was no evidence of thrombosis of the splenic vein. The spleen was still very large weighing 1520 Grams. It was greyish in colour and non nodular. There was no perisplenitis. On section it was seen that the splenic structure had been largely replaced by wide irregular alveolar spaces representing the dilated venous sinuses. On microscopic examination there were found to be filled with the peculiar large cells already referred to, which were also present in the pulp. Iron pigment was present between the connective tissue fibres of the trabeculae, partly converted into ferrous sulphide by action of H₂S from the decomposing bowel. Probably for this reason also the blood was very dark in colour, in no way suggesting an anaemia. There was nothing however in the appearances presented to account for the extreme pain which had brought the patient to an untimely death.

The liver was next examined. It weighed about 1200 Grams. A definite perihepatitis was present. There was a well marked cirrhosis of a coarse type and on section the cause of the pain was revealed. A huge primary cellied carcinoma filled up the centre of the liver and one could easily attribute his recent symptoms to such a cause. In the peripheral parts of the liver unaffected by the new growth there was a marked increase of interlobular connective tissue invaded by the endothelial type of cell peculiar to the disease. Parenchyma cells were well preserved and this may have accounted for the absence of jaundice. Dark staining pigment was present in the capsule and small vessels. Several lymph glands in the abdomen and thorax were enlarged. It is probably that they also contained the large typical endothelial cells.
Microscopic examination of the liver showed that the growth had arisen in connection with the hyperplasia of liver cells associated with the cirrhosis, and not from the invading endothelial cells. Whether this is an argument in favour of the non-neoplastic nature of the latter is somewhat speculative, but it raises the question "Is there a carcinomatous type of individual whose organs are particularly prone to undergo this pathological change?" or does the same factor operating in different spheres provoke on the one hand a comparatively benign and chronic hyperplasia of endothelial cells and on the other a rapid malignant growth which kills in a few months?

One is tempted to ask if the cellular pathology of a disease like lymphatic leukaemia finds a further expression in enloma, and does this in turn represent one aspect of a process which finds its expression in carcinoma.

(No note in the margin was probably due to the presence of the new growth in the liver.)
Case 4.

Post-Meningeval Neuritis.

Dr. Connie's Case.  6.25.
Case 4.

Post-Menopausal Neurosis.

In the drama of human evolution, civilisation was a late experiment. Five or six thousand years ago, our forefathers, few in number lived in temporary shelters, and gathered a scant substance from roots, fruit and fish. In a short space of time civilisation had entirely altered the conditions of life. Now we are massed together in towns, living on a strange artificial dietary, and sheltered by houses and warm clothing. The sudden change in environment has upset the balance between our instincts and our circumstances. The evolution of society has outstripped the evolution of the race and the resultant disharmony is now revealed in the protean manifestations of that bodily revolt, which we call disease. The artificiality of modern life has inspired an unnatural attitude towards the physiological activity of the body and in no sense has this been more marked than in the results of civilisation on the climaxes of women's sexual life. The phenomena of menstruation and parturition are now invested with all the attributes of disease, and the advent of the climacteric is viewed with considerable apprehension. A normal function has ceased to be a pleasure and physiological serenity is correspondingly lost. The results are so complex that their eventual issue is impossible to forecast. So intricate and interdependant are the various parts and functions of the superior mammals body, that it is hardly possible to disturb the balance of one part or function without impairing the integrity of the whole.

The significance of the foregoing statements I intend to illustrate by a case which might be classed as a post-menopausal neurosis.

Miss Kate McMillan, 51 years of age, a domestic servant by occupation was admitted to Ward 25 on the 1st of April 1928. She was born in South Uist and is unmarried.
Complaint: Drowsiness, periods of unconsciousness which come on without warning; and extreme constipation.

Duration: Symptoms intermittently present since the menopause five years ago.

History. The climacteric came on gradually 5 years ago, when patient noticed a progressive diminution in the menstrual flow. At first this was unaccompanied by symptoms, when quite suddenly "hot flushes" started. Her digestion, hitherto fairly good, was now impaired, and flatulence, borborygmi, and extreme dyspepsia became troublesome. Numbness in the fingers and toes was also noticed and loss of power in the arms and legs occasionally caused her to fall off her bicycle. She now became somewhat worried about her condition, and her concern was further increased when fits of unconsciousness came over her without warning. Thereafter she fell off her bicycle repeatedly. Occasionally the unconsciousness was preceded by a slight aura, and sometimes she attempted to evade the attack, without success, by the exercise of will power. Anxiety brought on the fits more frequently and she soon resigned herself to what she believed was the spell of a chronic disease. Invariably she woke up with little recollection of what had transpired during an attack. Sometimes she was injured in falling. She felt her strength being slowly sapped and with vomiting augmented her weakened state. Work became an effort and mental torpor ensued. Her bowels gave her little concern. At this time they moved only once a week or a fortnight. She appeared to be putting on weight and had now become breathless at times, with swollen legs and a puffy face. There was never any evidence of paralysis after a fit passed off. A doctor who was called in treated her constipation and soon she felt better. The fits became fewer in number and less prolonged. Now there was little definite unconsciousness but a dazed feeling persisted about once a week and when this affected her she was forced to hold on by some adjacent support. She noticed that she was becoming very sleepy and some days she would hardly open her eyes. A holiday on her native heath in South Uist resulted in a
marked improvement in her physical and mental state. The swelling of her legs was diminished and she was able to walk for miles without inconvenience. She also put on weight. Constipation was less marked and her anxiety proportionately lessened as her health improved. The dazed feeling was no longer present.

On returning to her situation patient states that she felt a different being. The large gloomy house oppressed her, and with a flood of recollection she remembered the recent trying time she had spent there. It was not long before she felt dissatisfied and "fed up with it all". Her mistress, in whose service she had grown old, made things as easy as possible but it was soon evident that the patient was relapsing into her former state. One day when left alone in the house she began to cook a meal for herself. She became somewhat nervous on leaning over the fire, but recovered sufficiently to watch in a spellbound fascinated manner, the bacon frizzle to a cinder, whilst she kept saying to herself "I must keep back from the fire". When the other servants returned 12 hours later, they found the patient in an unconscious state on the floor. When she awoke hunger assailed her, and she thought it was still morning. This was the prelude to the recapitulation of the condition from which she had previously suffered, though "flushings" were not now so frequent nor intense. Constipation was as bad as ever, and she became unconscious for hours every day, and severe headaches were almost as frequent. Flatulence and dyspepsia aggravated her other symptoms and when she took bananas, oranges, or tomatoes, an urticaria developed all over her body.

Breathlessness was still marked and occasionally palpitation troubled her.

The treatment of the constipation as before wrought a striking improvement in her condition, but the case presented so many features of interest that her Doctor sent her to
hospital for further investigation.

Previous History: The patient has been in domestic service most of her life. She was the 3rd child of a family of 8. Her mother died in an asylum, and her father was an invalid for years before his death. Only 3 members of the family are now alive. Two brothers were killed in France 10 years ago and this caused her a severe mental shock. The others were carried off by consumption in infancy.

Her life in service has been easy going, and a perverted intimacy sprang up with her mistress, with whom she admitted mutual sexual irregularities. About ten years ago patient frequently complained of a severe pain below the right costal margin associated with biliousness and vomiting. Frequently, a lemon colour developed in the skin after these attacks.

Appearance on examination. Patient is of fairly stout build 5ft. 4" in height and 11st. 3lbs. in weight. There is a trace of colour in the cheeks. The face is otherwise sallow. The expression is dull, listless and apathetic. The eyes are sunken and have a sleepy look. The intelligence is somewhat below average. There is no evidence of jaundice, Cyanosis or dropsy. Temperature is normal.

Physical Examination.

Alimentary System: Appetite and digestion good until the menopause. In her present condition before coming to Hospital there was lack of appetite; gastric discomfort; nausea, vomiting and flatulence after food with frequent eructations. These subjective phenomena were irregular in their time of onset, and did not always occur together.

Lips were weak and anaemic. Two complete sets of artificial teeth. Gums apparently healthy. Tongue moist and clean (in hospital). Mouth somewhat dry. The fauces showed no abnormal features.

The Bowels have always been constipated, seldom moving more than once a week since the menopause. The Hospital regime has
corrected this. The Benzidine reaction was negative.

**Abdomen.** Much superficial fat has given the abdomen a rounded appearance. No localised prominences. No striae gravidarum. Appearance that of elderly nullipara. No tenderness or rigidity of abdominal wall. Liver, spleen not palpable. Tympanic note on percussion over caecum and ascending colon. Mass of faces felt in descending colon. Nothing else to note.

**Haematopoietic System.** No enlargement of lymphatic glands in neck or elsewhere. Spleen not enlarged - Thyroid not palpable. Blood picture. Haemoglobin 85%. Reds 4,200,000. Whites 7,000. C.I. 0.99.

**Circulatory System.** No cardiac pain complained of; occasionally palpitation and dyspnoea. Swelling of the legs and puffiness of the face may have been associated phenomena. No evidence of cyanosis at present.

**Pulse.** No apparent thickening of arterial wall. Frequency 65 per min. Rhythm regular. Wave soft, gently rises and falls.


**Apex in nipple line.**

**Auscultation.** Heart sound closed. Faintly conducted but no evidence of pathological change.

**Respiratory System.** Breathlessness often associated with swollen feet. Respiratory arrhythmia is said to have occurred. Breathing is thoraco-abdominal in type. Frequency 16 per minute and of even rhythm.

Nothing referable to Naso-pharynx.

**Thorax.** The chest wall was well formed and covered. No apex beat could be seen.

**Percussion.** Dullness of both apices with diminished inspiration. Otherwise nothing to note.

The skin of the body was dry and marked easily. There was a mild degree of dermatographia. No eruptions seen. The hair of the scalp was fairly abundant, dry and brittle.
No oedema of the subcutaneous tissues was observed though patient stated it had formerly been present.

There was some degree of obesity.

**Urinary System.** No history of incontinence during the fits. Micturition at present is fairly frequent.

**Urine.** Calcium phosphate crystals seen.

No albumen, sugar or bile found, and no casts were present.

A few bladder epithelial cells observed.

**Reproductive System.** Referred to in case history.

**Nervous System.** Intelligence rather below average.

Patient emotional and apprehensive. When aroused from her sleepy state she may sit up in bed, and attempt to describe her symptoms vividly with many gestures. Drowsiness is a marked feature of the disease. Headaches have been of frequent occurrence. Articulation is not too good, and her speech has a slight syllabic element with occasional stammering.

The 2nd, 3rd, 4th and 6th Cranial nerves were fully investigated. The others showed nothing which referred to the condition.

**II. Visual acuity fairly good.** Patient does not require glasses. Arcus senilis present in cornea.

Differentiation of colours accurate but slowly elicited.

**III.** There was a slight ptosis of the left upper eyelid. No squint. No diplopia. Ocular movements free in all directions. Nystagmus not present.

**IV & VI.** The pupils were equal in size and shape. They reacted well to direct and consensual light. Accommodation was slower than normal.

There was no en- or exophthalmos.

**Motor Functions.** No fibrillar, or athetotic movements have been present at any stage of the condition. Never any paralysis and no present localisation of such can be determined. The skeletal muscles are not atrophoid. Co-ordination was apparently good at times other than the fainting attacks.
Reflexes. The knee and ankle jerks were equal in reaction and not exaggerated. The wrist and elbow jerks were normal in their response. Ankle clonus and knee clonus were absent. Babinski's sign was negative.

The pharyngeal reflex was interesting. When her throat was being examined, she bore a fairly complete examination without the least discomfort. Organic reflexes had never been impaired. Involuntary micturition or defaecation had not occurred.

Sensory Functions. At the onset of the menopause patient frequently complained of "pins and needles" in her limbs, "followed frequently by numbness. The "hot flushes" usually gave rise to a chill, headache and vertigo as before described. On examination, None of these phenomena were present.

Patient readily discriminates hot and cold objects placed against the skin, but two points placed 1" apart on the forearm were felt as one.

Otherwise nothing to note in the C.N.S. except that patient suffers from Claustrophobia - the fear of closed spaces. She loathes towns and large houses which she states bring on her attacks more frequently. She loves the country for its sense of freedom and fresh air.

Differential Diagnosis. We were confronted by conflicting facts. Was the condition described a direct sequela of the menopause? Was it a functional neurosis or was some organic disease present? At first sight the problem seemed very complex because the signs and symptoms of one disease were present with those of another and the discrimination and assessment of their place in the diagnosis was no mean task.

To begin with very few women pass through the menopause without some suffering or discomfort. The hot flushings are due to irregular vasomotor disturbance. General vaso-dilation suddenly occurs followed by a chill. These disturbances must depend upon some want of balance between the ductless glands,
consequent on the general metabolic processes that are taking place.

Flatulence, borborygmi, and dyspepsia are attributable to imperfect muscular control over the alimentary canal. The nervous system is deranged and various paraesthesiae appear, numbness, "pins and needles," loss of power in hands and arms, and legs. Mentally the patient may be profoundly changed. Disordered metabolism causes urates and phosphates to appear in the urine giving rise to frequency of micturition. Palpitation is usually dependent on the gastric disturbances of which flatulence in chief. To what are the signs and symptoms due? The more the phenomena of the menopause are studied, the more they appear to be the result of a disturbed endocrin balance. The cessation of those metabolic changes which cause menstruation, must necessitate a readjustment of the general metabolism of the body. Metabolism is largely controlled by internal secretions, and thus readjustment is not always at once possible. Consequent on the withdrawal of the ovarian secretion which has played the predominant role in the psychical life for many years, the body has to revise its tables of values. It is not surprising therefore that the effort at readjustment is somewhat of an experiment whose results depend largely on the physical and psychical adaptability of the individual. The experiment has usually a successful issue and the symptoms subside. This is not always the case however. Was there anything in the patient's condition to suggest that the disturbance of the menopause had produced more profound changes than are customary? Thence factors stood out clearly

1. The unconsciousness.
2. The drowsiness.
3. The extreme constipation.

This triad of symptoms was highly suggestive of Encephalitis Lethargica. The ptosis was an important accessory factor. On the other hand the long history, the absence of acute onset, and the slight physical signs were rather against such a
Moreover the lethargy in our patient's case was not rousable. There was no incontinence during her attacks and no history of transient conscious dysuria at the onset. Visual disturbances were not complained of, and there were no spontaneous involuntary movements. Further she retained no memory of events during her lethargy. Her present relatively healthy state was an additional argument against encephalitis. The absence of sugar in the urine and her obesity argued against diabetic coma. Epilepsy had an entirely different etiology and sequence of events. Uraemia was at once ruled out. Tumours and abscesses of the brain were contraindicated by the absence of fever, temperature, and localising symptoms and signs. The acute fevers involving the meninges could not have been responsible. We were thus left with the theory of a functional neurosis. How could this explain her fits of prolonged unconsciousness? Cerebral anaemia or oedema of the brain were feasible suggestions. How could these be brought about? To answer this satisfactorily it is necessary to return again to the disturbances of the menopause. It has been suggested that these do not always subside without leaving remote effects. One of these was at once apparent. There was a slight change in the thyroid secretion. It had suffered in the process of readjustment and a diminished quality or quantity of thyroxin was passing into the bloodstream. Not so much as to cause myxedema, but enough to give rise to obesity and some mental torpor. The dry skin and the brittle coarse hair may have resulted from this cause. But these were the least striking changes. The increased movements of the stomach manifested as borborygmi, flatulence etc and the spastic constipation had persisted too long to be entirely attributed to menopausal changes. Had then a vicious circle been established? Had the climacteric changes evoked a nervous reaction which was in turn to dominate and perpetuate those changes? There was a definite instability of the nervous system. The patient's apprehensive manner, her claustrophobia, her sexual
perversions all pointed to this fact. Did this neuropathic diathesis render the Central Nervous system more susceptible to peripheral influences? There is every evidence to show that it does and especially in this the case when there is some endocrine default. Now it seems likely that chronic peripheral stimulation will evoke a response from the division of the vegetative nervous system which is most affected. In our patient's case the digestive functions were the most disturbed. I venture to suggest that a hypersensitiveness of the vagus resulted and was to have far reaching effects. Years ago, Hess and Eppinger attempted to distinguish two types of neurotics— the vagotonic and the sympathicotonic, according as one or other division of the vegetative nervous system with its associated glands tends to overact. They summed up the results of vagotonia as laryngeal spasm, respiratory arrhythmia, low blood pressure, increased secretion and movements of the stomach and spastic constipation. There is an undue sensitiveness to foreign protein revealing itself superficially as dermographia or urticaria, and in the severe forms as anaphylactic shock.

The subjects of this condition tend to be fat and flabby: apprehensive but not excitable on the mental side.

This picture seems strikingly like that presented by the patient. The urticaria which she herself mentioned was a unique coincidence, and the spastic constipation was an important accessory. The question of the unconsciousness yet remained to be answered. How was it to be explained on this basis? The oedema of the legs and face quite independent of the urticaria seemed to indicate a weakened action of the heart. The circulation was not being maintained and stasis with anoxaemia of the tissues was resulting. The effect of this was augmented by the respiratory arrhythmia. In the second place the constipation and digestive disorders was causing a great deal of blood to accumulate in the abdominal lagoon. There was an associated slight anaemia. The circulation was thus becoming...
disorganised. Normally the hydrostatic effect of a varying level is equalised by the contraction of arterioles in other parts of the body. The assumption of the erect posture in man demands an adequate compensatory contraction of the abdominal wall and splanchnic arterioles to maintain the cerebral circulation. If this be lacking so much blood will accumulate in the splanchnic area that the arterial pressure in the aorta will fall markedly or the circulation may stop entirely. Thus in rabbits which have lax abdominal walls the animal may be killed on this principle, by holding it in the erect posture for some time. In this way the erect posture in man may be dangerous when the compensatory nervous reflex controlling the arteries and the tone of the abdominal wall is thrown out of gear. Everyone has experienced the phenomenon of petit mal where cerebral anaemia takes place for a few seconds. The patient was manifesting an exaggerated form of the last condition. The sluggish circulation was unable to maintain efficient oxygenation of the brain and the patient felt dizzy or lost consciousness at once. On falling to the floor the cerebral circulation was partly restored, and the condition became that of a prolonged syncope; the vital centres being little affected and a sluggish circulation taking place in the cerebral hemispheres.

When however the constipation was treated the condition tended to clear up. There was less vagus irritation and the abdominal lagoon was much diminished. Thus an effective cerebral circulation could be maintained.

Another less likely explanation depends on the anaphylactic factor. Urticaria is a vasomotor neurosis depending on variations in capillary permeability and tone. Flushings are probably also a result of vasomotor instability, and in all these conditions intestinal toxaemia is a causative factor. Thus a sudden oedema of the brain due to capillary permeation might easily cause syncope. However they arose, the patient
had no attacks in hospital due to careful attention to the state of the bowels. All sources of vagus stimulation were removed by a careful diet. Cardiac stimulants improved the tone of the heart and circulation. The blood pressure rose, and thyroid was administered for her obesity: Thyroxin 0.29 gr. T.I.D.

The results were extremely good. Her weight decreased. Mental acuity was increased and her interests in life broadened. A holiday at home and a change of situation were advised with strict injunctions as to careful regulation of the bowels. There was soon every evidence that the manifestations of the neurosis were subsiding. She was less drowsy after a week's treatment and able to be up and about a little each day, and she steadily gained in health, and was discharged from hospital feeling better than she had ever done before.

This case illustrated two important factors:
(1) That thought action to a patient may be a mental food or poison.
(2) That suggestion and example have a unique value in treatment.
Case 5

Acute Pneumonic Fever

Dr. Comrie's Case W. 25.
Case 6.

Rheumatic fever and the "Rheumatic Diatheses".

Rheumatic fever is a malady which is so notoriously common as to constitute a national problem of the gravest significance. In its acute forms in children when rheumatic carditis is so frequent a sequelae it has contributed more than any other disease to permanent disability of the individual and a proportionate loss of national efficiency. Its chronic manifestations such as osteo-arthritis, rheumatoid arthritis and so on, cost £17,000,000 amongst insured persons per annum. The seriousness of the disease cannot be overestimated. It is essential therefore that it be recognised at the outset, and treated as efficiently as possible. In this respect, as in so many others, the best efforts of the physician are unfortunately antagonised by constitutional and environmental factors, and the often unrealised operation of these etiological elements precludes effective treatment until permanent harm is done. The influence of constitution, environment and heredity is illustrated by the following case.

Robina Mitchell aged 22. 8 Wardlaw Place, Gorgie a kitchen maid was admitted to Ward 25 on the 21st February 1923.

The history was that whilst working in a hot, steamy restaurant she developed a headache and felt ill and depressed on the 15th Feb. She experienced some stiffness and pain in her wrists which was relieved by placing her hands in soda water. She was not allowed to go home however. Her weakness and lassitude continued and her legs seemed scarcely able to support her body. The next day (Sunday) she was unable to rise from bed. Legs and hands were swollen and the joints were painful. On Sunday night her neck was also swollen and a tender throat prevented her from eating. She was also sick and vomited frequently.
An intense pain in the back of her head and neck made her cry out. A doctor was sent for who administered some medicine which caused the patient to perspire freely. Soon toothachy pains shot all through her body and radiated down the legs to her heels. There was further stiffness and pain on moving the joints and in a short time she was unable to do a thing for herself. Constipation was very marked, and she was sent to hospital with a diagnosis of acute rheumatic fever.

Previous History. Always been troubled with sore throats. Scarlet Fever and Measles as a child. T.B. glands in the neck removed at the age of 5. Rheumatic Fever at the age of 14. Muscular rheumatism 2 years ago. No history of chorea, but patient has always been nervous.

Family History. Mother died of Bright's disease. The Father is in Ward 31 with osteo-arthritis. 2 sisters suffer from rheumatism. 2 brothers dead.

Environment. Home conditions poor. Patient keeps house to her father and has to cook his meals as well as work herself. She is a kitchen maid in a Restaurant where she works in a superheated steaming atmosphere from 8 in the morning till 7 at night.

State on examination. Pat. is a pale faced undernourished child with a sallow complexion. She is perspiring freely, but does not appear distressed by pain. The height and weight are below average and she looks anaemic. The neck is somewhat diffusely swollen and the temperature is raised.

The Alimentary System. The swollen throat has made eating difficult since her illness and sickness has been frequent. Otherwise nothing subjective, but she dislikes sugar. The front teeth are small and stumpy with blunt cutting edges. Very dirty and coated with tartar. Septic foci in carious sockets are oozing pus in the upper molars. The remaining back teeth have been worn down almost in a line with the gum. The pharynx is markedly congested and covered with a slimy mucus. The tonsils are much enlarged, ragged swollen and congested. No visible pus. The larynx is
reddened and shows catarrhal changes. A ragged yellowish adenoid mass could be seen by a rhinoscopic mirror in the posterior wall of the naso-pharynx.

The inferior couchæ in the nose were swollen and enlarged.

The upper posterior chain of lymph glands in the neck were enlarged and tender to the touch.

The bowels were constipated. This was corrected in hospital.

Nothing objective to note in abdomen.

Haemopoietic System. Leucocytosis of 10,000.

Secondary anaemia of 3,800,000.

Circulatory System. No pain or palpitation complained of.

Slight faintness and occasional dyspnoeæ at onset of attack, has now passed off. Anaemia manifested in the face.

Pulse. Arterial wall not thickened. On admission frequency increased to 100 per min. Regular in time and force. Volume fairly good but tension reduced. Under salicylate treatment pulse reduced to normal after 12 days.

Blood Press. 120 Syst. Diastol. 80.

Heart. Chest wall fairly well covered. Breasts rounded and firm. No pulsations in extra-cardiac regions seen.

Percussion. Heart is not enlarged. Apex in mid clavicular line.

Auscultation. Soft systolic apex bruit on admission. First sound in aortic area was faint. Under treatment both these abnormal phenomena disappeared. On a later examination no defect could be ascertained.

No exo-cardial sound. No thrill or pericardial friction.

General circulation good.

Respiratory System. Nothing subjective or objective to note.

Apices clear. No pleurisy.

Locomotory system. On admission both arms were held stiff.

Swelling of the wrists especially the right, tender to the touch.

Skin over them tense and glossy, and warm. Great pain on movement.

Some swelling and pain of elbows.
Swelling of the knees and ankles at home has subsided since admission to hospital.

Two years ago she states she had muscular rheumatism in the shoulders and arms. This took the form of severe shooting pains later followed by involuntary twitching all down one side.

The joints of the arm were rubbed with Methyl Salicylate, and pain disappeared with the swelling at all 3 joints in that limb, after a week's treatment.

The right shoulder and elbow still give pain on movement and that is all she now complains of.

**Integumentary System.** The skin is moist and the sweat has an acid odour. No rheumatic nodules could be seen or felt in the tendour. Skin eruptions were absent.

**Urinary system.** The urine was scanty in amount and brick-red in colour. On examination there was a heavy deposit of urates and a slight trace of albumen.

**Reproductive System.** Menstrual period regular and of 28 day type. No dysmenorrhoea. No menorrhagia.

**Nervous system.** Intelligence average. No abnormal subjective or objective phenomena to note.

There was little difficulty in deciding that the case was one of acute rheumatic fever, and the exhibition of Salicylates was at once indicated. The specificity of these drugs has of late been called in question. Their value in the pyrexial stage seems undoubted but evidence serves to show that their influence on the incidence of cardiac disease after the rheumatic attack is negligible. In the case under observation a definite fall in the temperature was seen after the administration of Sod. Salicylate and Sod Bicarb. $\frac{1}{6}$ gr XX, 4 hourly, and there was a corresponding decrease in the pulse and respiration rate. But no one line of treatment is of avail in the treatment of rheumatic conditions. It is known that there are rheumatic families in whom the tendency to the disease is well marked. The patient's father and two sisters are affected with rheumatic manifestations. Exposure, fatigue, and damp, are the precipitating causes. This
unfortunate patient has to work for 11 hours in a superheated atmosphere, than which nothing lowers the vital processes or causes more inefficiency. Diet is important for she is intolerant, to Carbohydrate in the form of sugar and is thus probably deficient in vitamin B.

The pre-rheumatic child is invariably "nervous" as the patient has been.

Her lymphoid system is in a bad state and probably always has been. There is a long history of recurring sore throat and glands in the neck. The lymphoid system has been converted from a defence against microbial infection into a nidus for their activity. The huge swollen tonsils and adenoids form an excellent culture medium and absorptive surface for bacteria and thus toxins.

The chronic constipation from which she suffers is an accessory toxic factor, and her general toxic state may be attributable to the defective lymphoid protection in the intestine.

The endocrine balance is badly adjusted, as is shown by two phenomena which occur after infection has taken place.

1. The irregular and abnormal sweat secretion.
2. The tendency to hyperpyrexia (not found here), which may be controlled by insulin.

The skin is inefficient in its response to cold and damp, and thus the marked effect of moist surroundings and damp houses on the incidence of the disease may be explained. There is also a sensitisation of the tissues to certain organisms and their toxins, particularly the streptococcus viridans and its allies and it is said that a phasic variation between this sensitivity and a relative immunity may occur all through childhood, thus explaining the frequent remissions and exacerbations. Certainly a somewhat similar state of affairs is found in some skin diseases where a condition may heal up in one part which has become locally immunised to it, only to break out in some other place.

The predisposing factors being so bad in what way could we improve the patient's resistance to microbial infection in the
The hygiene of the adenoids and the tonsils had to be considered. These had long since dropped out of the patient's defence corps, and had themselves become sources of further infection.

Their removal as soon as possible was thus indicated. The patient's environment presented difficulties. It was obvious that so long as she remained in her present situations she was simply laying herself open to further rheumatic attacks. Domestic service was suggested as giving more chance of escaping the disease. A good diet was essential to build up bodily resistance, and patient's previous method of eating when and where she could was severely-censured. Attention to the bowels was also impressed upon her. Regularity of life and diet were indicated for a readjustment of the endocrin balance which was not so far disturbed as to require drug treatment. The prevention of future chills was an essential element. The wretched state of the teeth and the fact that they were septic and worn down to the gums was a sufficient indication for the extraction of them all. By these measures it was hoped that the patient's resistance would be strengthened to combat successfully the latent mischief of the disease. Her present cardiac condition was good and remained so until she left hospital. But what guarantee had we that it would not be affected if a future attack developed? It is quite true that cardiac lesions are much more likely to occur in children than in adults in whom arthritic changes are more common, but this was not to be relied on. Have we then any vaccine which is likely to prove of service? Unfortunately opinion is still divided as to the causal organism. Most observers admit that it is a streptococcus probably saprophytic in ordinary circumstances but becoming pathogenic in a suitable soil. There was thus no effective vaccine therapy. Infection from individuals predisposed to the disease had also to be considered. Though not an infectious
<table>
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<td>February 28th 1928</td>
<td>Alice Mitchell 32 yrs</td>
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<th>Date</th>
<th>DIET AND MEDICINES</th>
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<td>28-2-28</td>
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[Graph and data chart]
disease, is may be mildly contagious in the early stages before manifestations appear. In the meantime, complications had to be avoided. The pyrexia had already been treated successfully by salicylates and the joint lesions had been reduced on the application of methyl salicylate. Rest for the general condition was indicated and patient was kept still in bed for 4 weeks after admission. Thereafter when no evidence of cardiac disease put in an appearance she was allowed up and about for an hour or so every day. Acute endocarditis which is the most common cardiac lesion following rheumatism usually puts in an appearance at the end of the first week. The endocarditis is usually valvular, the aortic valve being affected more than the mitral, but in some cases both. The valvular lesions arise as a result of the generalised endocarditis caused by the septicæmia. There is a fraying of the endocardium along the line of the valves and vegetations which later become organised form in the region. Faulty apposition of the valves in this way leads to either stenosis or incompetence with all their ghastly accompaniments. The left heart is much more frequently affected than the right since the systemic circulation causes more strain of the valves than the pulmonary.

The patient had so far escaped cardiac damage and it was unlikely that it would now develop. The pulmonary complication of any consequence is pleurisy and there was never any evidence of this.

In the absence of complications the treatment was that of the condition itself.

For the first week the patient lay in blankets with a long flannel garment with sleeves to the wrists. This was changed frequently during the sweating period. Recumbency was adopted as the best position since the lower extremity gave little trouble. Slight movements of the affected joints were carried out by the patient herself to prevent adhesions forming. The diet was chiefly milk diluted with mineral water. Abundance of fluids was indicated in the presence of such a loss by sweating and
barley water, and peptonised milk were frequently given.

On the 12th day after admission sponge cake, oatmeal and arrowroot were added to the milk diet. Aperients in the form of salal and magn. sulDh. were given with satisfactory results.

The only other drug used was Sodium Salicylate, and it certainly brought down the temperature. The pain in the joints was also lessened after its administration though local application of a salicylate preparation was also being carried out.

About 80 grains were given the first day and the dose was varied as the temperature responded to it. No toxic symptoms such as headache, tinnitus, vomiting, or haematuria made their appearance.

At the end of the second week the urine has assumed a lemon yellow colour and urates were absent. Pain in the right shoulder was all that was now complained of and sweating had ceased. The sore throat was giving less discomfort. Convalescence was not hurried. Though there was no apparent cardiac lesion, the bad family history suggested caution, and it was essential that the return to an ordinary active life should be graduated with care. The possibility of the development of chronic rheumatism with all its associated crippling had to be borne in mind. Infective arthritis and fibrositis often have their seed under these circumstances, and often open the way to osteo-arthritis which may be part of the general deterioration of advancing years affecting joints which have been weakened by strain trauma or infection in early life.

7 weeks from admission patient was discharged from hospital feeling greatly improved in health. All joint lesions had cleared up. Instructions for the removal of tonsils and adenoids were given. The septic teeth were to be extracted, and a more healthy situation sought if possible. By these measures it was thought that there would be a lessened chance of future infection.