

6169 (213)

Notes on the Diagnosis, Treatment and Prognosis

of

Kala Azar.

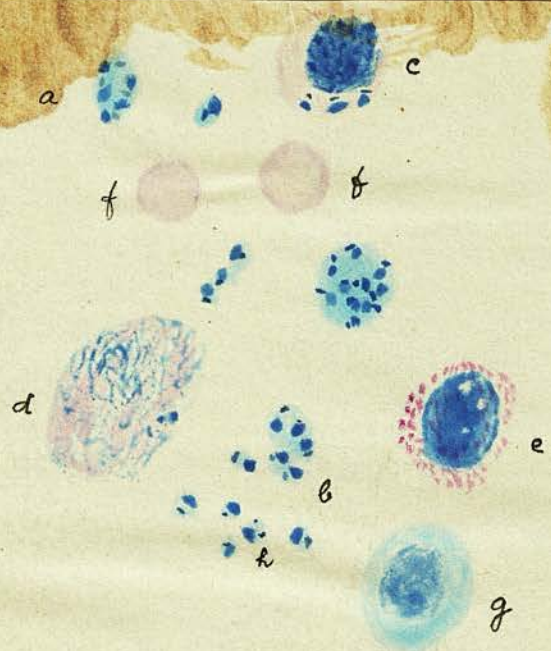
By

Ernest Muir.

M. D. 1910.

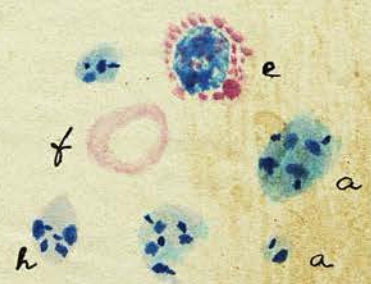


Splenic Blood in Kala Azar

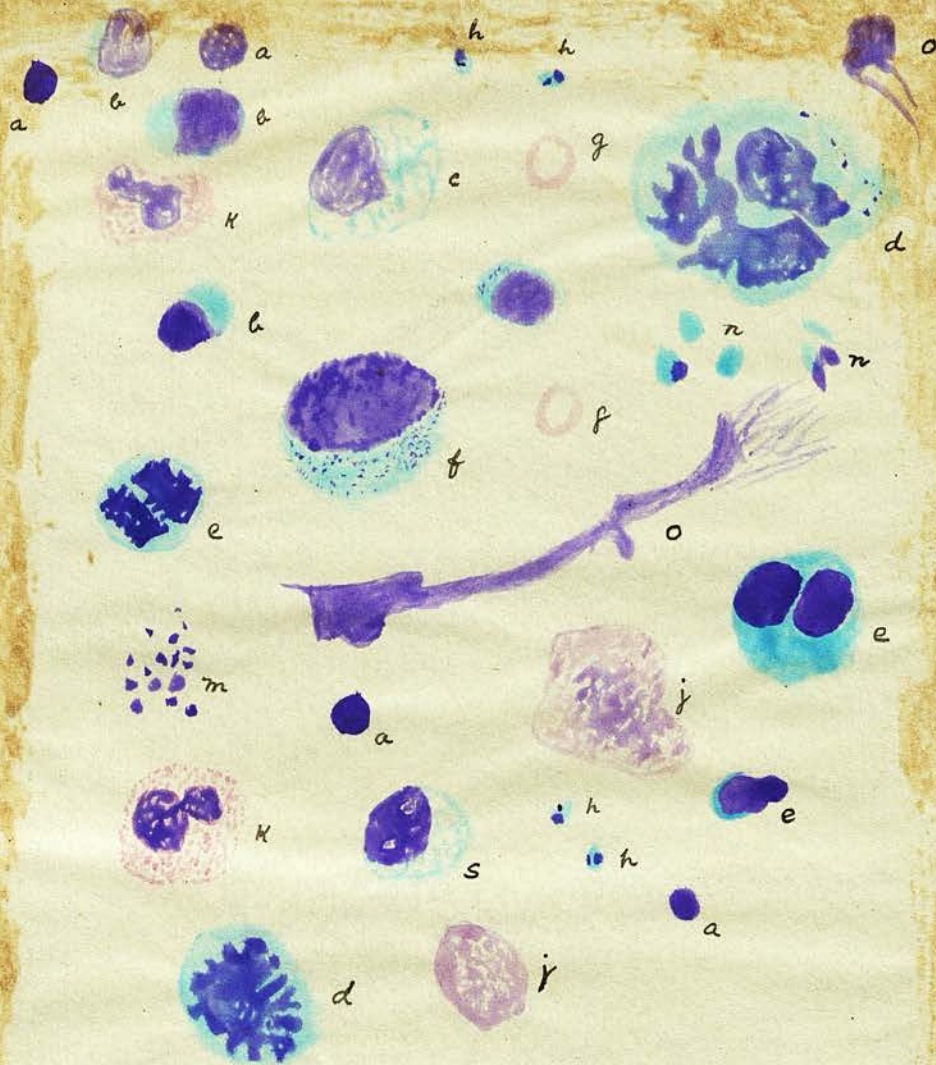


Case XV

- a. Groups of Leishman-Donovan - Bodies contained in a cell.
- b. Ditto with its cell burst
- c. Cell with violet nucleus, round and reddish protoplasm, containing three L.D.Bs in its protoplasm.
- d. Degenerate leucocyte containing L.D. Body.
- e. Mast Cells.
- f. Red Blood Corpuscles.
- g. Eosinophile leucocyte.
- h. Division of L.D. Bodies, where the micronuclei alone have divided



Case XIII

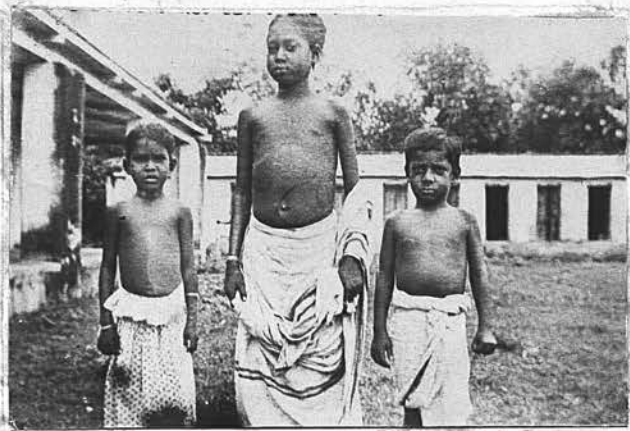


- |   |                                      |   |                            |
|---|--------------------------------------|---|----------------------------|
| a | Lymphocytes                          | m | Blood platelets            |
| b | Ordinary basophile mononuc.          | n | Small bodies stained blue. |
| c | Large basophile vacuolated.          | o | Ameboid movements.         |
| d | ditto division forms.                | s | Vacuolated basophiles.     |
| e | Ordinary basophile - division forms. |   |                            |
| f | Large basophile containing granules. |   |                            |
| g | Red Blood Corpuscles.                |   |                            |
| h | Leishman Donovan Bodies.             |   |                            |
| j | Degenerated leucocytes.              |   |                            |
| k | Polymorph. Neutrophiles.             |   |                            |

Blood of Spleen in Kala-azar  
 Taken from case XX





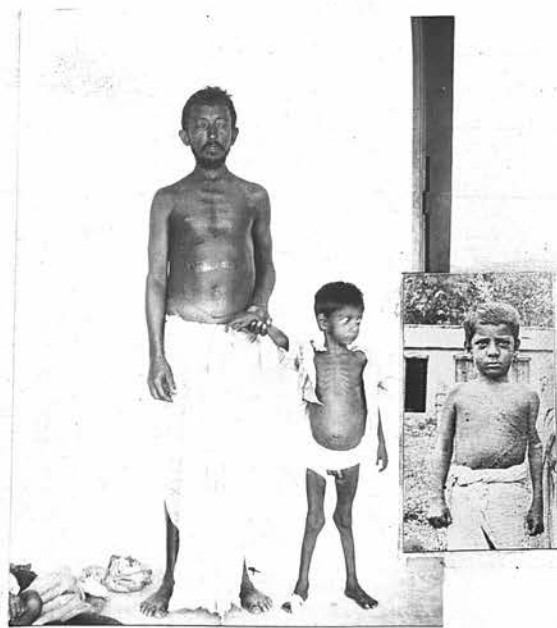


Cases II I XVII



A  
Group  
of  
Kala Azar  
Patients

Cases XVII + III



Case XVII  
after treatment.

Case XVII before treatment



Case XVI



Cases XV XXII XIV



Cases XV XIV XXII





Case XI



18 months after  
he left hospital.

Case IX



Case XII



Case XIX



Cases XX



### THE DIAGNOSIS OF KALA AZAR .

Kala Azar is a disease, the characteristic symptoms of which are fever, enlargement of the spleen and liver, certain changes in the blood, as well as certain secondary symptoms dependent on the above.

The fever is generally acute in its onset, lasting continuously except for a short remission in the early morning.

There is a tendency for the fever to become of a lower type after an indefinite time, that time varying with the individual and with the treatment employed. In many cases there is a double remission in the 24 hours as may be seen in the Charts of Cases 1, and 12. This double remission however is at once destroyed by the presence of any septic process in the body; indeed, if that septic process be severe enough, it has the effect of changing the type of fever entirely to a complete intermission.

This is to be noticed also in the above named charts. The fever of Kala Azar is accompanied by a burning sensation of the skin, especially that of the limbs and also a burning sensation of the eyes.

When the fever reaches the low type the patient becomes so accustomed to it often that he declares he has no fever, and only complains of a feeling of weakness and an enlarged and painful spleen. I have had a patient declare that he formerly had fever but now has none, while the thermometer showed a temperature of 102°.

On the other hand the thermometer may show no fever for several days and weeks and yet a splenic puncture will give

blood full of Leishman-Donovan-Bodies, as in Cases 13 and 16.

The great difference between the fever in Malaria and that in Kala-Azar is the rigor in the former.

In the first onset of Kala Azar there may be a certain amount of rigor, but it is very slight compared to that in Malaria. The natives themselves know the difference well and a diagnosis between the two diseases can generally be made with a fair amount of certainty by asking the patient whether the onset of the disease is accompanied by rigor or not. As the fever gets less it tends to come on only in the late afternoon or at night and to pass off in the morning. The time of the onset of the fever in Kala Azar thus helps in its diagnosis from Malaria, seeing that fever in the latter generally sets in about noon. I have often however had out-patients complaining of the symptoms of ordinary quartan fever, and, when this was treated with quinine, of the symptoms of daily fever of the type of Kala Azar, while a much enlarged spleen has pointed to the latter disease lying latent during the time of the quartan malaria.

The enlargement of the spleen in Kala Azar is perhaps its most notable symptom. When the fever has the acute form the spleen enlarges rapidly, but when it takes the low type it enlarges more slowly and tends to become very hard. When the fever ceases the spleen as a rule becomes smaller. The spleen may become so large that it fills practically every region of the abdomen.

This is in contrast to Malaria where the spleen seldom reaches to more than two or three inches below the costal margin.

This shows the absurdity of trying to tell the amount of Malaria in a district where Kala Azar exists by the "Spleen Index". In "The Practical Study of Malaria" by Stephens and Christophers, on page 264 this method is mentioned thus "It seems clear that the comparison of the Malaria of widely different regions by means of the per-centage of enlarged spleens in the children is not possible. We have however found that in Bengal the parasite rate and the spleen rate in children varied proportionately, the spleen was however nearly always about double that of the parasite rate".

Now, of the one thousand patients or more which we often treat in a week in Kalna, and which are drawn from the Burdwan, Hughli, and Nadia districts, well known as the unhealthiest districts of Bengal, about 90 per cent or more are often Kala Azar patients in the winter, while only 2 or 3 per cent are Malaria. Almost all these Kala Azar patients have enlarged spleens. There may be a certain number of Kala Azar patients who have the malaria parasite in their blood, but it is not common here seeing I have as yet failed to find it, and Dr. Chatterjea of Calcutta, who is a great authority on both diseases, writes in the Indian Medical Gazette that he has never yet found the parasites of both diseases in one patient. The statement quoted from "The Practical Study of Malaria" may be correct for the part of Bengal examined, but it certainly is very far from true as a general statement.

The enlargement of the Liver. While enlargement of the spleen is a constant symptom in Kala Azar, enlargement of the liver is by no means so constant, though it generally does occur to some small extent. In Cases 1 and 14 the liver was very much enlarged. In some cases the enlargement of the liver is accompanied by absence of bile in the stools and great constipation. In these cases purging with magnesium sulphate leads to a speedy diminution in the size of the liver. In others, as in case 1 and 14 especially, the motions are well coloured from the beginning and the liver only disappears slowly after the spleen has almost gone. I think it is very probable that a process of fibrous tissue formation alternates with a process of contraction of that fibrous tissue in many cases. The former process leads to slight enlargement of the liver and the latter to diminution in the size of the liver. The former process goes on in the active form of fever, the latter during the latent period of the fever. The two processes tend to keep up a balance of size so that the liver neither gets larger nor smaller. A common result of this process of cirrhosis of the liver is the formation of ascites, as in Case 21. Ascites is a very common condition here and, in my experience, has in most cases been preceded by a history similar to that of Kala Azar. Where the liver is enlarged there are generally large veins to be seen over the surface of the right side of the abdomen. I have sometimes had a little difficulty in distinguishing a much enlarged liver from an initial liver abscess, but have generally found that the organ in the latter

is much more tender, and that in the latter disease much relief was at once given by the administration of large doses of Ipecacuanha.

Changes in the blood While there may be a marked diminution in the number of the red blood corpuscles, (I have found as few as 950,000 per c.m.m. in one case)- the most striking changes are in the leucocytes. Most important among these are the diminution in the per-centage of the polymorphonuclear leucocytes and the relative and absolute increase in the number of basophile leucocytes. A great many vacuolated neutrophiles are found and others are found in various stages of degeneration. They are often found with Leishman-Donovan-Bodies in their protoplasm as in the blood taken from Cases 13 and 15. The basophiles on the other hand are sometimes found in the spleen blood in a state of division as is shown in the illustration of the blood from Case 20. In Case 1 a careful search of three slides failed to show a single neutrophile. In some cases, besides the basophiles found in ordinary blood, a form of large mononuclear leucocyte is found with active amae**h**oid movements. Some of the basophiles take on a deeper stain than others both in the nucleus and in the protoplasm. The blood taken by means of a puncture from the spleen or liver generally abounds in Leishman-Donovan-Bodies shown in the illustrations. This consists of an oval body which takes on a blue or bluish-red colour with Leishman's stain. Within it lies a macronucleus stained light violet, and a micronucleus stained darker violet. When the fever is of a low

type this body is found as just described, but when it is acute, division forms are found as shown in the blood from Cases 13 and 15. When two L.D.Bs. are found in one capsule, the size of the capsule is about half the size of a red blood corpuscle. When 4 or more are found, it is larger than a red corpuscle. As many as 9 may be found in one capsule as shown in the illustration.

When the division is going on rapidly, numerous division forms are to be seen with the micronucleus divided and the macronucleus undivided. Mast cells are often found in the blood of Kala Azar patients in fair abundance. With regard to taking spleen punctures - many have regarded it as a dangerous and unjustifiable proceeding. I have never yet seen any bad results from it. The following is the process followed. A tightly-fitting all-glass syringe is used. This is boiled for ten minutes and then dried leaving the piston sufficiently moist only to ensure suction. A certain number of slides are laid out ready on a table near the patient.

An assistant standing on the right side of the patient presses with both hands on the right margin of the spleen so as to make it lie as much as possible to the left and at the same time stretch the abdominal wall over it. A point as near to the ribs as possible is selected for the puncture. The skin over this spot is cleaned with turpentine and spirit and the needle inserted at right angles to the spleen. This last point is most important otherwise the needle may slip along the surface of the splenic capsule and push the spleen in front of it. One drop of blood

is sucked up into the syringe and the needle withdrawn. The assistant continues to press on the spleen for almost five minutes after. The patient must always be lying on his back and must continue to lie without moving for half an hour after the puncture is made. Slides are made in the ordinary way from the blood in the syringe.

As to the nature of the L.D.B. there has been a great deal of speculation, but one cannot help being struck with its resemblance to the malarial parasite especially that of quartan fever. While the process of enlargement does not go on inside a Red-Blood Corpuscle it consists of gradual division till a certain size is reached when the capsule bursts. The capsule containing 9 parasites in the blood of Case 15 looks very like the appearance got in the parasite of quartan malaria. As a result of the condition of the blood the patient has often a blackish appearance which is very striking and gives rise to the name of the disease, which means "Black Fever". In many advanced cases there is a diminution in the coagulability of the blood which may lead to purpura or haemorrhage from any slight wound. There is also a tendency to the formation of septic processes in different parts of the body. Suppuration of the middle ear is found in a large proportion of cases. (See Case 8 ).

Inflammation of the gums is even commoner (See Cases 1, 14, 15). It often ends in necrosis of a part of the lower jaw. Cancrum oris is another common symptom ( Case 19 ), and gangrene of the throat is also a very serious result (Cases 5 and 7) which

may lead to death by asphyxia or rupture of a blood vessel. There is also a tendency to form abscesses or sloughs at any part of the body where there may be slight injury.

Kala Azar may last for a very long time without either being cured or ending fatally as in Case 13 where it had lasted 5 years. It may last far longer even than this when the patient is treated.

I know of a woman who has had Kala Azar for about 13 years. The fever becomes active at times and then after-treatment becomes latent again. To sum up, the most important points to be observed in diagnosis are :-

- (1) The size of the spleen and liver.
- (2) The continuation and type of the fever.
- (3) The state of the tongue, which is generally clean.
- (4) The colour of the skin and general appearance of the patient.
- (5) The differential leucocyte count.
- (6) The presence of Leishman-Donovan-Bodies.
- (7) The fact of the fever not yielding to quinine
- (8) The absence of Widal's reaction.

Still Kala Azar in its initial stages, that is during the first 3 or 4 weeks, may be very difficult to diagnose on account of the spleen not being enlarged to an appreciable extent. In this stage I have found it much resembled by the initial stages of liver abscess, where however the liver is enlarged and tender to a greater extent than in Kala Azar. Again I have found it resembled by a low fever dependent upon a chronic gleet. Examination

Examination of the urine however easily made the diagnosis clear. Again Dengue, which is not uncommon here in the months of June, July, and August, has to be distinguished, and in this the type and duration of the fever are chiefly useful in diagnosis.

The diagnosis from Malaria is not difficult, as a rule examination of the blood revealing the malarial parasite, and the fever in almost all cases yielding to quinine.

### TREATMENT OF KALA AZAR

Treatment of Kala Azar may be divided into prophylactic and curative measures. Until there is a proof to the contrary I think that it is wise to take as at least a working hypothesis in prophylactic treatment the theory that the chief, if not the only, carriers of the disease are bed-bugs.

This theory, apart even from the experimental proofs brought forward by Dr. Patton and others, seems to me to answer to every fact known about the infection with Kala Azar in this district.

The fact that the disease is seldom limited to one member of a family as is borne out in Cases 9 and 10 and in Case 23, while those in houses a short distance off are not affected is in favour of this theory. I frequently have a whole family of 5 or 6 members brought to me, every one of them suffering from this same disease.

The infrequency with which the parasite is found in the peripheral blood, and the fact that it is never found there except when the disease is in its active form explains the fact that many escape infection.

The disease is found in many countries besides India. It is common in Syria, and Arabia and is found in Egypt.

In Syria it is found in the valley of the Jordan but not on the higher lands. In India I have found it in those villages where there is most jungle, especially bamboo jungle which is very dense and shuts out the sun and wind, while in districts

where the land is cultivated Kala Azar is unknown. While out in camp this winter in the Hooghly District I found three villages of coolies who had come from Chota Nagpur some seven years ago. Their villages had no jungle surrounding them. The inhabitants of these villages were entirely free from Kala Azar, while in the surrounding Bengalee villages almost every house contained one or more patients.

In the oldest villages the disease was worst and especially among the better class people who live in houses which are built of brick, and therefore last many years. As to the reason of this - I think that it is very probable that the fact of the inhabitants of older houses and the houses surrounded by bamboo jungle being most affected is due to the fact that such houses are generally very damp and peculiarly favourable for the cultivation of bed-bugs, while huts built of split bamboos have to be renewed year by year and are thus unfavourable for the cultivation of bugs.

The unwillingness of the natives to cut down the bamboo jungle inspite of their, in many instances, realising its unhealthiness is chiefly due to two causes. Firstly, the bamboo makes a very profitable crop and requires practically no labour, Secondly it affords privacy to their women. In many places I have seen the ruins of large villages which have almost disappeared, only one or two houses being left amid the bamboo jungle, and on my enquiring the cause the invariable reply has been "Spleen Fever".

Kala Azar is more common in valleys, as there is more moisture, and on alluvial soils as the water stands and does not filter away so quickly as it does in sandy or gravelly soils. The year before last (1908) the Ganges sunk very rapidly after the rains and along with it the tanks and smaller rivers very quickly dried up. The result was that Kala Azar was very much less. This last year on the other hand there were floods in the rains and the river has not sunk nearly so low; the tanks accordingly have also much more water in them and, in consequence, the Kala Azar patients have been about 3 times as many as the former year. With all these considerations in mind it is easy to see how ineffectual in this part of Bengal at least would be the method proposed by many for stopping the so-called malaria fever. The destroying of mosquitoes would possibly have a beneficial effect on the few malarial patients, but on the very large majority who have Kala Azar it would be ineffectual. A much more useful measure would be the cutting down of all bamboo and other thick jungle and the planting in their place of large trees at suitable intervals.

Besides this there is the impossibility of destroying the mosquitoes which breed on the flooded paddy fields in the rains, while the removing of jungle would probably be welcomed by most villagers, if it were done by the orders of Government.

Beyond this the destruction of old houses would be a useful measure. Fumigation of plastered houses seems to me to be useless as the bugs remain deep in under the plaster and the fumes could never reach them.

A mere destruction of jungle or of old houses while advantageous therefore would not free a region of Kala Azar entirely. It would be best to follow out the plan mentioned in Major Rodger's book on "Fevers in the tropics", and remove the residence to, at least 400 yards from the former site.

We have found bugs travel from one house to another house a few yards away, but never to the distance of 400 yards.

With regard to the Curative Treatment of Kala Azar many attempts have been made. Quinine by the mouth has been recommended in large doses. In Kalna however we have found Cinchona Alkaloids much more effective than quinine. Cinchona Alkaloids, a bye-product in the manufacture of Quinine, is supplied by the Botanical Gardens at Calcutta.

One pound of the Alkaloids is mixed with 6 oz. of pure Sulphuric acid and 120 ounces of water. After standing it for a short time the mixture is filtered and diluted with an equal quantity of water. To each ounce of this infusion 16 grains of Ferri Sulphate and 40 minims of Liqor Arsenic Hydrochlor are added. The dose of this mixture for an adult is one drachm three times daily. Seeing that most Kala Azar patients are constipated, 6 drachms of Magnesium Sulphate to the ounce is added in these cases.

If necessary, and especially in cases where the liver is enlarged, a powder is given according to the following prescription :-

Rx	Pulv. Jalap	grs	1½
	" Rhei	"	1½
	" Calomel	"	1
	Sodium Bicarb	"	1
	Podoph	"	1/3

If this powder given every morning is not sufficient to secure a good motion, it is supplemented in the evening with castor oil.

In giving the cinchona mixture and in the treatment of Kala Azar generally it is most important to keep the bowels freely open. This treatment is generally sufficient to reduce the high form of fever to the low type, but I doubt if it is ever sufficient to eradicate the disease.

The natives have a habit of cauterising with red hot irons over the spleen. In Syria I have frequently seen setons used over the spleen, with beneficial results.

Those who advocate the use of quinine have also recommended the hypodermic injection of quinine bihydrochlorate or other non-irritant preparations of the drug.

In my experience the injection of quinine has only been beneficial when there has been local irritation at the point of injection and the benefit has been in proportion to the amount of irritation, there being most benefit of all where an abscess or a slough occurred. The treatment is in fact similar to the native plans of cauterising and using the seton. This fact is borne out by most of the cases given in this thesis.

In dealing with the diagnosis of Kala Azar, I have mentioned that the great characteristic of the blood is the diminution in the number of polymorphonuclear neutrophile leucocytes, which should be about 75 per cent in normal blood.

The injection of an irritating fluid is almost invariably followed by a distinct increase in the number of the

leucocytes. This is very strikingly shown in Case 1, where, on the first examination of the blood no neutrophiles were found, but, when the blood was examined ten days later, a hypodermic injection having been made in the meantime, 57 per cent of neutrophiles were found. It is not necessary to give an injection sufficiently irritating to cause very much pain as a rule, though as a rule a quicker result can be got where the pain is more severe. On the other hand where the patient is very weak a very small injection may produce a slough, while a very much larger injection would have produced but little effect on a less advanced case. The fluid that I have been in the habit of injecting is a solution of 4 grains of Quinine Sulphate in one drachm water with sufficient Sulphuric Acid to dissolve it. Of this solution I give from 20 to 90 minims according to the size and condition of the patient. When the patient is in the hospital I generally begin with a small injection and judge by the amount of reaction the dose of the subsequent injections.

I have never yet found this method of treatment fail where I have got the patient in time and have been allowed by the patient or the friends to continue the treatment for a sufficiently long period. I generally give the injections into the Latissimus Dorsi Muscle in adults, and in small children into the gluteal region.

During the last 3 or 4 months I have been giving on an average more than 60 injections weekly. In an out-dispensary which I hold weekly in a district where Kala Azar is especially prevalent

the people have come to realise the benefit of the injection to such an extent that they never object to its being given, and many patients insist upon its being given. This is the more striking when one bears in mind the strong aversion of Bengalis to bearing pain.

The child of one of our dispensers was suffering from Kala Azar, I gave an injection of Quinine Sulph. Mixture with the result that there was considerable swelling at the site of injection but the spleen and fever at once subsided. The swelling at the site of injection also subsided. About a month after there was a slight return of fever and the spleen enlarged slightly. The site of the original injection again became swollen and painful upon which the fever and spleen subsided. This happened three times to a slighter degree each time. Thereafter the boy has had no return of fever or enlargement of the spleen.

As to how often injections should be given and how long they should be continued, one has to judge most by the size of the spleen and liver and by the general condition of the patient. The cessation of the fever is never an indication for stopping the injections unless the spleen is rapidly diminishing in size and the patient rapidly increasing in weight. As to the frequency of giving injections : the effect should always be kept up. As long as there is pain on pressing the last point of injection another may not be necessary, but it is often well, where the patient can be got to endure it, to give several small injections in different parts of the body either at

the same time or at short intervals, as the combined effect of them all acts more rapidly in producing a sufficient reaction. It seems probable from the large numbers of degenerate neutrophils which are found in Kala Azar Blood, that the effect of the parasite is to cause their destruction at a greater rate than they can be reproduced.

The effect of the injection is to produce a stimulation in the reproduction of neutrophils, sufficient to outbalance their destruction.

A similar effect is often produced automatically by the various septic processes mentioned among the symptoms of Kala Azar, such as Cancrum Oris, Disease of the middle ear, gangrene of the throat, etc. It has been shown however in the various cases how this process may lead to very serious results, death from asphyxia or haemorrhage, etc. While there is a tendency to the formation of these septic processes in the body, they do not form in many cases, while in others a chronic purulent condition of the middle ear or a chronic suppuration of the gums or the constant formation of small wounds due to the scratching of the skin which is frequently covered with itch (due to a native prejudice against washing the skin in Kala Azar) is sufficient to keep the Kala Azar in abeyance, so that, though it is not cured, yet it remains latent or of a very low and chronic type and may thus last for many years. I have more than once met with adults who show the scar of some huge wound of the face. On my enquiry they have told me that 20 or 30 years ago they had "Spleen Fever" but that when the wound

appeared on the face the spleen and fever disappeared at once. My chief difficulty in treating Kala Azar patients is to get them to continue the treatment long enough and to begin it in time.

The disease is apt to become latent without being eradicated, and the patient is generally so content with this that he considers it unnecessary to have any further treatment.

It is always important at the outset of treatment in advanced cases to attend to the mouth, lest there should be any suppuration of the gums or throat. It is also advisable where possible to keep an advanced case in bed and to take care that he avoids chills. Kala Azar patients are peculiarly apt to take pneumonia with a fatal result as in Case 14.

Seeing the digestive system is not much affected in most cases it is advisable, whenever the fever is not high, to keep the patient on a full, though simple diet. I have tried limiting the patient to a milk diet but have found that the patient's strength was apt to suffer as compared with those who had a more generous diet. Where milk in large quantities can be digested it has a very beneficial effect. When the giving of a large quantity of milk is followed by undigested motions it is generally advisable to stop the milk for a short period and then by means of such a powder as that mentioned above, get the motions regulated. The milk should then be begun again and increased by slow degrees. Dysentery is not uncommonly found in advanced cases. In children I generally use an emulsion of castor oil in large doses, and in adults ipecacuanha in 20 grain doses.

It is difficult to say how the dysentery is caused but I think it is not improbable that it is caused by the formation of ulcers homologous to cancrum oris and the other septic processes mentioned above.

There is one fact about which there can be no doubt and that is that Kala Azar is very much affected by seasonal influences.

In Kalna we meet with comparatively few cases in the hot weather or in the early part of the rains. Towards the end of the rains the numbers of Kala Azar patients begin to increase again, but it is in November and December and January that we have sometimes as many as 400 Kala Azar patients coming in one day. This is probably due to the effect of the cold during these months, the heat of summer having the effect of subduing the disease. The sun seems to have a definite effect also in increasing neutrophile leucocytosis and it may be partly in this way that the heat of summer acts in limiting the disease.

It is also during the damp season at the end of the rains that bugs are most rife and thus there are then increased opportunities of contracting the disease.

### THE PROGNOSIS OF KALA AZAR

The Prognosis of Kala Azar is generally supposed to be far from hopeful. This impression is very much helped by the course taken by the disease in the few Europeans who have lately contracted it. The cases given in connection with this thesis however show that a more hopeful view may be taken with reason. Of the 23 cases, which are chiefly far advanced cases, given 12 are known for certain to have been cured and to have remained in perfect health for periods of one year or more. Those which did not recover all came under treatment after the disease had continued for 6 months or more, or else they left hospital before a complete cure could be effected.

Speaking generally, I think there is no doubt that Kala Azar (or at least the form of the disease which we are familiar with here) is curable in almost all cases if it be got in time, i.e. within the first 3 or 4 months of its course, and if the treatment be continued for a sufficiently long time.

In more advanced cases however, while there are many, like Cases 1 and 17, who will recover, there are also others which have reached a stage in which they do not react to the treatment.

The nature of the temperature is of little help in prognosis as a high temperature is common in the initial stages and those in whom the disease is much more advanced may have a normal temperature at intervals, when the disease becomes latent.

The size of the spleen and liver do not form an absolutely prognostic sign, as a very large spleen may disappear in a very short time with treatment, while a much smaller spleen may resist treatment.

The safest method of prognosis seems to me to be got by watching the amount of reaction when the injection of a definite amount of an irritating fluid such as a solution of Quinine Sulp. is given. This reaction is shown by the amount of rise of temperature over what there was before, by the amount of diminution in the size of the liver and spleen and by the relative increase of the number of neutrophile polymorphonuclear leucocytes.

Division forms of Leishman-Donovan-Bodies indicate an active state of the disease but do not form an absolute factor in the prognosis.

One of the worst signs in Kala Azar is a certain appearance of the skin where it loses its glistening appearance and takes on a livid colour similar to skin beginning to become affected by a spreading gangrene. I have never seen a patient recover when this appearance is found, but it is only got after many months of the chronic disease.

Case I Panchu Dashi, admitted to hospital on February 12th 1909, age 11 years.

Patient had a history of 6 months continuous fever at the time of admission to hospital. On examination of abdomen on admission the spleen reached to the umbilicus and the liver reached to 3 inches below the costal margin in the right nipple line. Blood was examined on February 5th, a week before admission of patient to hospital. Although three slides were carefully examined no neutrophile (finely granular eosinophile) leucocytes were found; thus 100 per cent of the leucocytes were basophile. Numerous bodies were found which were evidently vacuolated degenerate polymorphonuclear leucocytes. After the examination of the blood an injection of 3 $\bar{v}$  of Quinine Sulp. Mixture was given in the leg. This was followed by a high rise of temperature. On February 14th there was found to be an abscess at the seat of injection. This was opened when the temperature became normal. The patient had at the same time been treated by giving a mixture internally, containing Cinchona, Iron, Arsenic and Magnesium Sulphate.

The abscess when opened was found to contain a slough, which was evacuated.

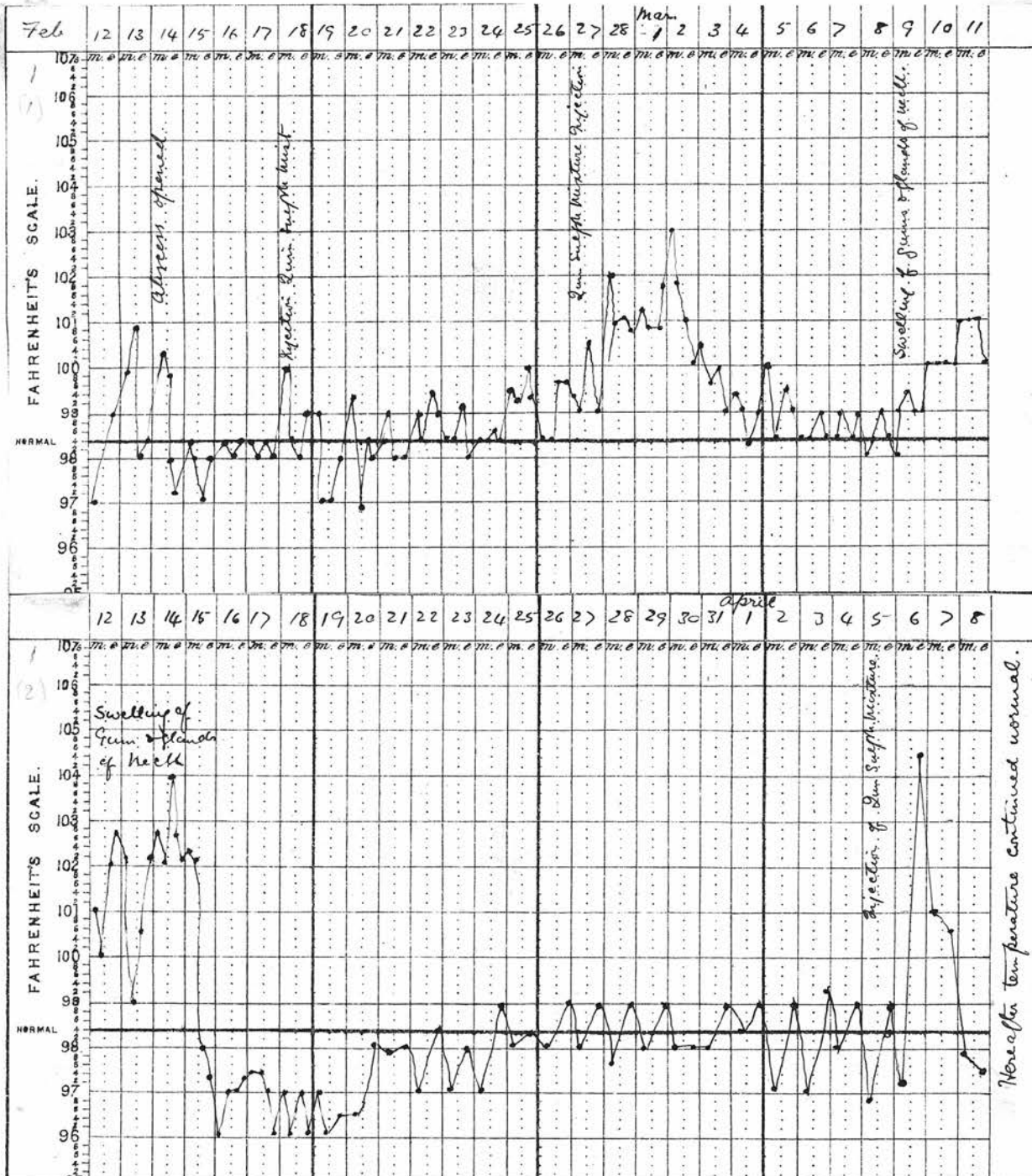
On February 15th the blood was again examined, when 57 % of neutrophiles (polymorph) were found, 10 % of lymphocytes and 32 % of large mononuclear basophile leucocytes. The spleen and liver were much diminished in size, the former only reaching to within 1 inch of the umbilicus and the liver being only 1 inch from the costal margin in the right nipple line.

The patient was treated also with calomel and saline purges, almost every day, without which there was no evacuation of the bowels.

On February 25th there was again a distinct rise of temperature. Another injection of quinine sulphate mixture was given hypodermically which was followed as before by a sharp rise of temperature, after which the temperature again became low. On the 9th of March the gums became swollen as did also the glands of the neck. This was accompanied by a rise of temperature, which reached its summit on the 14th at  $104^{\circ}$ , after which it sank rapidly to subnormal, the mouth condition having also subsided. On March 24th the temperature began again to rise slightly above normal in the evenings. On April 5th another injection of Quin. Sulp. mixture was followed by a sudden rise and fall of temperature after which the temperature remained normal and the patient began rapidly to put on weight. The photograph marked Case I shows the patient a few months after leaving hospital. The patient has now continued in robust health for over a year. In the accompanying temperature charts, the daily double rise of temperature may be seen at such places as a septic process is not taking place.

The spleen disappeared much more rapidly than did the liver, the latter long continuing to show enlarged veins over its surface externally. These have however long since disappeared and both spleen and liver are now normal.

In the photograph the sizes of the spleen on admission to hospital and at the time of taking the photograph are indicated on the abdomen with painted lines.



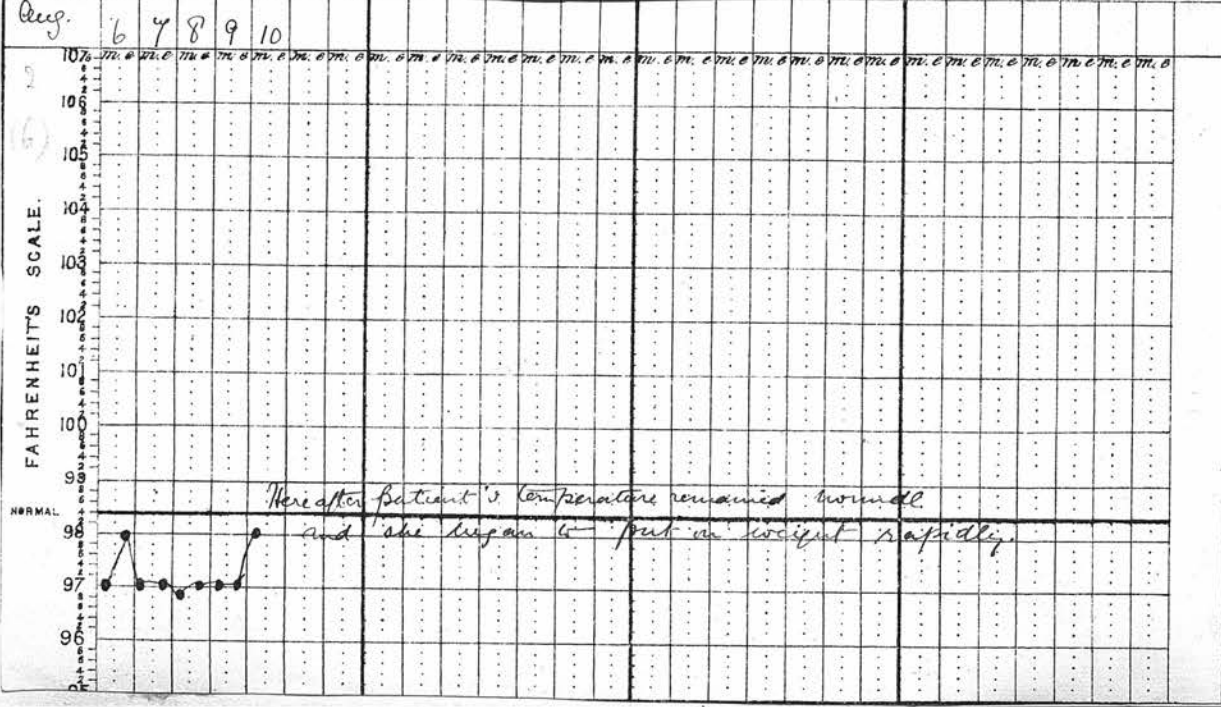
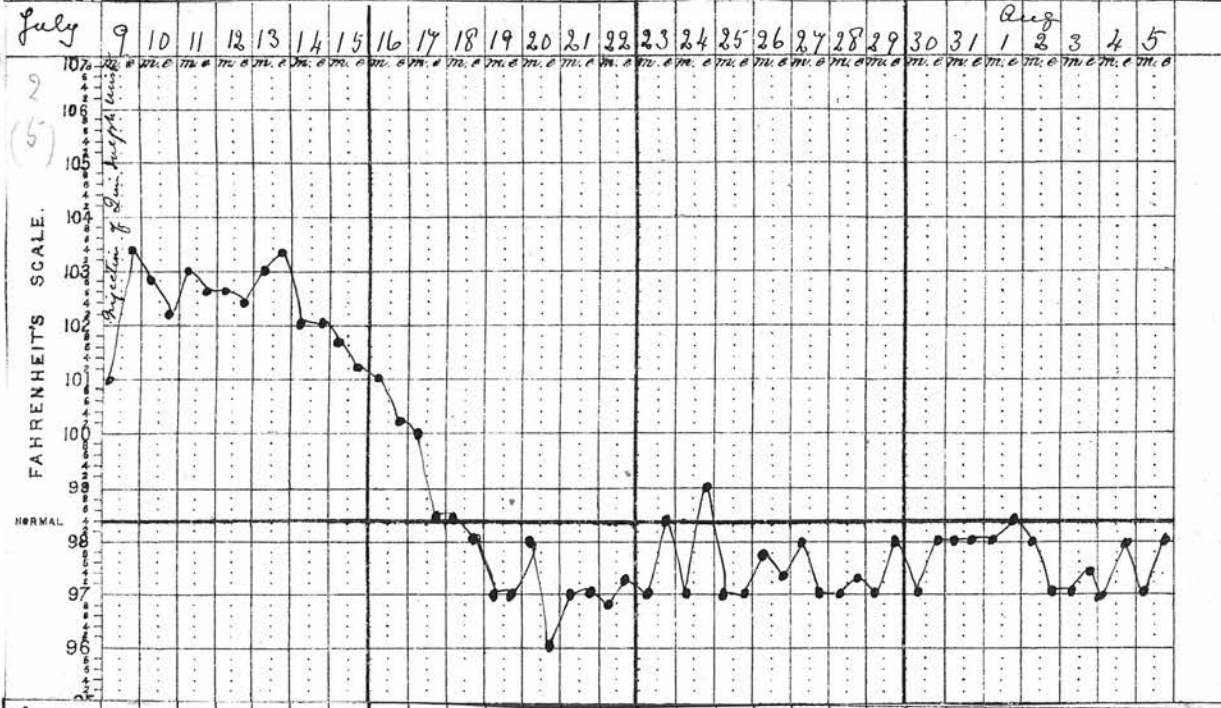
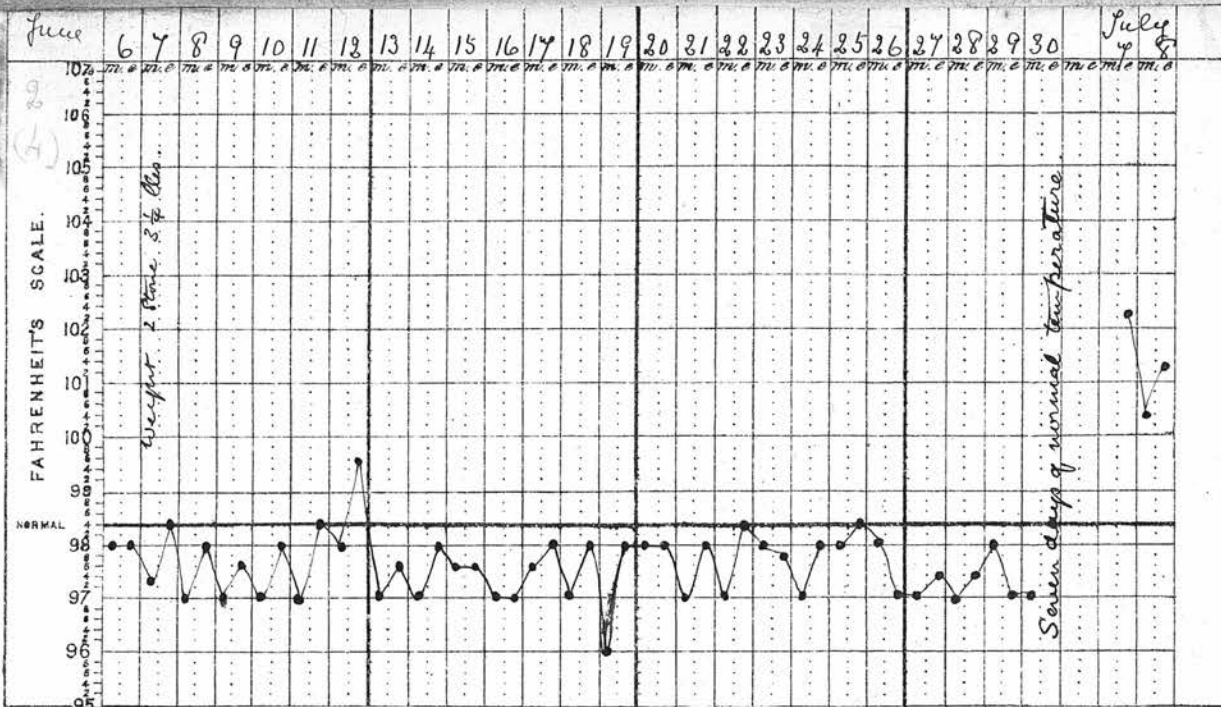


Case II Ruth, aged 7 years. Admission March 14th.

Spleen was considerably enlarged on admission. Injection of five grains of Quinine Bihydrochlor were given hypodermically in different parts of the body daily for some time, but without apparent beneficial effect. On the 27th of March the temperature rose to 102.6 and was accompanied by suppuration in the mouth. On the 4th of April an abscess formed in her back at the site of one of the injections upon the opening of which on the 10th the temperature soon assumed the normal. As the slough in the abscess had not been completely evacuated, an abscess reformed accompanied by fever. On the evacuation of this the temperature remained normal. On the 14th of May there was considerable inflammation of the right ear which had been painful for some time. This was accompanied by a rise of temperature for two or three days. Thereafter there was no more rise of temperature and the patient gained considerably in weight, while the spleen became so small that it could hardly be palpated under the ribs.

The patient remained well for nearly a month, but on July 7th the temperature became high and the spleen enlarged once more. An injection of Quinine Sulp. mixture was given on the 9th and on the 13th the temperature began to go down, reaching the normal on the 17th. The patient has since had no more fever and has put on weight rapidly. The photograph marked Case II shows her some weeks after the fever had finally disappeared. The temperature charts which are given in full show the effect of the inflammatory process in causing a rise of temperature followed by absence of fever.





Case III Bijay, aged 5. Admitted October 20th.

History of high remittent fever for three months before admission. Cinchona and Iron and Arsenic mixture was given internally and injections of quinine sulp. mixture were given inter-muscularly but patient did not react to treatment. Legs became swollen, skin became of a dark, livid colour. After being  $4\frac{1}{2}$  weeks in hospital, he died apparently from the state of the blood the solid constituents of which were very much reduced in amount.

Case IV A boy aged 13 who was seen as an out-patient. When I first saw him a differential blood count gave the following :-

Polymorpho Neutrophiles	37 %
Coarse granular Eosinophiles	6 %
Lymphocytes	$36\frac{1}{2}$ %
Large Mononuclear Basophiles	$12\frac{1}{2}$ %
Degenerate forms	6 %

The immediate cause of my seeing the boy was his having sustained a severe injury to his spleen which was enlarged to beyond the umbilicus.

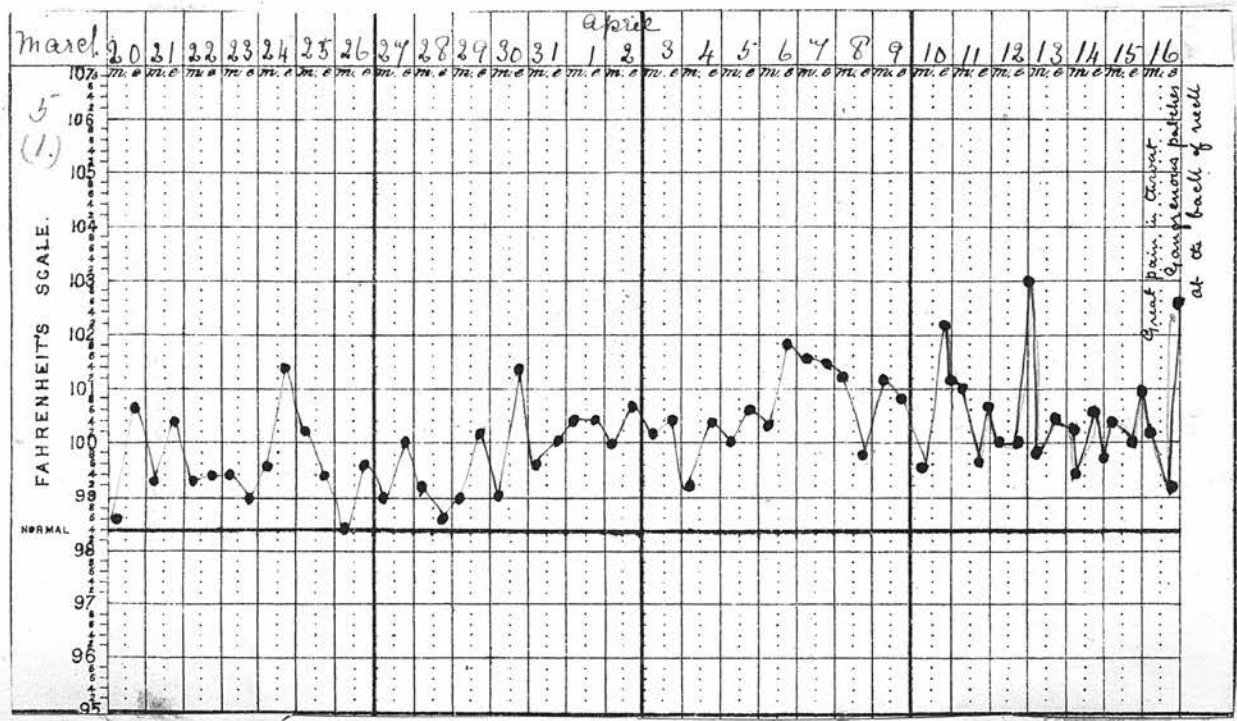
This was accompanied by very considerable pain in the splenic region and by a high rise of temperature.

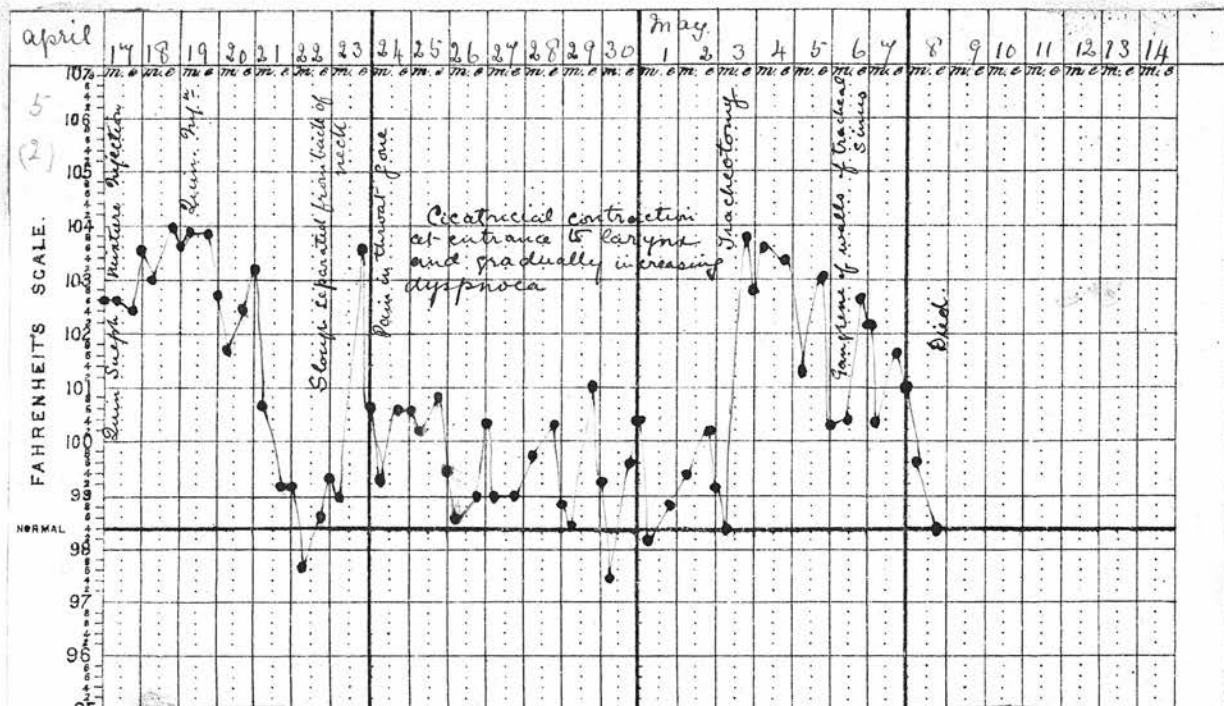
When I saw him next however after treating him for 2 weeks with cinchona etc., the pain had considerably decreased, the spleen had diminished in size and the temperature had become normal. The boy became steadily better and the last time I heard of him he had had no more fever and his spleen had almost become impalpable under the costal margin.

Case V Khudu, aged 9. Admitted on March 20th.

History of 5 months fever on admission. He was given frequent injections of Quin. Sulp. mixture hypodermically and cinchona, etc. internally as a result of which spleen became smaller.

In the 2nd week of April ulcers of a gangrenous nature began to form in the pharynx, affecting the uvula, soft palate and the posterior part of the arythino-epiglottidean folds. Fluids were returned in large measure by the nose when drunk. As the laryngeal ulcer healed and contracted the opening of the larynx became contracted and there was considerable dyspnoea. The stricture was dilated with bougies but the relief to the dyspnoea was only temporary. Tracheotomy was performed which was followed by great relief for 4 or 5 days, when gangrene began to appear in the sinus leading to the trachea, resulting in sudden blocking of the trachea from which he died. There was gangrene at the back of the neck at the same time.





Case VI. Panchu Chatri, aged 11 years. Admitted on July 24th.

History of ten months fever before admission.

The father, who was an intelligent man, gave the history that the fever during the 1st four months lasted a few days at a time and then got better. Thereafter the fever became high and continuous. He was treated for 3 months by a native doctor without benefit. Thereafter he was treated as an out-patient at our dispensary with cinchona and iron mixture with the result that the high temperature became low, but did not cease.

On admission to hospital the spleen was 4 inches below the costal margin in the left nipple line and extended to beyond the umbilicus.

The liver extended to 3" below the costal margin in the right nipple line.

Without strong purgatives he seldom passed a motion, and even then they were clay-coloured. After continuous

administration of calomel jalap and magnesium sulphate the motions became gradually tinged with bile and were fairly green 3 weeks after admission to hospital, while the liver had decreased so that it was hardly palpable under the ribs.

Injections of quin . Bihydrochlor. were given hypodermically every 2 or 3 days after admission. They were followed by a certain amount of pain at the sites of injection, and the spleen began to steadily decrease in size. Still the fever, though it continued more or less low, never stopped and the patient's weight, though it did not diminish, did not increase either. About 6 weeks after admission I began to give injections of Quinine Sulp. mixture which caused local pain and swelling and the temperature took a more swinging character, while the appetite became decidedly better. The weight did not increase however. The patient was removed from hospital and I heard that he had died shortly afterwards.

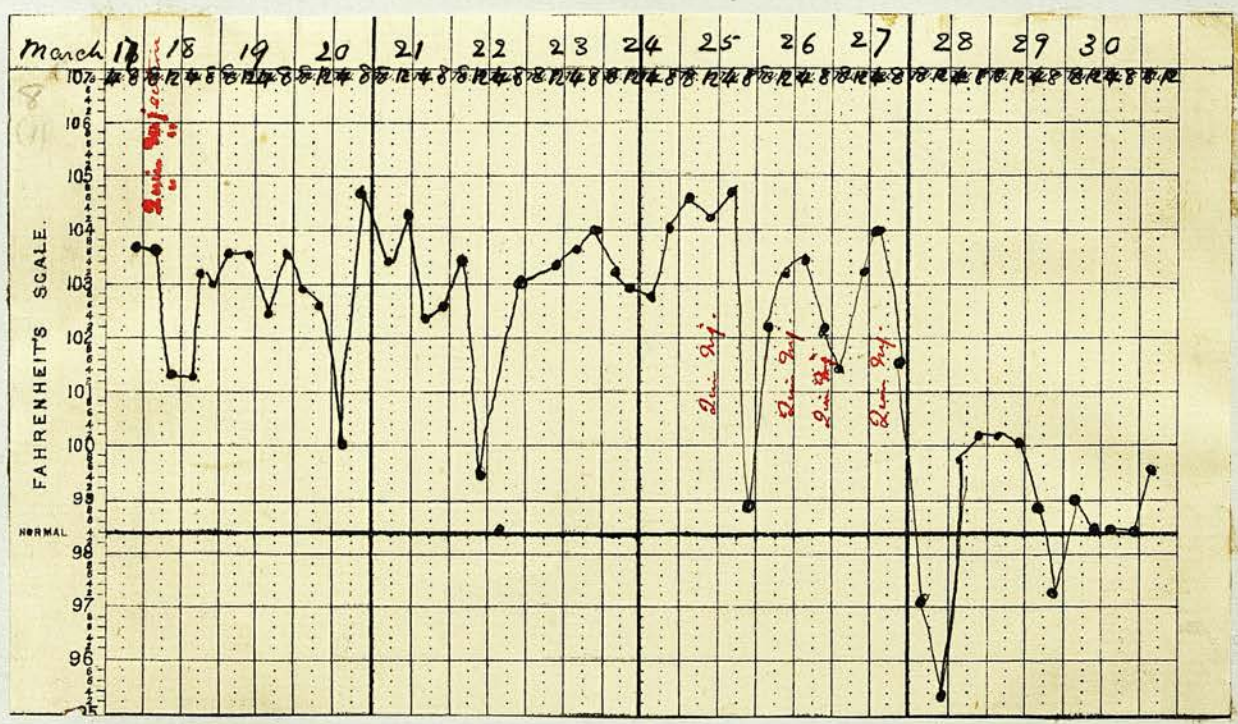
The delay in beginning treatment seemed to have been too long and the tissues seemed not to have had power to react to the treatment.

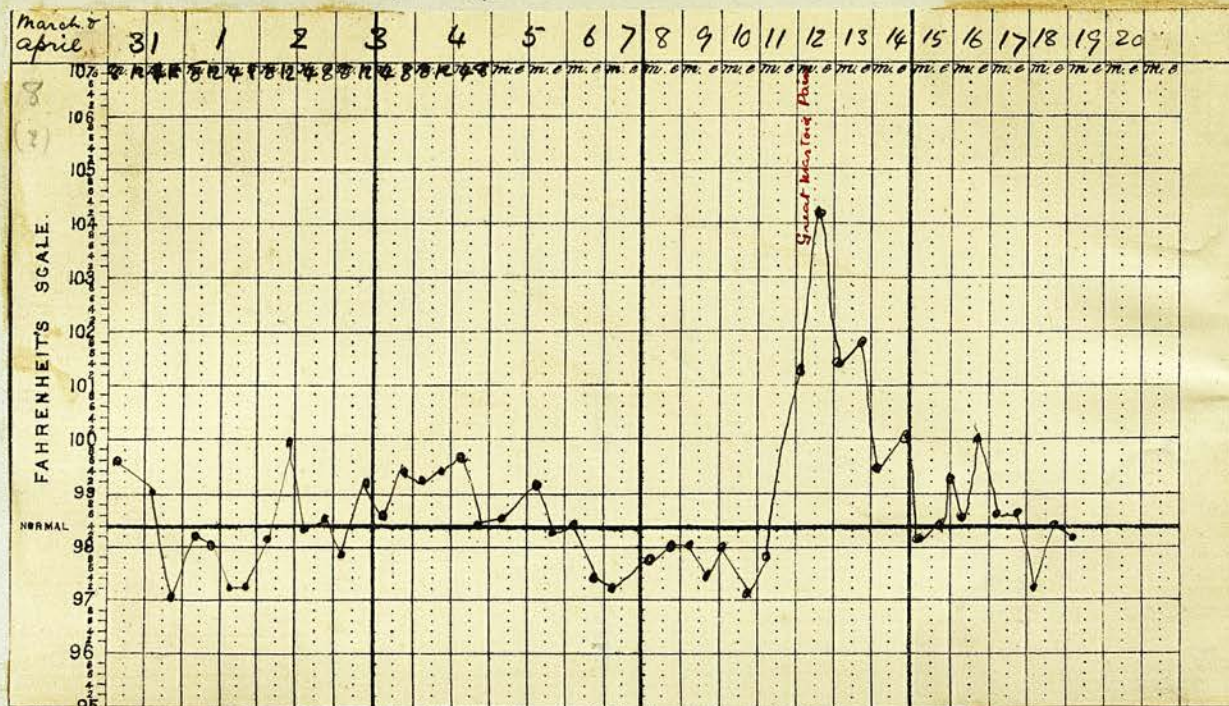
Case VII Nitya was admitted on the 30th March.

He developed gangrene in the region of the tonsils and died suddenly from haemorrhage due to the perforation of an artery in that region.

Case VIII Suraj aged 28, female. Was admitted on March 16th 1907 with a much enlarged spleen.

Quinine by the mouth and quin. bihydrochlorate subcutaneously produced little affect on the temperature. On April 11th there was severe pain in the region of the mastoid, which was relieved by cutting down to the bone and the applying of carbolic poultices. Her temperature went to 104.2 deg. F. on the 12th. On the 13th the temperature came down to normal and she has had no fever since. (1910).





Case IX Atul, aged 9 years, was admitted on the 12th of February 1909. Had had fever since the 31st of January which did not yield to quinine.

Spleen had become rapidly enlarged till it reached to the umbilicus at the time of admission. On auscultation of the chest points of dulness were formed at both bases with rales which decreased on passing upwards.

Injections were given hypodermically of Bihydrochlorate of Quinine, which caused a good deal of pain.

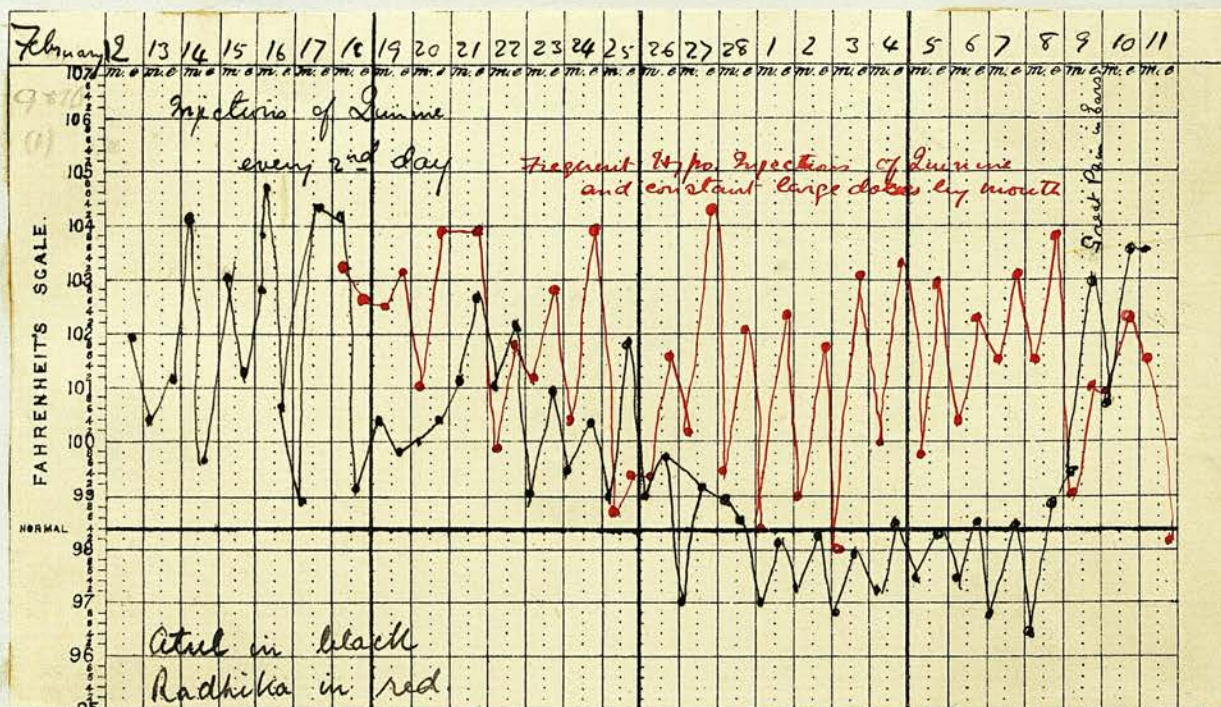
The temperature became normal on the 1st of March and remained so till the 8th of March when the temperature suddenly rose, accompanied by great pain in the middle ear. Fever lasted till the 28th of March when the temperature became normal. There has been no fever since. The photo of Case IX was taken 18 months after patient was discharged from hospital.

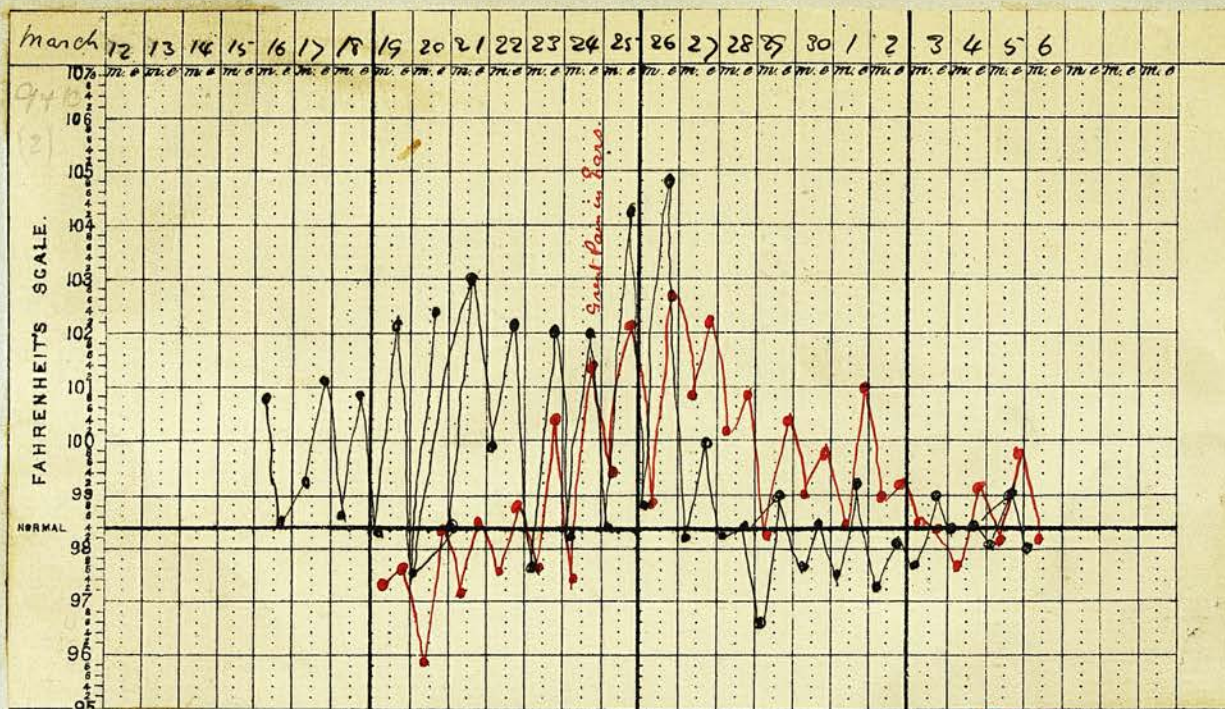
Temperature chart is given.

The coincidence of the disease in onset and course is striking in this and the next case.

Case X Radhika, aged 4 years, brother of Atul. Admitted on February 17th.

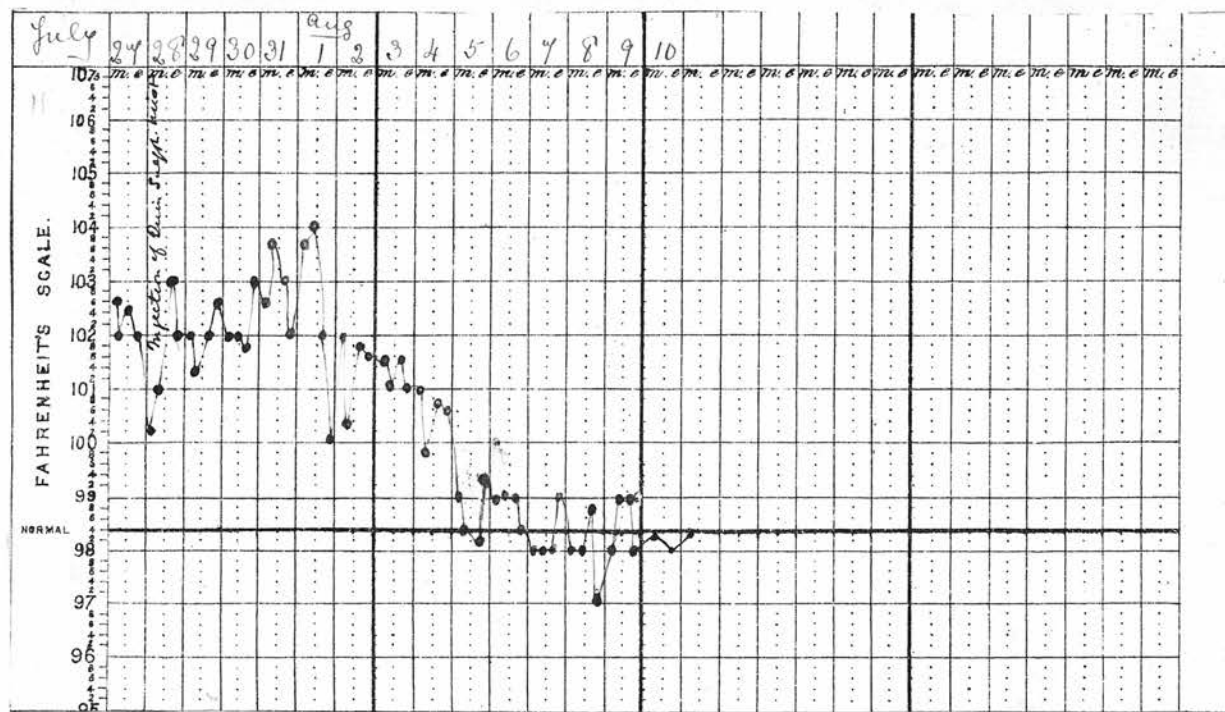
Treated with hypodermic injections of Quinine without much effect. Great pain in ears developed on the 24th of March followed by cessation of fever shortly after. Charts of Atul and Radhika below.





Case XI Gour, aged 12, admitted on July 27th. Spleen at time of admission extended to about one inch beyond the umbilicus. Liver enlarged to two inches below the ribs in the right nipple line. An injection of m 30 of quinine sulph. mixture was given hypodermically on the 28th of July, which was followed by considerable local pain. The temperature soon became reduced and became normal on August 10th. Temperature remained normal till he left hospital, when both spleen and liver were very much diminished in size.

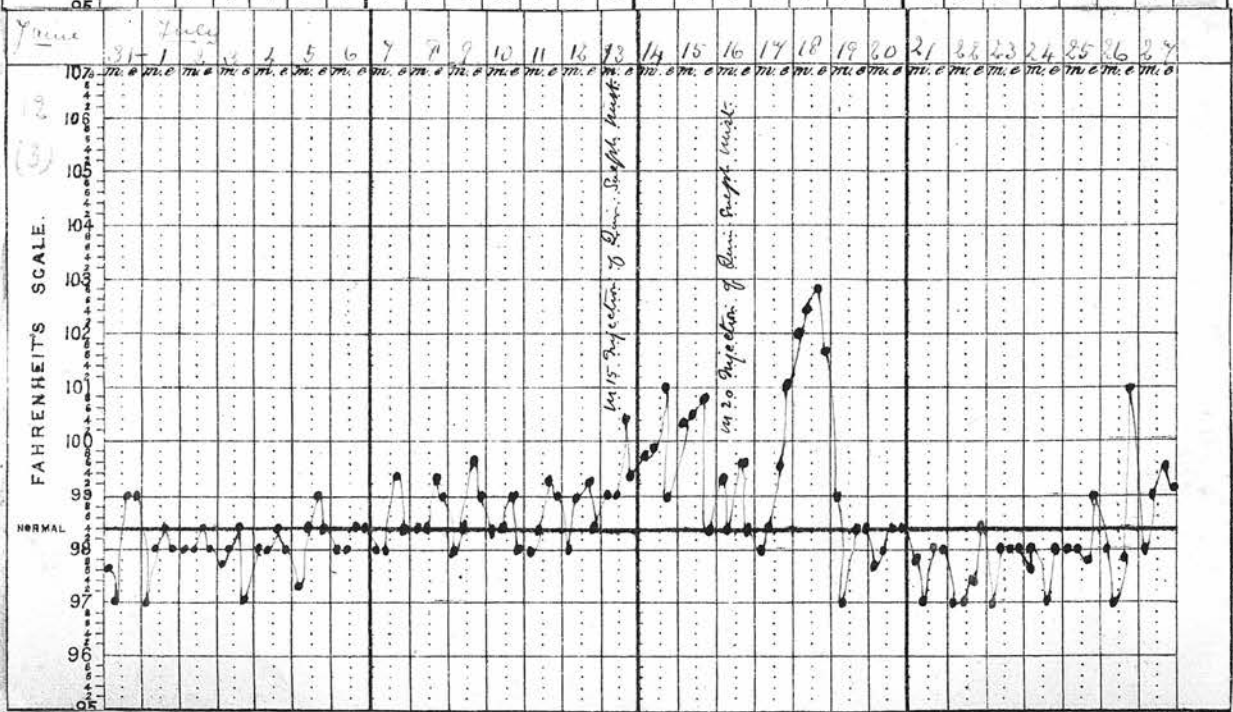
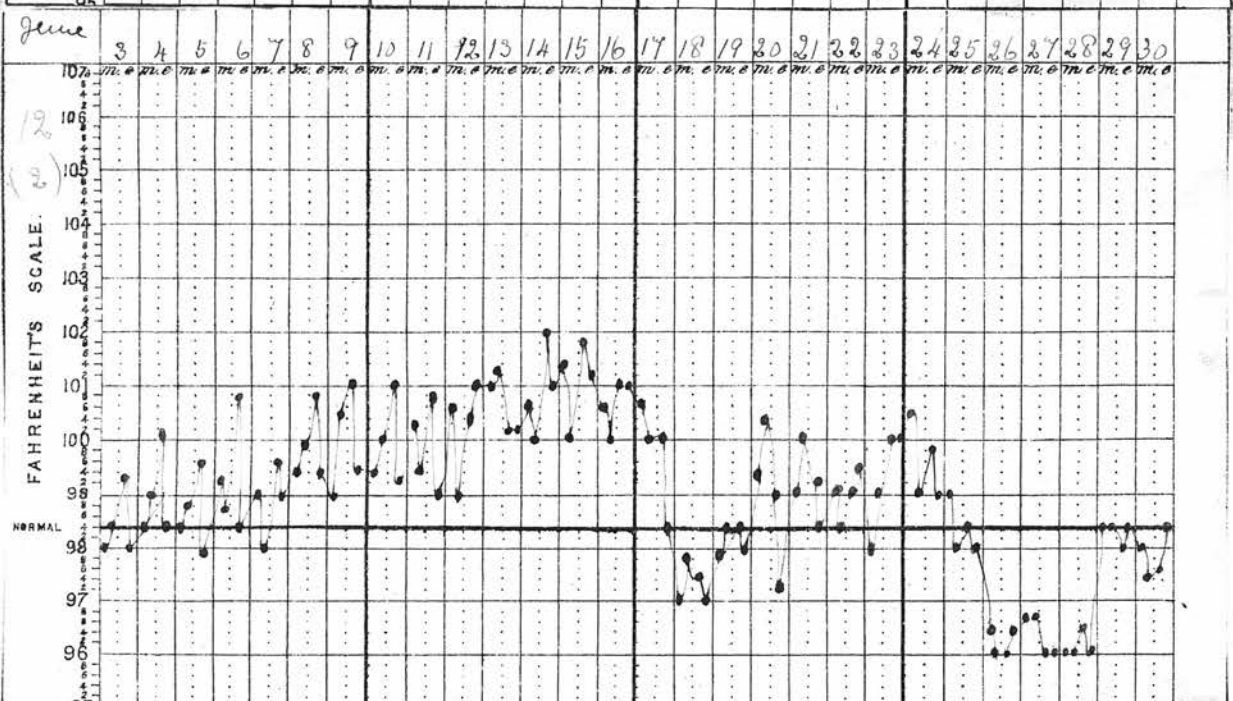
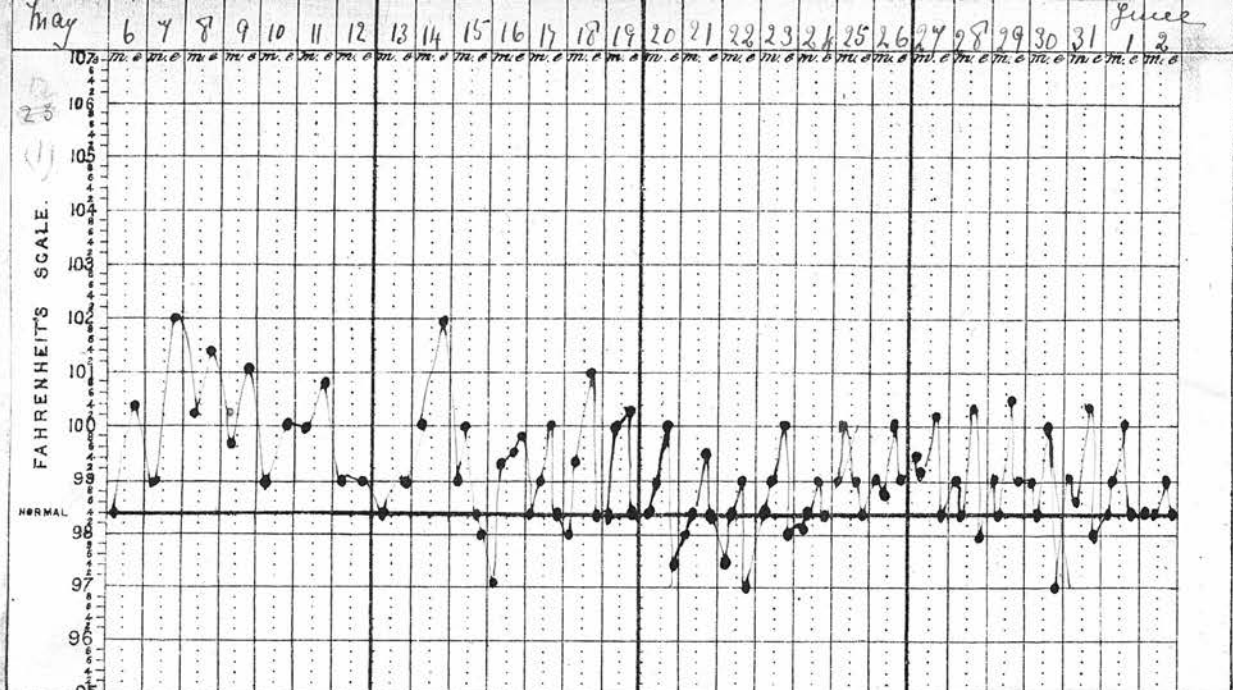
Patient was very constipated, the motions being clay coloured. Photo taken about time of admission.

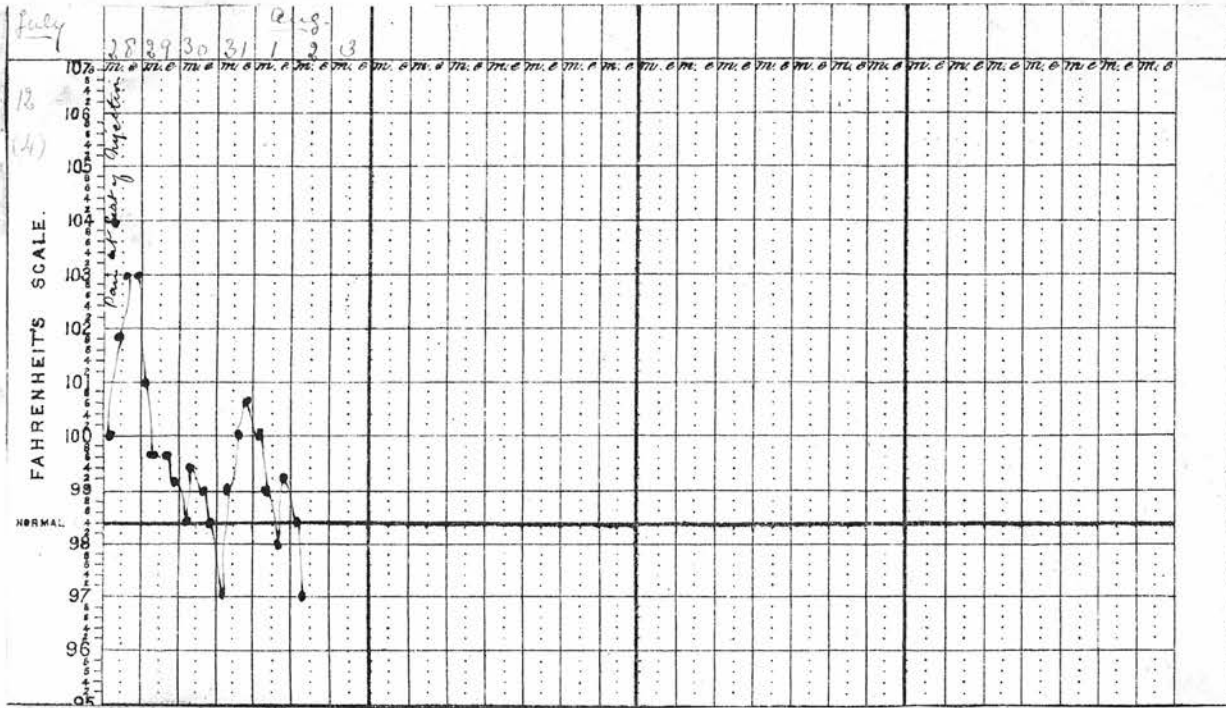


Case XII Jacob, aged 6 years. Admitted on May 6th.

Had a low temperature, irregular. Had severe dysentery, which after some time yielded to treatment with Castor Oil Emulsion. Spleen on admission reached to near the umbilicus. Injections of Quinine sulph. mixture m 15, were given on the 13th of July and again m 20 on the 17th of July.

The temperature rose rapidly on the 18th of July to 103 and became normal again on the 19th. It rose again on the 26th, when an abscess formed, and remained low after the 1st of August. He has had no more fever since the beginning of August. Photo was taken after patient had been about two months in hospital. Temperature charts given in full.





Case XIII Poteshwari, aged 8 years. Admitted on the 20th of December.

History of fever first when 3 years old. During these five years there had been fever from time to time. Fever had been worse for the last two months. Fever was always worst at night. There had never been any ague. Spleen was enlarged since patient was three years old.

On admission spleen and liver were very much enlarged.

In the blood taken by splenic puncture I found numerous Leishman-Donovan-Bodies, division forms in groups of 2, 4, 6, 8, and 9 being very many. A differential leucocyte count gave only 15 per cent of Polymorphonuclear neutrophiles, the rest being basophile. An injection of Quin. Sulp. mixture m 40 was given on the 22nd. Temperature reached the normal on the 24th when patient left hospital as the mother was needed urgently at home. An illustration of some forms found in this blood has been given.

Case XIV Bhanta, aged 11 years. Admitted November 30th 1909.

Liver and spleen were both very much enlarged, but especially the liver as is seen in the photograph marked "Case XIV." There had been a history of continuous fever for twelve months. On admission liver was 4 inches below the ribs in the nipple line. The spleen was 3 inches below the subcostal margin in the left nipple line. The motions were slightly hard but well-coloured. The blood from a liver puncture was examined on the day of admission, Leishman-Donovan-Bodies were found and a differential

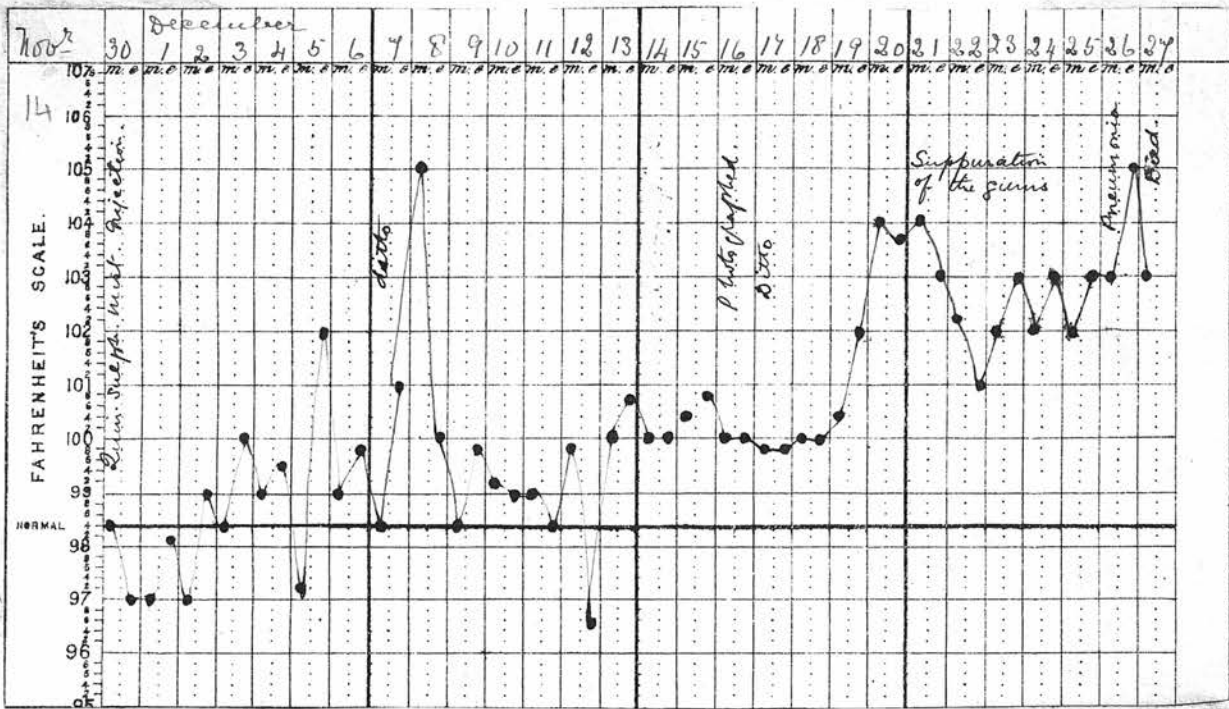
leucocyte count was got of polymorphonuclear neutrophiles 59 per %  
 Basophiles 41 " %

A hypodermic injection of 30 m of Quin. Sulp. Mixture was given on November 30th and again on December 7th.

The second injection was followed by a rapid rise of temperature for 24 hours after which it subsided to a maximum of 100 degrees F., but the spleen became considerably smaller (as shown in photo).

The liver also became slightly smaller. On the 17th he had another similar injection. On the 20th his gums began to swell as did also the glands of the neck, while the spleen became rapidly smaller. On December 26th he began to develop pneumonia and died on the 27th. At the time of death the spleen had shrunk to half its original size and the liver was considerably smaller.

In the photographs the markings on the abdomen indicate the size of the spleen and liver below the ribs on the 14th of December. The wider circle round the spleen indicates the size of the spleen on admission a fortnight before. Temperature chart given.



Case XV Bolai, aged 10 years.

History of 6 months fever before admission. Admitted on December 14th 1909. Was treated as an outpatient for 3 weeks before admission. On November 26th an injection of m 30 of Quin. Sulp. mixture was given hypodermically.

The blood from a splenic puncture was examined on December 16th. Leishman-Donovan-Bodies were found swarming in every field of the microscope, some of them single, but most of them in groups of 2, 4, 6 and 8 and many in a state of partial division. The spleen on admission extended to 1½ inches beyond the umbilicus and to 3 inches below the ribs in the left nipple line.

The patient was given an injection of quinine sulph. mixture upon admission, which caused slight reduction in the size of the spleen, as seen in the photographs taken on the 16th instant by the inner of the two spleen markings.

Shortly after admission patient began to have considerable swelling of the gums with discharge of pus from between the gums and the teeth. There was also considerable painful inflammation of the glands of the neck. This was followed by a high night

temperature while it lasted, but whenever it subsided the temperature became normal.

Due to my being away for six weeks injections were not given during that time, but the patient was treated with cinchona alkaloids and iron. On the 14th of February I again took a splenic puncture. Leishman-Donovan-Bodies were almost all single and far fewer in number. On patient's admission the relative count of leucocytes had given only 4 per cent of polymorpho neutrophiles; it now gave 22 per cent.

The spleen was however very nearly the same size as upon admission.

Case XVI Dashi, aged 27, female. Admitted on November 25th 1909. History of 6 months fever.

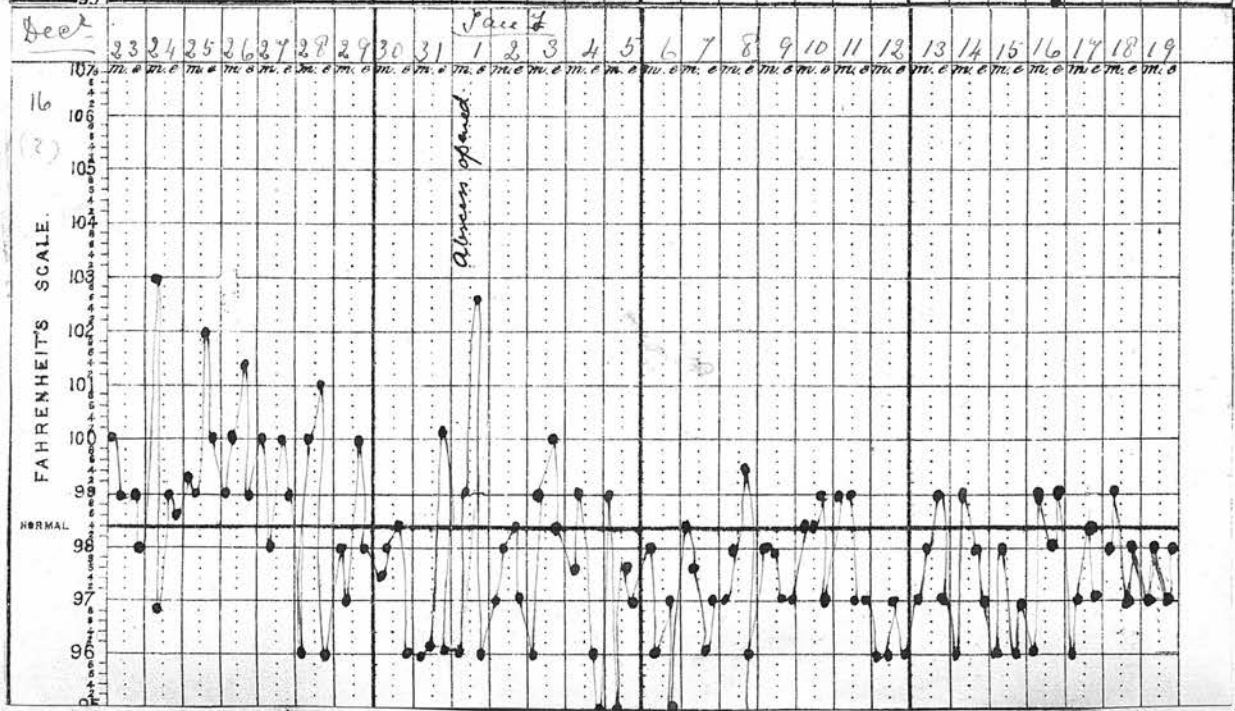
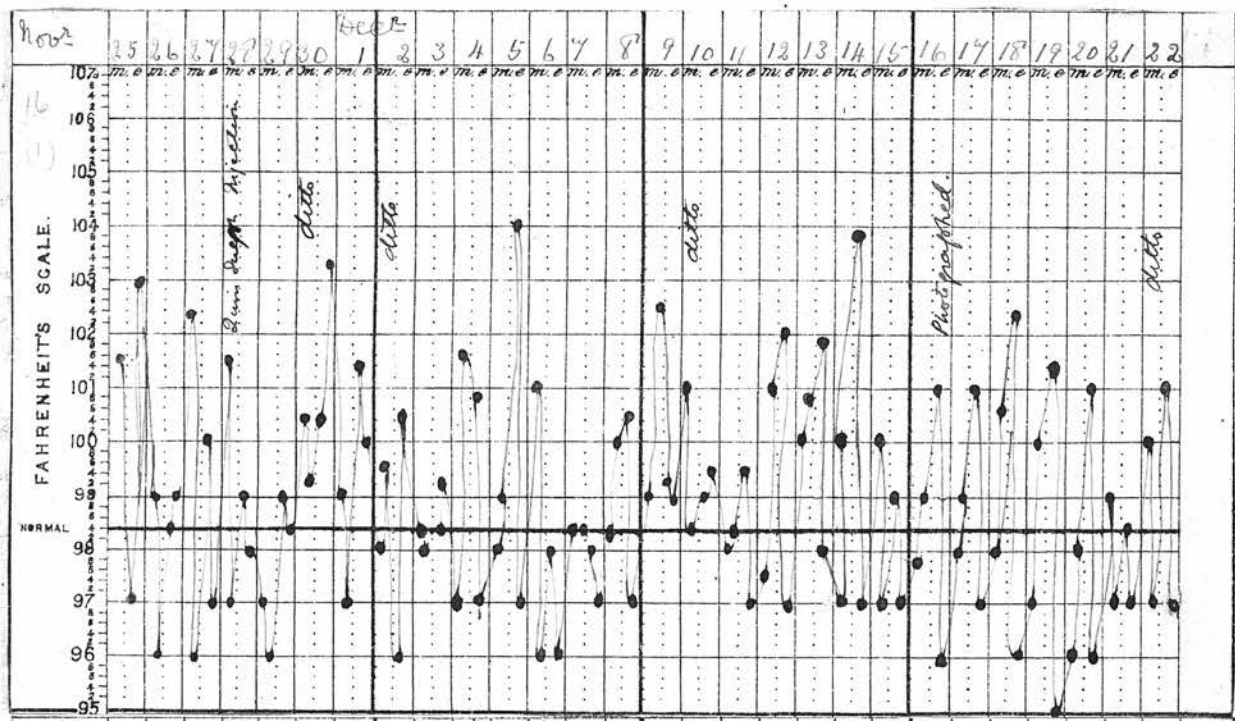
Spleen on admission extended to 3 inches below the ribs in the left nipple line. The fibres taken from a spleen puncture at admission showed Leishman-Donovan-Bodies in abundance.

The differential leucocyte count gave only 9 per cent of polymorpho-neutrophile leucocytes, the rest being basophiles and degenerate forms.

She was treated at intervals with injections of Quin. Sulp. mixture with the result that an abscess formed in the posterior fold of the axilla, which was opened on the 26th of January. The spleen became rapidly smaller as did also the liver.

The diminution of size in these organs is shown in the photograph which was taken on the 16th of December. The diminution of size in the spleen was much more rapid however during the

presence of the abscess. After the opening of the abscess the temperature remained normal till the patient left hospital on January 26th, with the exception of occasional slight rises to 99°. On January 6th another spleen puncture was taken. There were still abundant Leishman-Donovan-Bodies but the proportion of polymorphs had risen to 30 per cent.



Case XVII Bijay, aged 5 years. Admitted on September 22nd 1908.

History of 6 months fever before admission. Frequent injections of quin. sulph. mixture were given with the result that two abscesses formed consecutively in his two gluteal regions.

These were accompanied by very rapid diminution in the size of the spleen and patient began to put on weight rapidly. The two photographs taken at the time of admission and after he was cured show better than any description the completeness of the cure. As the patient lives only a few hundred yards from here I have plenty of opportunity for observing that there is no return of the disease.

Patient is as well as he was when the second photo was taken at the time of writing, viz :- February 1910.

Case XVIII Karuna, aged 13 years. I was called out to see patient who had been two days or probably longer in labour. I found the head impacted in the pelvis and delivered a dead child with forceps.

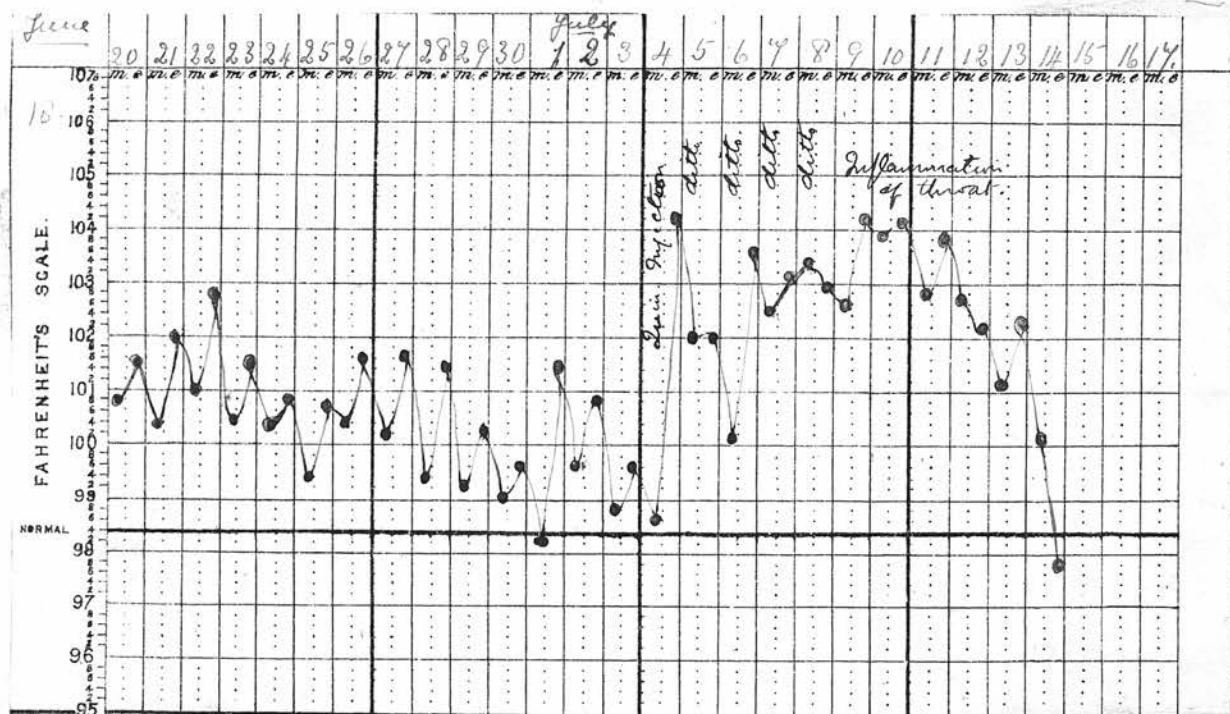
There was a history of fever previously for two months.

After delivery there was at first fever due to the septic condition of the vagina, caused by the usual interference of native midwives previous to my being called in.

This rapidly subsided as the wounds became clean with douching. The patient was brought into the hospital the day after delivery. On the 4th of July her temperature became normal in the morning, but in the afternoon of that day the liver began to enlarge as did also the spleen. The liver in a couple of days

reached to  $2\frac{1}{2}$  inches below the costal margin. The spleen which could not be palpated before below the ribs enlarged rapidly till it was within two inches of the umbilicus. At the same time the temperature went up to  $104^{\circ}$ . There was nothing to account for the fever in the region of the vagina. Injections of bihydrochlorate of Quinine were given daily.

On the 10th and 11th the throat became swollen and tender but quickly healed up again. As the throat healed the temperature fell rapidly to normal and did not rise again. As the throat became swollen the liver and spleen began to rapidly decrease in size again. Chart given.



Case XIX Charan , aged 20.

When admitted, patient had a spleen extending to about one inch from the umbilicus. He informed me however that his spleen had filled almost the whole abdomen but was rapidly diminishing in size.

Patient when admitted had a large sloughing wound of the right cheek communicating under the zygomatic arch with the cavity of the mouth.

After admission the wound continued to slough for about 3 weeks when it had reached from the right ear forward to the outer canthus of the right eye. The right eye became destroyed and there was a dangerous bleeding due to ulceration into a vein on the inner side of the wound.

The wound gradually became clean and there was no more fever.

The patient then insisted upon going home for three weeks, during which time his legs became so bent at the knees and fixed by fibrous contraction that his tibiae and femora were parallel to each other. On the patient's return slow extension gradually straightened the limbs. By this time the spleen could not be palpated under the ribs. The mouth was so fixed by fibrous contraction of the wound on the face that patient could not open his mouth more than one inch. Both the Kala Azar and the wound on the face were cured, but the patient seemed so much reduced that he could not regain strength and he died shortly after.

Possibly if we could have supplied him with better nursing he might have recovered.

The photograph shows patient about the time of admission to hospital. Internal medicinal treatment consisted of cinchona, iron, arsenic and nux vomica.

Case XX Panchu, aged 6.

Was treated by me two years ago for inflammation anterior to the hip-joint. An incision was made but no pus could be found. The leg which was bent at the hip joint was extended and kept straight by a special splint for about two months. After this the patient was able to walk about, the leg showing no more tendency to flexion and the pain having entirely disappeared.

No further trouble ensued in connection with his leg. On admission to hospital again two years after this, the patient had an enlarged spleen which however gradually disappeared. He had had a history of continuous fever for about a month, but this had disappeared after the incision was made in front of the hip. After the leg was healed however the low fever very soon began again and the spleen began again to enlarge. He was treated for this as an out-patient with cinchona, etc., but was only brought at very irregular intervals. After about a year or more of this fever patient was brought in the end of January in a very much reduced condition.

The spleen extended on his admission to beyond the umbilicus. Injections of turpentine were made in his back but the reaction to them was not very marked. On February 15th I took a splenic puncture. Leishman-Donovan-Bodies were found, but not any double forms. The proportion of polymorpho neutrophiles was

7%. Numerous division forms of leucocytes were formed as shown in the illustration on page 2. Some of the basophiles took on much deeper stains than others. Some of the basophiles were vacuolated and others contained granules of a deep purple colour.

Bodies which took on a light blue colour were also found some of them containing a dark purple body like a nucleus. Degenerate forms of leucocytes were also found, marked j in the illustration..

Case XXI Panchugopal, aged 25.

I was called out to see him at a village about 10 miles away and found patient very thin and weak with ascites and swelling of the legs. After removing 400 ounces of fluid with the trocar and canula, I found that the spleen was enlarged almost to the umbilicus.

I sewed up the wound with a purse-string suture and ordered cinchona, iron and arsenic and digitalis mixture and left with the patient a large quantity of magnesium sulphate<sup>half</sup>, telling him to take sufficient to produce 5 or 6 motions a day. I also ordered him to take about 4 pints of milk a day. I was called back almost a fortnight later and found the patient stronger and able to sit up. This time I removed about 200 ounces of fluid and continued the same internal treatment. The site of the first trocar had slightly supplicated externally. The spleen was smaller.

After another 3 weeks I again removed a small quantity of fluid. The patient by this time was able to stand up. I

continued the same treatment internally as before. The spleen had almost disappeared. There had been slight suppuration at the 2nd trocar wound also. The next I saw of the patient was about 6 weeks later when he was able to come and see me himself.

Since then there has been no return of fever, spleen or ascites and the patient is stout and strong and able to do heavy farming work. There was no albumen in his urine.

Case XXII Phatik, aged 18. Admitted on December 3rd 1909. On admission spleen extended to beyond the umbilicus. On taking a spleen puncture numbers of Leishman-Donovan-Bodies were found.

Differential leucocyte count gave :-

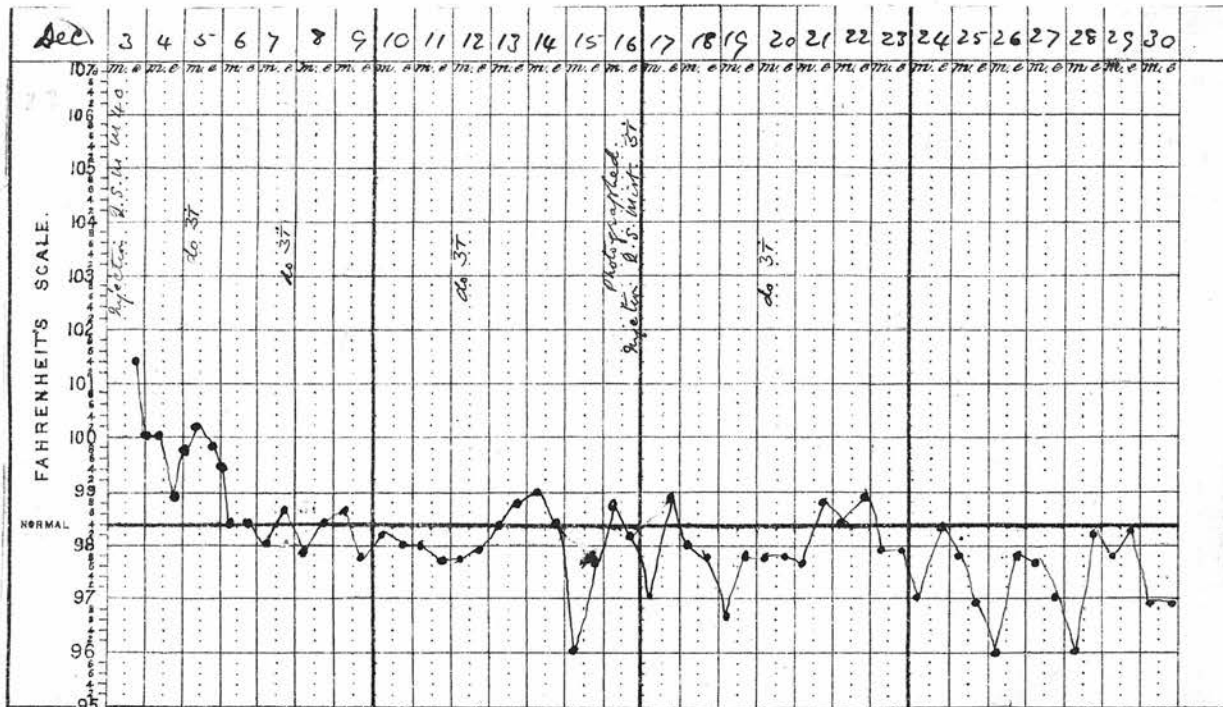
Degenerate leucocytes	16 per cent
Polymorpho neutrophiles	15 " "
Mononuclears basophiles	38 " "
Lymphocytes	31 " "

Under frequent injections of quinine sulph. mixture the temperature became normal. The spleen became smaller as is indicated in the photo taken in December 16th. The liver was scarcely enlarged at all from the first.

Patient continued in hospital for 4 weeks and left with the spleen very much reduced in size and the temperature continuing normal.

He was advised to stay longer but refused. I have heard that he has had a return of the fever since leaving hospital. In the chart the temperature though subnormal is irregular in its

rise and fall, an indication that the disease though subdued is not entirely eradicated.



Case XXIII Bhupan, aged 3, the son of one of our employees developed a very large liver and spleen. Frequent injections of quinine bihydrochlorate were given, some of which caused considerable local irritation and an abscess formed at the site of one of them. About the same time suppuration formed at the root of one of the teeth of the lower jaw. This was followed by necrosis of about an inch of the jaw.

During these two septic processes the spleen and liver rapidly decreased in size and when at last the suppuration in the mouth ceased the temperature became normal. The boy was sent to another part of Bengal to school where Kala Azar is not prevalent.

Two and a half years have elapsed but there has been no return of the disease.

It should be mentioned in connection with this case that his mother has been suffering from this same disease for some years in its chronic form. She has been treated frequently with cinchona mixture but has not yet entirely recovered, the disease remaining latent and becoming active at times. It is probable that the child received the infection from its mother.

APPENDIX

Since writing this thesis I took the photograph (given below) of some of the patients attending the dispensary at Kalna. The spleens, and, when they were much enlarged, the livers, have been outlined in white.

The duration of the fever, as stated by the patients, has also been marked. These periods are, taking the patients from left to right, and the back row first, :-

- (1) Many Years (he could not tell definitely).
- (2) Four Months.
- (3) ~~XXXXXXXXXX~~ Six Months.
- (4) Seven Years
- (5) Four Months.
- (6) 14 Years
- (7) Six Months
- (8) Two Years
- (9) Two Years
- (10) Six Years.



So it will be seen that, of ten patients with palpable spleens, taken at random, the average of duration was at least three years. Any error that may have been made would be on the side of making the periods appear shorter than they really were.

The boy whose fever had lasted off and on for 14 years has an enormous spleen, but it is considerably smaller than it was formerly. The reduction in size was due to an injection of turpentine, which formed a swelling fluctuating on pressure. When this was opened it was found to contain a small slough and a considerable quantity of blood.

We have been using turpentine hypodermic injections lately with considerable effect, proving that it is the irritation of the injection which has the beneficial result and not the mere absorption of the drug injected.

(2) Two other interesting cases were omitted from the thesis. One is of Lakshman, a sweeper, who had Kala Azar for some months. He was treated with quinine and cinchona by the mouth without being cured entirely. He became very much reduced in strength, and very anaemic. He had several fits of an epileptic nature one day. An injection was given him hypodermically, which produced an abscess. From that day (some two years ago) he has had no return of the fever. His wife also had the same fever. She also recovered on receiving an injection which produced a small abscess on the back, and she has had no return of the fever.

She had a typical attack of typhoid fever in the interval between two attacks of Kala Azar fever.

This patient and his wife came from Chata Nagpur district, where Kala Azar is practically unknown. Those who come to Kalna from such districts are especially liable to Kala Azar.

The other case is of Madhu, whom I had treated for some time for Kala Azar with Cinchona mixture, with the result that the fever was stopped.

I was, some time after, called in to treat him for a sharp attack of typhoid. He recovered from this.

Two weeks after the typhoid fever disappeared, the Kala Azar began again with a rapidly enlarging spleen.

It will be thus seen that Kala Azar has no tendency to either neutralise or to be neutralised by Typhoid fever.

There is a diminution in the number of leucocytes in both diseases.