A T H E S I S

on

S L E E P I N G S I C K N E S S;

Being an Account of the Investigations of the Commission of the Royal Society, in Uganda, the Nile Valley and Sudan, from May 1903 to February 1905.

by

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Introductory.

I was directed by the Government of India in April 1903 to proceed to Uganda to investigate Sleeping Sickness on their behalf, inorder to obtain exact information regarding it, so that measures might be taken to prevent it's gaining an entrance into India. A Commission had just been appointed by the Royal Society for this purpose. The Government of India, through the Secretary of State, asked permission from the Royal Society for me to join the Commission as their Representative. This sanction was given, and I met the Commission in Uganda on 25th May 1903. The Commission was composed of Col David Bruce F.R.S. Dr Nabarro and Myself. We worked together until Aug 1903, when Col Bruce left for England. Dr Nabarro left shortly after. I continued the work alone elaborating and extending the investigations in Uganda until Nov 1904. I then conducted an expedition to Lake Albert and from there down the Nile through the Sudan and Egypt. The object of this expedition was to determine for the Uganda Administration, whether Sleeping Sickness was present on the shores of Lake Albert and if so, to determine exactly the distribution of the disease and the fly on the Lake and down the Nile: and further, for the information of the Government of Egypt, how far, if at all, the fly extended into the territory of

the Sudan; a matter of great practical importance in view of the possible northward spread of the disease into Egypt.

I propose, in this Thesis, to bring forward the results of the work of the Commission. The work done by us up to the time of Col Bruce's departure for England has been published in the Reports of the Sleep-Sickness Commission of the Royal Society No 4, Nov 1903. The investigation, carried on by me until my arrival in England, on leave, in Feby 1905, has formed the subject of a Report, which has been submitted to the Royal Society. The Royal Society having decided to publish this Report, it is now being printed by the Stationery Department at the request of the Royal Society. I had the assistance of Lieut Gray R.A.M.C. in the work from March to Nov 1904, but the investigations were under my direction, and I was entirely responsible for them from the time of Col Bruce's and Dr Nabarro' departure. The Report presented by me to the Royal Society was drawn up by myself. Having thus detailed the work done in conjunction with my Colleagues on the Commission and that done by myself, I shall now, set forth the results of our researches in their entirety and proper sequence.

Since in this Report a good deal of detail will be given, the propositions, that this Thesis brings

forward evidence to prove, may be briefly stated:-

1. That sleeping sickness is caused by the entrance into the tissues of a species of trypanosoma.

2. That this species is, probably, that discovered by Forde and described by Dutton from the West Coast of Africa and called by him the Trypanosoma gambiense.

3. That so-called cases of Trypanosoma Fever from the West Coast are cases of sleeping sickness in the earliest stages.

4. That enlargement of lymphatic glands containing trypanosomes in large numbers is the essential feature of Trypanosoma Fever: sleeping sickness is Trypanosoma Fever with in addition, signs and symptoms due to changes in the nervous system, and the appearance of these symptoms synchronises with the appearance in number of the trypanosomes in the cerebro-spinal fluid.

5. That 70 to 80% of the general population of the sleeping sickness areas of Uganda are in the early stage of the disease.

6. That monkeys are susceptible to sleeping sickness, and show the same symptoms and run the same course, whether the trypanosomes are derived from cases of trypanosoma fever, or from the cerebro-spinal fluid of cases of sleeping sickness. The pathological

changes found in man in cases of sleeping sickness can also be reproduced in monkeys.

7. That dogs, rats and guinea-pigs are partially susceptible, but donkeys, oxen, goats, and sheep have proved absolutely refractory.

8. That the trypanosomes are conveyed from the sick to the healthy by a species of tsetse fly, Glossina palpalis, and possibly certain other varieties of tsetse flies (Glossina pallidipes, morsitans, fusca and longipennis).

9. That the distribution of sleeping sickness and Glossina palpalis correspond.

10. That sleeping sickness has recently infected the fly belt of the Albert Lake and it has spread down the banks of the Nile to Wadelai (about 100 miles); it will continue, under existing circumstances, to spread until it reaches the limit of the fly belt on the Nile.

11. That sleeping sickness is, in short, a human tsetse fly disease, and the lymphatic system is mainly involved.

The stage at which our knowledge of the etiology of this disease in Uganda had reached on the arrival of the Commission was, that the cause of the disease was a streptococcus (CASTELLANI). Whilst searching for this organism in the cerebro-spinal fluid of sleeping sickness cases, Castellani saw, in 5 cases a trypan-

osoma, but, at that time, he was of opinion, that this was an accidental concomitant, like Filaria perstans. Accordingly the Cmmission had to determine, 1) The exact cause of the malady,2) How it was spread from the sick to the healthy. In a Conference held on the 22nd March 1905, between the Royal Society, Colonial and Foreign Offices, the Royal Society, in a Memorandum, held that these facts had been satisfactorily proved by the researches of the Commission in Uganda. This Memorandum was based on the Reports submitted by their Commission on sleeping sickness in Uganda.

2.General description of the Country.

Before commencing to give an account of the investigations, it is desirable to give a brief description of this, comparatively little known, country, in which the disease is working such serious damage. The sleeping sickness areas are, at present, limited to the margins of the great inland Seas, the Victoria and Albert Nyanzas and a part of the Nile valley.

The area of Lake Victoria is, roughly, equal to that of the whole of Scotland. The disease is, at present most severe on it's northern shores and islands, but it also extends along it's Eastern and Western shores into German territory. In the British Protectorate from east to west the Lake is bounded by, a portion of British East Africa, Usoga and Uganda Province

proper. There are numerous islands scattered about its northern end of which the Sesse group is one of the most important.

The Administrative Headquarters of Uganda are at Entebbe, situated on a Peninsula on the northern shore in Uganda Province. The Station is situated above the fly belt. It was here the Commission had it's Laboratory and Hospital built, and this was, also, it's Headquarters, cases being brought in from the sleeping sickness areas as required. The native Capital of the country is at Mengo or Kampala, about 25 miles north of Entebbe. The Equator passes through Entebbe, which stands about 4,500 feet above the level of the sea. At Jinga in the Usoga Province, the Nile takes it's origin, and flows over the Ripon Falls at this point: it continues it's course northwards, and at a place called Fajao it passes over the Murchison Falls and becomes the Victoria Nile. It joins the Nile from the Albert Lake, and the united streams form the river, which flows towards Egypt, as the White Nile. At Khartoum it is joined by the Nile from Abyssinia called the Blue Nile. The united streams flow past Omdourman to Egypt. The Albert Lake forms part of a rift valley which includes Lake Albert Edward, the two being connected by the Semliki River. The Albert Lake is at a lower level than the Victoria, being 2,170 feet.

The waters from this Lake, as already mentioned, join those from the Victoria Lake and flow north.

The vegetation round these Equatorial Lakes is very dense. A common form is the ambatch(Herminiera elaphroxylin). In the sheltered waters large masses of the well-known Sudd (or more correctly Sadd) accumulate. . The Sadd is formed by papyrus clumps becoming detached, and then coming together, forming little groups. Their roots become united below the water by the accretion of water weed and other vegetable substances, and in this way a peaty mass is formed just below the surface, from this the papyrus continues to grow as from a soil. In any question of 'Clearing'— this would be an extremely difficult problem- the removal and keeping down of the Sadd, because it's roots sometimes go 20 feet into the water, and the fringe is often 40 to 50 yards wide, and it accumulates again with great rapidity. As we shall see it is in this dense vegetation near the Lakes that the Glossina palpalis (the transmitter of the parasite of sleeping sickness) is abundantly present.

The geology of this area has not been fully worked out, but it would appear that the Victoria Lake is a large, though shallow, depression, of which the larger of the numerous bays and inlets are , probably,

and in some cases certainly, due to faults. The north of the Lake is fundamentally composed of gneissose rocks, frequently covered with laterite, while deposits of sedimentary rocks occur containing iron deposits in places. Earthquakes are felt not infrequently, and the way the drainage flows, northwards away from the Lake, suggests probable faulting in the neighbourhood.

The natives belong to the Bantu Negroes. Johnston states ''That the present population of Uganda is composed of three main elements. First, the Pygmy-Prognathous type. Second, the West African Negro type, which constitutes the bulk of the population at the present time, and which, no doubt, invaded Uganda in succession to the original Pygmy-Prognathous settlers when the land was mostly covered with great forests. The third element, in the composition of this population, is the Gala herdsman from the north and north east.''

The staple food of the natives is the banana. They, also, eat sweet potatoes and in certain parts a root called Mahogo. They drink a beer made by fermenting the juice of the banana.

Many of the tribes are entirely unclothed, thus exposing them to the bites of insects of all kinds. Some wear a cloth made from the bark of a tree, but this is frequently discarded when working.

The population of Uganda proper is said to be about one million, that of the Province of Unyoro about 110,000. The population is densest at the margin of the Lake. The reason for that is, that the chief trade of the country is conducted on the Lake shores. The canoes (the chief means of communication in the country) bring tobacco &c &c for sale here. Unfortunately, this part of the country is in the tse-tse fly belt, hence the very rapid spread of sleeping sickness. Since the disease commenced in Uganda in 1900, the deaths from sleeping sickness have reached the appalling total of 100,000. At the present time it is about 1,000 per month. This, in a sparsely populated country like Uganda, has had a most disastrous effect. The Government are adopting the wise procedure of being guided in their attempts to combat it, by the results obtained by scientific research. We will proceed to discuss these investigations in detail.

3. The cerebro-spinal fluid of every case of sleeping sickness taken by lumbar puncture during life contains trypanosomes.

The cerebro-spinal fluid was obtained by the following procedure. The patient was placed under chloroform, he was turned on his right side, his legs were well flexed on his thighs and his thighs on his

abdomen. His head was depressed towards his chest. The fore finger of the left hand was then placed on the highest point of the left iliac crest and the thumb on the spinous process, which was on a level with this point. The needle was inserted into the interspace immediately below, and just to the right of the middle line. It was pushed straight home. In sleeping sickness cases the fluid generally came out under considerable pressure. About 20c.c. of the fluid was collected. This was then centrifuged for 20 minutes. The whole of the supernatant fluid was carefully poured off. The sediment was immediately examined under a low power, 150 to 200; Zeiss 16 mm apochromatic objective and No 12 or 18 eyepiece do very well. The sediment contains, occasionally, a few red cells and other cellular elements, which will be referred to later in detail. The trypanosomes may be numerous in the cerebro-spinal fluid, and in some cases can be seen in the uncentrifugalised fluid, but, as a rule, they are scanty and require to be carefully sought for. Every case of sleeping sickness in Uganda, which we have examined (about 150), has shown trypanosomes in the cerebro-spinal fluid.

Other species of these parasites have been carefully worked out, and a good deal is known regarding their morphology. Amongst the best known are, the Trypanosoma lewisi, described, in rats in India, by

Timothy Lewis F.R.S., Army Medical Department, the Trypanosoma brucei, the cause of Nagana in Africa, discovered by Col David Bruce F.R.S. R.A.M.C., the Trypanosoma evansi discovered by Mr Evans of the Veterinary Department of India, and which causes the disease called Surra, which gives rise to a large mortality amongst horses in India; and there are several others described, which produce disease in animals. In addition to those found in warm blooded animals, there are many varieties found in the blood of fish, frogs &c &c. In man, however, this parasite had not been observed until Forde and Dutton, recently, in the blood of a man in the West Coast of Africa discovered it. They did not then, associate the presence of the trypanosome with sleeping sickness. The work of the sleeping sickness Commission in Uganda has, however, been repeated in the West Coast and Congo (where sleeping sickness is endemic), and has been completely confirmed.

In Plate 1. which is a drawing of a number of trypanosomes seen in a film made from the blood of a monkey, injected with the cerebro-spinal fluid from a case of sleeping sickness. The film was stained by Leishman's method. The general characters of the trypanosoma, as described below are depicted.

From the examination of a number of trypanosomes from different cases of sleeping sickness, the following

details of measurement were obtained:-

Length.	Chromatin Dots	Distance of micro-nucleus from posterior end.
μ.	per cent	μ.
21.5	10	0.5
19.0	70	0.2
29.4	10	0.4
26.4	10	1.0
21.8	0	9.25
Av. 21.7	20	9.47

As a study of the plates will show, the parasite posses a micro- and macro-nucleus. The micro-nucleus stains much more deeply than the macro-nucleus by the Romanowsky method. It has been called a centrosoma. From or close to the centrosoma, a deeply stained lime will be seen to take it's origin, this is the thickened margin of a membrane, which is attached to the protoplasm of the parasite, by means of this membrane it is propelled through the fluid. The thickened margin ends in a whip-like process, the flagellum. The small parasite moves with great rapidity in the cerebro-spinal fluid. It has a somewhat eel-like motion. After the cerebro-spinal fluid has been kept outside the body for some ten minutes (at room tempt, 70° to 80° Fah), it comes to rest. It generally moves with it's tail in front, but the reverse is also, frequently, seen. It is customary to call the flagellar end, anterior and the other pos-

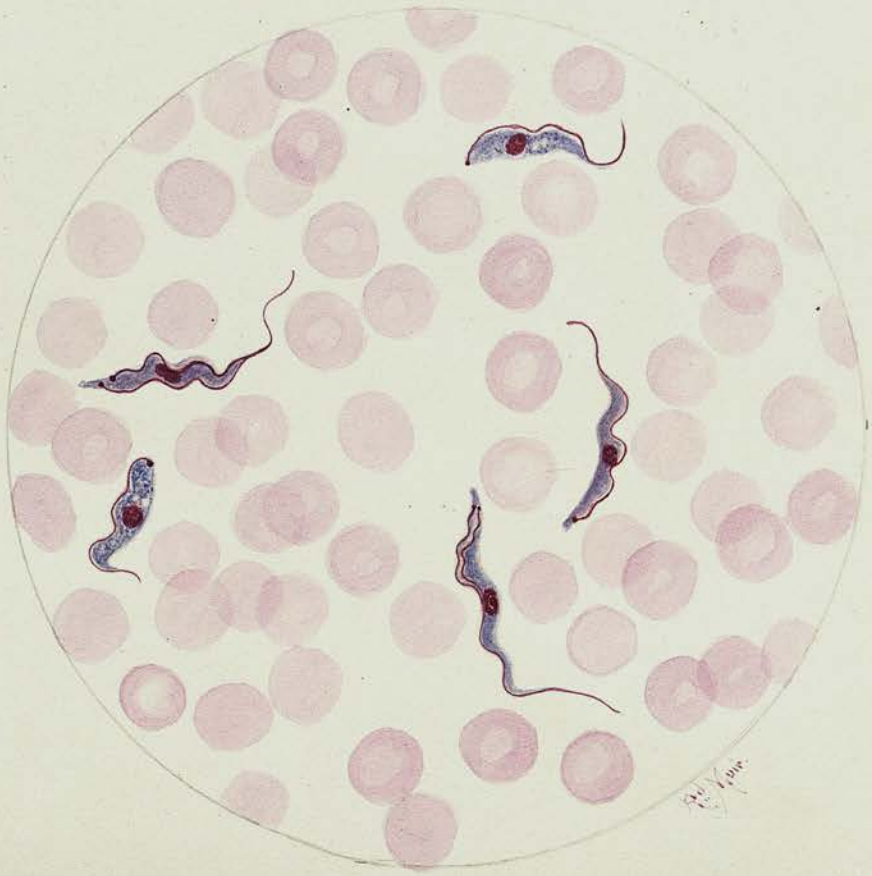


PLATE 1., Film of blood from Monkey (Cercopithecus) inoculated with cerebro-spinal fluid from Sleeping Sickness case. Shows characters of Trypanosoma of Sleeping Sickness, division forms are seen. Stained Leishman's method. × 1,000.

terior. This parasite reproduces itself by simple division, the centrosoma divides and then the membrane splits into two, the nucleus and protoplasm also undergo division. The resulting new forms may remain attached, and in this way rosette formations are produced. No definite sexual reproduction has up to the present been demonstrated in the parasite. Having thus seen that trypanosomes are present in the cerbro-spinal fluid of all cases of sleeping sickness examined at Entebbe, it became necessary to determine, whether cases coming from other districts also showed the parasite.

4. Trypanosomes occur in the cerebro-spinal fluid of cases of sleeping sickness in other districts than Uganda. It will be remembered, that the view held by Sir Patrick Manson, that Filaria perstans was etiologically connected with this disease, was found to be incorrect, because in Kavirondo, where sleeping sickness was very prevalent, Filaria perstans was not found in any of the cases. This might well have been the case with the trypanosoma also; accordingly, a careful investigation of the cases from this area was made. The result of this examination showed, that trypanosomes were present in the cerebro-spinal fluid of all cases examined in Kavirondo. Thus an important question was satisfactorily answered. A further objection might

have been raised, namely, that trypanosomes may, also, be present in the cerebro-spinal fluid of patients suffering from other diseases.

5. The cerebro-spinal fluid of cases of disease other than sleeping sicknes does not contain trypanosomes.

Inorder to control the above observations, the cerebro-spinal fluid of a number of cases suffering from other diseases was examined with negative results in every case. By this observation, we obtained a satisfactory answer to a question of great importance. The next question to be answered was

6. Are trypanosomes present in the peripheral blood of cases of sleeping sickness.

If trypanosomes are present in the cerebro-spinal fluid, it was considered highly probable that, they were, also, present in the blood. The result of our investigations showed, that they were present in every case examined.

They may be , occasionally, found by the examination of a stained film, made from a drop of blood from the finger, but, as a rule, in order to be certain of their presence, it is necessary to get rid of the red blood corpuscles and to use a much larger quantity of blood, 10c.c. of blood is taken from a vein at the bend of the elbow and citrate of potash solution added to prevent clotting. It was thought, at first, that the parasites

would be driven down with the blood corpuscles, but on trial, it was found that the filariae and the trypanosomes resist the centrifugal action. The 10c.c. of blood was centrifugalised for 10 minutes, the clear fluid was pipetted off and again centrifugalised. This procedure was repeated 4 times. The sediment, after each centrifugalising, was examined for the parasite. By this method,the trypanosomes were found in every case of sleeping sickness examined. This examination of the blood is an extremely tedious process,as a simpler and quicker method, the examination of the juice of the lymphatic glands (cervical) is much to be preferred.This leads us to the next proposition

7.Enlargement of lymphatic glands and especially the cervical group is a constant feature of sleeping sickness and trypanosomes are found in number in these glands.

The reason why glandular enlargement occurred so constantly in cases of sleeping sickness had never been satisfactorily explained, although the condition had been recognised for a very long time. Slave dealers in Equatorial Africa were in the habit of feeling the necks of slaves before purchasing them, and rejecting those having marked glandular enlargement. The natives of Uganda,today,will tell you, that they are quite certain that when the glands of the neck enlarge, they will

sooner or later die of sleeping sickness, they then begin to eat up any livestock they may have e.g. goats, chickens &c &c.

Some of these enlarged lymphatic glands were excised, inorder to study their structure and contents, whilst doing so, I found trypanosomes in number in the juice, so much so, that it was perfectly easy to demonstrate them in a small drop of juice removed by a hypodermic needle, thus greatly facilitating the diagnosis of the disease. They are easily seen in the fresh preparation, because their active motion renders the detection easy. Stained preparations show a number of breaking down forms, demonstrating that a destruction of trypanosomes is taking place there. Some structures resembling the Leishman bodies are also seen.

In the perivascular spaces in the brain and other organs in sleeping sickness exactly the same cells are seen, that occur in the enlarged glands in this disease vide Plate 4.

This observation has been of considerable practical importance, because,we are now in a position to recognise a case of sleeping sickness, even in the earliest stage; the enlargement of the glands first arrests attention and the puncture can be made and the diagnosis arrived at in a very short time. By detecting early cases, we may be able to prevent

the infection of 'Clean Fly Belts'.

In order to compare the frequency of the occurrence of the parasite in the peripheral blood and the lymph juice, some 60 cases of sleeping sickness at all stages of the disease were examined. A drop of lymph was taken from the gland by a hypodermic syringe and blown out on a slide and examined fresh. Trypanosomes could always be found after about 5 minutes search. At the same time a drop of blood was taken from the finger of the same case, and a film made on a slide and stained by Romanowsky's method and the whole film examined. The result of this investigation showed that the trypanosomes could, only occasioally, be found in the slide and then only after prolonged searching. We see from this, that the trypanosomes are constantly present in the lymphatic glands in number, whilst in the peripheral blood they are present in very small numbers and only, occasionally, sufficiently numerous to be detected in films.

8. Do trypanosomes occur in the blood of the general population?

Early in the research we were met with a curious problem; cases were admitted suffering from slight fever and enlargement of lymphatic glands, but with none of the nervous phenomena associated with sleeping sickness: on examination of these cases the blood

and, at a later date when the method was known, the lymph juice from the enlarged glands were found to contain trypanosomes. These cases could be explained in one of two ways, as being, either cases in an early stage of the disease (and this proved the correct explanation) or they might have been cases of infection by another variety of trypanosoma.

It will be seen, that at this stage , it was important to make a large number of observations on the population both within and without the sleeping sickness areas, inorder to determine the presence or absence of trypanosomes in the blood of the population of these areas. In June 1903, the Commission, accordingly, commenced and completed this observation. A body of men that we found very suitable for this purpose, was the Hut-Tax labourers, i.e. men who come to Entebbe from all parts of the Protectorate, both from sleeping sickness and non-sleeping sickness areas, and work for one month, inorder to pay off their Hut-Tax, which amounts to R3/- (about 4/-) per head. We were, therefore, able to examine a large number of men, from both areas: I, also, went to Nairobi, in British East Africa, where no sleeping sickness has occured. The final results of the research are shown in the table.

Incidence of Trypanosomes in the blood of general population.

A.- Sleeping Sickness Area.

District.	Number of cases examined. June 1903.	Trypanosomes	Filaria
Sesse.	18	6	13
Bussi.	11	6	10
Busiro.	29	7	6
Mugema.	12	1	4
Kome.	1	0	1
Bugaba.	1	1	1
Sewaia.	1	0	0
Kagera.	1	1	1
Nkumba.	6	1	2
Total	80	23	38

Incidence of Trypanosomes in the blood of the general Population.

B.- Non-Sleeping Sickness Area, Uganda.

District.	Number of cases examined. June 1903.	Trypanosomes	Filaria
Kampala.	4	0	2
Toro.	1	0	0
Makoto.	2	0	0
Jalamba.	2	0	1
Singo.	4	0	0
Buganga.	3	0	0
Nakolia	2	0	1

B.- Non-sleeping sickness Area, Uganda. (cont)

District	Number of cases examined. June 1903	Trypanosomes	Filaria
Kalagalla	1	0	0
Matuntotora.	2	0	0
Kibali.	1	0	0
Kiwangoli.	1	0	0
kikanda.	1	0	0
Bulamwezi	6	0	3
Mawokoto.	12	0	7
Buddu.	6	0	4
Busibika.	6	0	2
Singo.	3	0	2
Unyoro.	10	0	1
Total	67.	0	23

C.- Non-sleeping sickness Area, East Africa

District	Number of cases examined. July 1903	Trypanosomes	Filaria
Nairobi	50	0	0
Grand total	117	0	23

Incidence of lymphatic gland enlargement of the general Population.

D.- Sleeping sickness Area.

Two districts, the Sesse and Kome Islands were examined in June 1904. The result of the examination

showed that the percentage of cases having enlargement of lymphatic glands, especially of cervical glands was very high, about 70%.

Having thus seen that a trypanosoma is present in the blood of a large percentage of the general population of the sleeping sickness areas the question to answer was

9. Is the Trypanosoma the same as that found in Sleeping Sickness cases?

This problem was attacked in the following manner 1) By keeping under observation at Entebbe, away from the fly belt and, therefore, from fresh infection, 5 men (natives), in whose blood the parasite was found, but, at the date of finding them, early in 1903, they presented none of the usual signs of sleep-sickness, and in the cerebro-spinal fluid the trypanosomes were not found. 2) By following the after history of the cases in whose blood we found the trypanosoma in June 1903, and the cases of enlarged glands examined in June 1904. 3) By a study of the morphology of the two parasites and by noting the effects of experimental inoculation in a series of animals.

10. Do cases of Trypanosoma Fever pass into Sleeping Sickness?.

We have had for 2 years under constant observation 5 cases of natives at Entebbe and one European, who contracted the disease in Uganda, is at

present in London under medical supervision. The history of these cases is as follows:- Two of the natives died of Pneumonia in April 1904. In this connection, it is interesting to note that the Drs Cook of the C.M S. Mission Hospital, Mengo, have observed a marked increase in the admission rate to their Hospital for Pneumonia within the last two years, suggesting that Trypanosomiasis lowers the resisting power of the tissues to invasion by the pneumococcus and other bacteria. Of the other cases under observation, two now show undoubted signs of sleeping sickness. With the commencement of these signs, the trypanosomes began to appear in the cerebro-spinal fluid. They were under observation about a year before the signs of sleeping sickness became definite. As these men have never returned to the sleeping sickness areas, all chance of reinfection has been avoided. The remaining case, up to Feby 1905 did not show any definite signs of sleeping sickness.

The European was seen by Col Bruce, in London, in Dec 1904. He was then sick and in the opinion of Col Bruce showed signs characteristic of sleeping sickness.

This case is further of importance, as showing that the white man is not immune to sleeping sickness and compares with the case of the Lady Missionary from the Congo. The results of these important cases are shown in tabular form below:-

Name.	Trypanosomes		Time under observation	Result
	Blood	C.S.F.		
Karala Barigi	+	+	March1903 to April 1904.	Died Pneumonia April 1904.
Bara Risgallah	+	—	ditto.	ditto.
Jordien Murjan	+	+	March 1903, signs of S.S. became marked Aug 1904.	
Tabula	+	+	March 1903 signs became marked about Dec 1904.	
Kumsasaba.	+	—	March 1903.	Apparently well
J.M. (European)	+		April 1903	Probably in early stage of S.S.

In addition to these 6 cases, the after history ofthe men in whose blood we found the trypanosomes in June was investigated a year later. The result of the investigations was very interesting and suggestive, it showed that many of these cases have since died of sleeping sickness, and others were apparently well. This observation supports the view that the condition called Trypanosoma Fever is simply the early stage of sleeping sickness, and that sooner or later, according to the lesser or greater resisting powers of the individual, they will pass into the last stage of the

disease. A common cause of lowered resistance is famine, through failure of the banana crop, which at best forms a poor dietary.

In addition to those cases, which have passed into the last stage of the disease, a certain number appear to be quite well. An interesting question arises Do any of these cases ultimately acquire sufficient immunity to destroy the parasite and recover?. In fact become 'Salted'. The disease, in the light of recent researches, has been too short a time under observation to answer this question. It is not, however, absolutely impossible, that a certain proportion will be found to acquire immunity to the parasite.

From a study of these data, we learn that the early stage is generally a prolonged one. It will be seen that some of the cases have gone on for nearly 2 years from the time the parasite was first detected in the blood and no doubt the patients had harboured the parasites for some considerable time before that examination. In man, it is a matter of difficuty,to determine the exact duration of the disease from the first inoculation, but it may be safely said, that it is a prolonged stage in the majority of cases, probably 2 years and in some cases more. The next question is

11. Can any difference be made out microscopically between the Trypanosoma of sleeping sickness and that of trypanosoma fever?

It was thought at first by us, that the trypanosoma of sleeping sickness was shorter, had more chromatin dots and that the micro-nucleus was situated nearer the end than the other. It was found, however, that on injecting the cerebro-spinal fluid into a monkey the trypanosomes became quite as long as those found in the blood of man, the other differences also disappear. Further very considerable variation in size and shape of the same species of trypanosoma occurs from day to day in the same animal, and even in the same film of blood considerable differences in the morphological features are observed. For these reasons little or no stress can be laid on the morphological characters, as a means of distinguishing the different species of trypanosomes. We, therefore, have to ask

12. Are these trypanosomes pathogenic to animals and can any specific difference be made out between them by animal experiment?

It is unnecessary to give all the experiments in full, but typical experiments will be given, in extenso, to illustrate the effect on Monkeys.

Experiment 1, Monkey, male, Macacus rhesus.

To note the effect of sub-cutaneous injection of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness.

March 23 1903. Injected 10c.c. of cerebro-spinal

fluid taken P.M. from Case 18 Kaperi, under the skin of the left side of the monkey.

May 11. As the injection of cerebro-spinal fluid on March 23 has not given positive results, this monkey was again injected under the skin with 2c.c. of cerebro-spinal fluid from Case 41 Warosansa.

May 28. The trypanosomes were found in the blood for the first time. This is evidently due to the second injection 17 days ago.

June 3. This monkey has been ill for the past week and has gradually been growing thinner and weaker. This afternoon he had a convulsive seizure, affecting the right side more than the left, he has clonic spasms of the right arm and leg, with twitchings of the face and eyes.

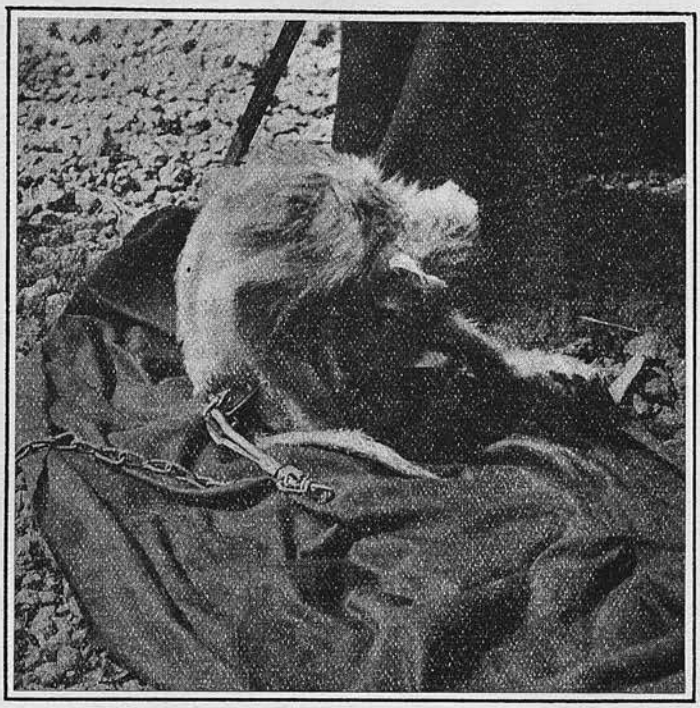
June 4 The trypanosomes are numerous in the blood. His condition has considerably improved. There is no sign of paralysis. The right knee jerk is diminished. He is able to climb into his box.

June 11. The trypanosomes are still more numerous to-day.

June 18. The trypanosomes are scanty.

June 23. During the last 10 days the monkey has shown symptoms of sleeping sickness. He sits all day with his head sunk on his chest evidently asleep.

The following photograph shows his appearance at this time:-

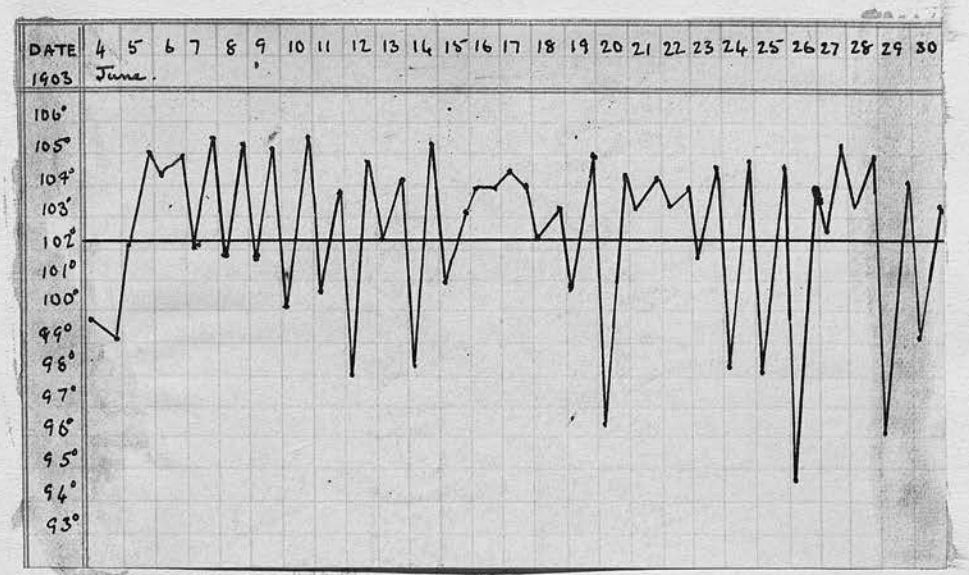


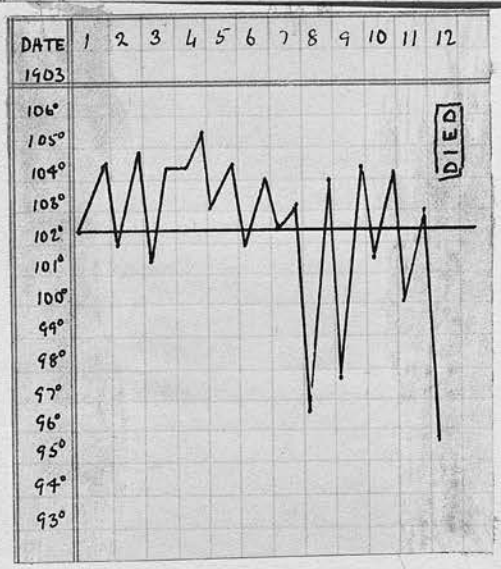
July 10. Since the last entry the appearance of sleep-sickness has become more marked. The animal sits still all day with eyes closed and head sunk on chest. He is extremely emaciated, but has no marked signs of paresis. He can still climb into his box. As he sits in this lethargic condition the muscles of the arm and trunk frequently show marked twitching, a symptom often seen in the last stages of sleeping sickness.

July 12 Died at 11.30 A.M.

The following chart represents the temperature curve from June 4 to July 12. From March 24 to May 23 the temperature remained absolutely normal. No observations

were made from May 24 to June 3.





The following table shows the presence or absence of trypanosomes in the blood:-

Date	Parasites in the blood.		
	Filaria	Malaria	Trypanosomes.
1903 April 7.....		—	—
,, 8		—	—
,, 9		—	—
,, 11		—	—
,			

Table (cont)

Date	Parasites in the blood		
	Filaria	Malaria	Trypanosomes
1903.			
April 14		—	—
,, 22	—	—	—
,, 30	—	—	—
May 7		—	—
,, 14		—	—
,, 21		—	—
,, 28		—	+
June 4		—	+
,, 11		—	+
,, 18		—	+
,, 25		—	+
July 1		—	+
,, 10.		—	+

Post-mortem. Immediately after death. The body is extremely emaciated. There is an ulcer in the right groin about the size of a shilling. The inguinal and axillary glands are enlarged. The mucous membranes are pale. The right pupil is dilated, the left is normal.

On opening the body the omentum is seen to be studded thickly with hard tubercular nudules, and the surface of the liver and lungs are also seen to be tubercular.

On removing the calvarium the dura mater is found to be healthy. On the surface of the left hemisphere

is seen a caseous mass the size of a bean, which is adherent to the dura mater and evidenfly tuberculous in origin. The surface of the brain is pale in colour and the vessels only slightly injected.

Microscopical examination of the blood from the heart showed numercus trypanosomes.

Remarks.-During life this animal presented the appearance of a typical sleeping sickness case. Even in the act of eating, his eyes would close and his head fall forward on his chest, and he would sit apparently scund asleep. Itwas disappointing to find on post-mortem examination that the animal was tubercular.

This case when placed beside Ex 60 (vide below) and the two are compared, it will be agreed that this monkey owed it's symptoms to the trypanosomes and not the tubercle. Compare also Exs 34, 95, 96, 54. This monkey was brought from England, these monkeys (Macacus) do not harbour the malaria parasites, as the local ones do (Cercopithecus).

Experiment 34,Monkey, male, Macacus rhesus.
To note the effect of injecting the cerebro-spinal fluid from a case of sleeping sickness into the vertebral canal of a monkey.
April 8 1903. Injected 1 c.c. of cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness into the spinal canal of this monkey.

This experiment ran a very similar course to

Ex 1. The animal died on Sept 10 1903. The P.M. showed no tubercle.

Experiment 95. Monkey Cercopithecus sp.

To note the effect of injecting cerebro-spinal fluid from a case of sleeping sickness into the vertebral canal of a monkey. This experiment was in all respects similar to the above.

Experiment 54. Monkey, Cercopithecus sp.

To note the effect of injection of cerebro-spinal fluid from a case of sleeping sickness into the brain cavity of a monkey. The trypanosomes appeared in the blood of this animal on the 29th day and the disease ran a course similar to Ex 1.

The above experiments have dealt with the effects of the injection of cerebro-spinal fluid containing trypanosomes into monkeys.

The following experiments deal with the effect of injection into monkeys of blood containing trypanosomes from cases showing no symptoms of sleeping sickness.

Experiment 60.- Monkey, Macacus rhesus.

To note the effect of the subcutaneous injection of blood from a case of trypanosoma fever.

April 15 Injected subcutaneously 2c.c. of blood containing trypanosomes from Case 66, Tabula, Marine.

May 7. Trypanosomes appeared in the blood for the first

time today, 22 days after injection.

May 14. The trypanosomes are noted as being very numerous.

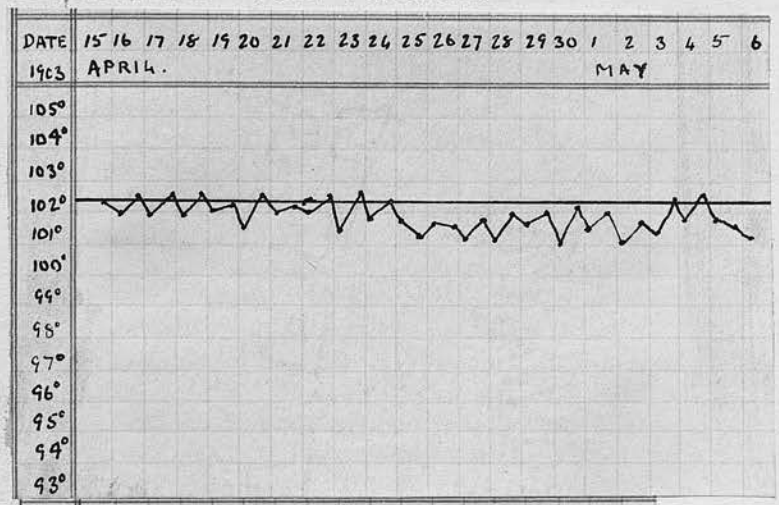
July 2. Up to the present this monkey has shown no signs of being ill. Today, however, he appears listless and less energetic. Temperature observations resumed.

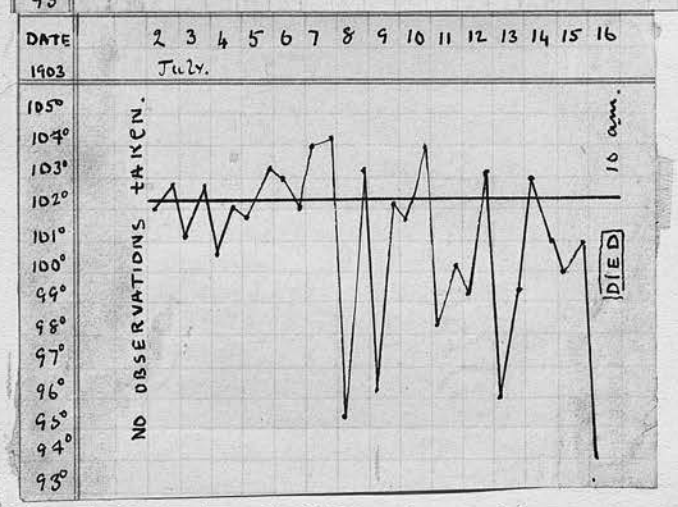
July 15. For the last fortnight, this monkey has presented the same picture of sleeping sickness as noted in Experiment 1, monkey. He sits about all day with his head sunk on his chest, evidently asleep. He has become emaciated and puffy about the face.

The following photograph shows his appearance at this time:-

The following chart represents the temperature curve. From April 15 to May 6 the temperature remained normal.

No observations were made from May 6 to July 2, when observations were resumed:-





The following table shows the presence or absence of trypanosomes in the blood and cerebro-spinal fluid:-

Date	Parasites in blood.			Parasites in C.S.F.	
	Filaria	Malaria	Trypan.	Filaria	Trypanosoma
1903.					
Ap 15	—	—			
,,23	—	—	—		
,, 30		—	+		
May 7		—	+		
,, 14		—	+		
,, 21		—	+		
,,28		—	+		

Table (cont)

Date 1903	Parasites in blood.			Parasites in C.S.F.	
	Filaria	Malaria	Tryp	Filaria	Trypanosoma
June 4		—	+		
,, 11		—	+		
,, 20		—	+		
,, 25		—	+		
July 1		—	+		
,, 16		—	+		+

July 16. Died at 10 A.M. Post-mortem at once.

The body is much emaciated. The pupils are equal and normal. The axillary and inguinal glands are enlarged. On opening the body there is no increase of the fluid in the peritoneal, pericardial or pleural cavities. There are no signs of tubercle in the mesentery, spleen, liver or lungs.

On removing the calvarium, the dura mater is found to be normal. On reflecting this membrane the surface of the brain presents a striking resemblance to that found in man in cases of sleeping sickness. The convolutions are flattened; there is some injection of the superficial vessels; the sub-archnoid fluid is in excess, filling up the sulci and giving them the ground glass appearance so often described in cases of sleeping sickness. Fluid taken from the lateral ventricles and examined microscopically shows trypanosomes. The brain was removed entire for future minute examination.

The heart, is normal in appearance. Blood taken from it and examined microscopically shows many living trypanosomes, many of which present peculiar forms.
The lungs, show no signs of tuberculosis. They are somewhat congested, otherwise normal.
The liver, is congested and presents a nutmeg appearance.
The spleen, is congested, dark in colour and firm in consistence.
The kidneys, are normal. The intestines appear healthy and present nothing noteworthy macroscopically.
Remarks.- This is a noteworthy case and should be compared with monkey Experiment 1. As far as one could judge this animal presented the typical appearance of sleeping sickness during life, and the brain after death looked like the usual sleeping sickness brain in miniature. The organs showed no signs of disease, so that one is bound to look upon the injected trypanosomes as the cause of death. But the trypanosomes, which were injected into this monkey, were taken from the blood of a case of trypanosoma fever, from Case 66, Tabula.
The trypanosomes although injected subcutaneously, have found their way into the cerebro-spinal fluid, and given rise to symptoms which closely resemble those of sleeping sickness in man.

This result is certainly suggestive and in our opinion, goes far to prove that we are dealing with one species of trypanosoma, and that Tabula and others are

are in the incipient stage of sleeping sickness.

The following additional experiments were done with the blood from cases of trypanosoma fever, and the general features presented were in all respects similar to the above described experiments.

Ex 56 - Monkey, Cercopithecus sp.

To note the effect of injection into the vertebral canal of blood containing trypanosomes from Case, 66 Tabula. Trypanosomes appeared in the blood of this monkey 10 days after the injection.

Ex 61- Monkey, Macacus, rhesus.

To note effect of injection into the vertebral canal of blood containing trypanosomes from Case 66, Tabula. The trypanosomes appeared in the blood of this animal 22 days after the injection. As shewing the prolonged nature of the disease, this was still alive at the end of 1904, the trypanosomes being still present in the blood. This experiment compares with some of the human cases, which are still alive and may acquire sufficient immunity to destroy the parasite and so recover.

Ex 121.- Monkey, Cercopithecus sp.

To note the effect of injection of blood containing trypanosomes from Case 66, Tabula into the brain of a monkey through the foramen magnum.

Ex 123.- Monkey, Cercopithecus sp.

To note effect of injection of blood containing tryp-

anosomes from Case 64, Jordien Murjan, into the brain of a monkey through the foramen magnum.

These experiments on monkeys show that the trypanosomes derived from the cerbro-spinal fluid of sleeping sickness cases and the trypanosomes from the blood of persons showing no signs of sleeping sickness, can both give rise to a chronic and fatal disease in the monkeys, whish bears a striking resemblance, in it's last stages to sleeping sickness in man

The minute examination of the brain of one of our experimental monkeys, injected subcutaneously with cerebro-spinal fluid containing trypanosomes from a case of sleeping sickness, which was sent to Englamd and which died, after an illness of 2 years there, showed exactly the same lesions, which Mott originally described as being found in cases of sleeping sickness in man.

These experiments, therfore, afford strong evidence that the trypanosoma is the cause of sleeping sickness and that trypanosoma fever is an early stage of this disease.

Although we found monkeys the most useful animal for these experiments, we have also used in our experimental work, dogs, jackals, cats, guinea-pigs, rabbits, rats donkeys, oxen, sheep and goats.

Experiments on the effect of the injection of these trypanosomes into dogs.

The native dog of Uganda is not very suitable for experimental purpoeses, as they nearly all harbour ankylostomes and many die of this.

The conclusion arrived at, from a study of the few cases under observation, was that the trypanosomes of sleeping sickness and trypanosoma fever can live and multiply for some time in the blood of the dog, but tend to disappear sooner or later, and that whether derived from cerebro-spinal fluid of sleeping sickness cases or from the blood of cases of trypanosoma fever show no difference in their action in the dog. Also it would seem that the pup is less susceptible than the adult, as the calf is less susceptible to piroplasma, than the grown up cattle.

The disappearance of the trypanosomes from the blood of dogs is interesting and makes the dog the connecting link between the susceptible monkey and the refractory goat &c. This suggests that a percentage of men may, also, be able to destroy the parasite.

Ten experiments were made on dogs and pups. It is unnecessary to give the full details. The results were as above summarised.

Experiments on the effect of the injection of these trypanosomes into cats.

The cat was found to react in a very similar manner to the dog. Both varieties produced the same effect. The trypanosomes developed in the blood and

after a time disappeared. The animal showed no deterioration of health throughout the whole observation. Kittens reacted in a similar way.

Experiments on the effect of the injection of these trypanosomes into guinea-pigs and rabbits.

It was found at first that the injection of cerebro-spinal fluid from sleeping sickness cases or the blood from trypanosoma fever cases, did not produce the disease in animals, but, later, it was discovered that on injecting large quantities of the cerebro-spinal fluid and blood into these animals, that a very slow and chronic disease was induced with both strains.

Three guinea-pigs were injected with cerebro-spinal fluid from sleeping sickness cases and three with blood from trypanosoma fever cases. Three rabbits were injected with the one strain and three with the other strain of trypanosomes, with the above mentioned result, which was exactly the same in both cases.

On the effect of the injection of these trypanosomes into donkeys, oxen, sheep and goats.

All these animals remained completely refractory to both varieties of trypanosomes. they were again inoculated with large quantities of the fluids after long intervals, many active trypanosomes being present in the fluids at the time of injection. In all cases the results were negative, the animals remained quite refractory, and they were kept under observation for

nearly 2 years. This reaction in cattle was interesting because we were able to demonstrate that

13, Other varieties of pathogenic trypanosomes are found in animals in Uganda.

We were asked by the Administration in Aug 1903 to give an opinion on a herd of sick cattle, of which a considerable number had already died. We found in the blood of all the cattle , which were sick, a trypanosoma. This strain was taken to Entebbe and carefully studied and the results of our observations showed, that it was quite different in it's reactions in the same series of animals to the trypanosoma found in sleeping sickness e.g. dogs died in a fortnight with trypanosomes swarming in the blood. It was, probably, Trypanosoma brucei or a closely related species. We called it the Jinga Trypanosoma (after the locality). THe history of these cattle is interesting. They were brought about April 1903 from the foot of the Elgon Mountain, which is a very healthy district, to Jinga: on the march they halted at several places. At one of these near the mouth of the Nzoia river, we, subsequently, discovered a belt of fly, Glossina pallidipes. It was at this point that the cattle became infected and it continued to spread at Jinga, because the Glossina palpalis (which we proved experimentally was able to transmit this variety of trypanosoma) was very abundant

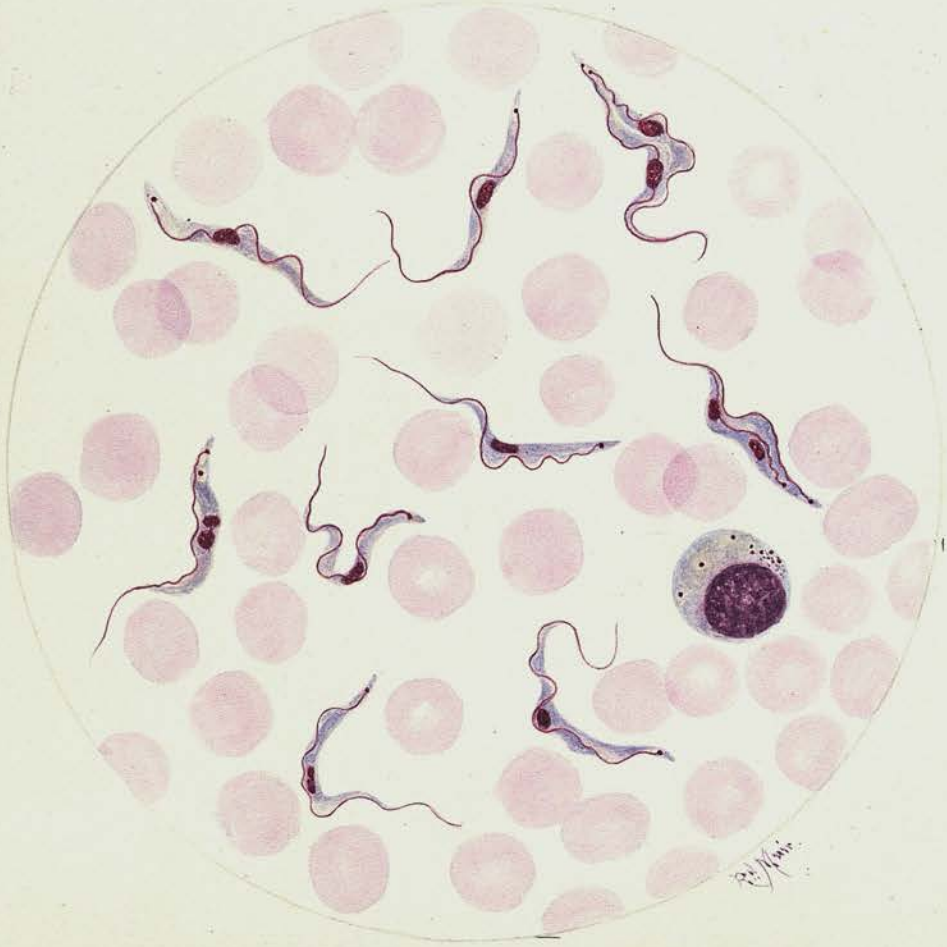


PLATE 2., Film of blood from dog suffering from the Abyssinian Fly Disease. Shows the characters of the Trypanosoma found by us in this disease. ×1,000.

here. In addition to this one, two other varieties of trypanosomes, which also gave rise to disease in animals, were discovered by us. One which produced disease among the mules on the Abyssinian Boundary Commission. The other was found in a sick mule in Uganda. These two latter showed certain variations from the Jinga variety in the reactions in animals, but both are quite different from that of sleeping sickness. It will be seen that we are dealing in Uganda, not only with the human variety of trypanosoma, but also with 3 varieties (1 of which is, probably, Tryp brucei), which give rise to disease in animals. All the varieties are conveyed by the Glossina palpalis, as we were able to show experimentally. Plate 2., shows the Abyssinian variety.

14. The trypanosomes of sleeping sickness and trypanosoma fever are identical.

No difference can be detected either, in their morphology or their behaviour when inoculated into various animals. The evidence brought forward points very strongly to the two varieties of trypanosomes being one and the same and that species is, probably, the Trypanosoma gambiense.

15. Have Bacteria any relation to the etiology of sleeping sickness?

As already mentioned it was held by Castellani that a streptococcus found by him was the cause of

sleeping sickness. This organism was found by him only in the tissues after death or when the patient was dying.

Inorder to test this point, a series of observations were made during life and after death. During life, cultures were made from the lymphatic glands, blood and cerebro-spinal fluid in broth and agar. The result of these observations showed, that in a certain proportion of cases in the last few days of life (the longest was 10 days before death), when the patient was moribund a bacterial invasion occurs, but this is purely terminal and is not met with in all cases. Cultures made from the heart blood, cerebro-spinal fluid and lymph glands after death, in a considerable number of cases, remain sterile. The organisms found in these terminal invasions are generally cocci, because the great majority of these advanced cases have foci of suppuration due to jiggers in the hands and feet. Pure cultures in broth of the streptococcus, obtained from the cerebro-spinal fluid were injected into healthy monkeys, and monkeys having trypanosomes in their blood without appreciable effect, showing that, these organisms have very low pathogenic powers and can only gain a footing in the tissues when the resistance is greatly lowered. It is certain they play no part in the etiology of sleeping sickness. The var-

ious signs and symptoms are produced by the trypanosoma alone; of course a case may be cut short by an intercurrent disease e.g. Pneumonia, as in diabetes and other diseases. Plate 4. shows diplocccci in the brain.

16. The History and distribution of sleeping sickness in Uganda and the Nile basin.

The first cases of sleeping sickness were reported by the Drs Cook in April 1901. These cases came from Usoga. A year later the disease was found to be epidemic in Usoga and had spread into the neighbouring parts of Kavirondo and Uganda.

Dr R.U.Moffat C.M.G. P.M.O. is of opinion that '' the disease is not indigenous to Uganda, but has been imported, within recent years, from the Congo basin. This he thinks is no matter for surprise when we consider that the opening up of Equatorial Africa has led to inter-communication between the countries and districts, which in earlier days were absolutely cut off from each other''. He is inclined to explain the first appearance of the disease in Busoga, by the fact that a large number of Emin Pasha' Sudanese, accompanied by a multitude of slaves from the Congo Territories west of Lake Albert, were brought in and settled in Usoga.

Since the Autumn of 1903 the disease has broken out on the north east shores of Lake Albert, and is slowly spreading down the Nile valley, and the lat-

est information shows that the disease has also extended south to the Albert Edward Lake. So we see that the shores of the Victoria, Albert and Albert Edward Lakes as well as the Nile basin are affected by the disease. A point of great importance is, that the disease since it's commencement in 1901, has never involved the country inland from the great waterways. In the opinion of the Uganda Prime Minister, Apolo, a strip 10 to 15 miles wide would cover the affected area and any cases found futther inland are imported. This peculiar distribution of the disease suggested that there must be a special reason. Since we have seen that the cause of the disease is a trypanosoma, the disease cannot be conveyed in clothes of food or directly from man to man, but must, probably, be carried by some blood sucking insect. This led the Commission to ask themselves the following question

17. Does the distribution of sleeping sickness coincide with the distribution of any biting insect?

On the analogy of Nagana a tsetse fly was suggested. But the Tsetse fly was not supposed to occur at altitudes of 3000 feet, Mr F.J.Jackson in a despatch to the Foreign Office dated Sept 27, 1901, writes '' I may add that there is species of tsetse fly found along the wooded portion of the Lake shore here at Entebbe. It is plentiful in the Botanic Gardens''. The Commission had also observed this fact. Specimens

were sent to Mr E.E.Austen of the British Museum (Nat History). They were identified as Glossina palpalis (Rob Desv). Mr Austen writes '' this is the West African species and it's occurrence in Uganda is very interesting and was quite unexpected by me, though it is true that another species, Glossina fusca, occurs both in West and East Africa''

Without entering into details it is desirable to mention a few facts about these flies. The name Tsetse fly was and is, probably, associated with the Glossina morsitans, which transmits the fly disease in cattle in Zululand and in other parts of Africa. It was with this variety or a closely allied one, the Glossina pallidipes, that Bruce made his classical experiments on the Trypanosoma brucei in Zululand, which has been the starting point of the work which has since been done on insect transmitted disease, including malaria. In addition to these species, we have in Equatorial Africa the larger varieties, Glossina fusca and longipennis. These are the varieties, which are found in British East Africa and Uganda. It is a curious fact that the Tsetse fly seems to be confined to Africa. It has not been found in India or elsewhere. Both male and female suck blood, and in captivity it is impossible to keep them alive without feeding them on blood. In this way they differ from mosquitos. Our

MAP SHOWING THE DISTRIBUTION OF SLEEPING SICKNESS IN UGANDA.

The Red Dots show where Sleeping Sickness is prevalent.
The Black Dots where it is absent.
The Crosses represent cases imported from Sleeping Sickness area.

KERI
Dufile
NIMULI
RIVER NILE
WADELAI
TENGRI R.
VICTORIA NILE R.
FAJAO.
FOWEIRA.
BUGUNGU
MWANGA'S
MAHAGI SOGHIR.
MAHAGI KEBIR
BUTIABA
R. WAJA.
ALBERT NYANZA.
R. ITITI.
UNYORO
LAKE KWANIA.
L. SALISBURY.
R. HOIMA.
R. KAFU.
LAKE CHOGA.
R. SEMLIKI
R. NGUSSI.
MRULI
BUYAGA
BUGANGEZI
SINGO.
BULAMWEZI
BUSERERE.
L. MDOLOGOMA.
CRATER
Mt. ELGON
R. NILE.
USOGA.
UGANDA PROVINCE.
BWEKULA
CHAGWE.
NAPOLEON G.
EAST AFRICA PROTECTORATE
R. KATONGE.
BUTAMBALA
MAWAKOTA
BUSIRO
RUISAMBA.
EQUATOR.
EQUATOR.
KABULA.
BUDDU
LAKE ALBERT EDWARD.
SESE IDS.
MAVIRONDO GULF.
ANKOLE.
L. KACHIRA
KOKI
VICTORIA NYANZA.

30° 31° 32° 33° 34° 35°
4° 3° 2° 1° 0°

Scale of Miles.
0 10 20 30 40 50 60 70

MAP SHOWING THE DISTRIBUTION OF CLOSSINA PALPALIS.

The Red Dots show localities where Tsetse Fly was obtained. ●.

The Black Dots where other biting Flies obtained but no Tsetse. ●.

4° 30° 31° 32° 33° 34° 35°

3° 2° 1° 0° 1° 2° 3° 4° 5° 6° 7°

KERI
Dufile
NIMULI.
RIVER NILE.
ACHO.
AVOI
QWADELARI
TENGRI R.
VICTORIA NILE R.
FAJAO
FOWEIRA.
MAHAGI SOGHIR
MAHAGI KEBIR
A. WAGA.
ALBERT NYANZA.
KIBERO
UNYORO.
R. FITI.
LAKE KWANIA.
L. SALISBURY.
R. HOIMA.
R. KAFU.
LAKE CHOGA.
R. SEMLIKE.
R. NGUSSI.
MRULI
BUYAGA.
BUGANGEZI
SINGO
BULAMWEZI.
L. MPOLOGOMA.
MT ELGON
CRATER
R. NILE.
USOGA.
UGANDA PROVINCE.
BWEKULA.
KIADONDE
MAPOLOTIG.
EAST AFRICA PROTECTORATE.
R. KATONGE.
BUTAMBALA.
MAWAKOTA.
BUSIRO
NZOIA RIVER
L. RUWAMBA.
EQUATOR
EQUATOR.
KABULA.
BUDDU.
SESE Is.
KAVIRONDO GULF.
LAKE ALBERT EDWARD.
ANKOLE.
L. KACHIRA
KOKI.
VICTORIA NYANZA.

experience in Uganda showed, that they were most active in the day time about 12 O'Clock. They seldom bite in the night time. They have a very direct flight and make very little noise. They at once insert their long proboscis and fill themselves with blood in a remarkably short time, about 30 seconds. The bite produces less local reaction than that of the mosquito. The natives pay little or no attention to it, and as they are mostly unclothed, they are very frequently bitten. The fly when at rest crosses it's wings in very characteristic fashion, they are folded on it's back like a pair of scissors. These flies, unlike the mosquito, produce only one larva at a time, they are, therefore, called pupifera. This fact may turn out to be of some practical help in any attempt to exterminate it. When the pupa is laid, it is quite white, contracts, and is seen to be segmented. After a time it increases in size and becomes black in colour. It seeks a sheltered place and comes to rest. When kept in a dry place in the course of about 4 weeks it hatches out into a fully formed fly. The darkening is no doubt protective, as it is much less readily seen and, therefore, less liable to be destroyed. A curious feature was noticed in the larvae hatched out in the Laboratory, namely, that the fly in captivity tended to abort. It produced extremely small pupae, which were not viable. Plate 5 shows the various

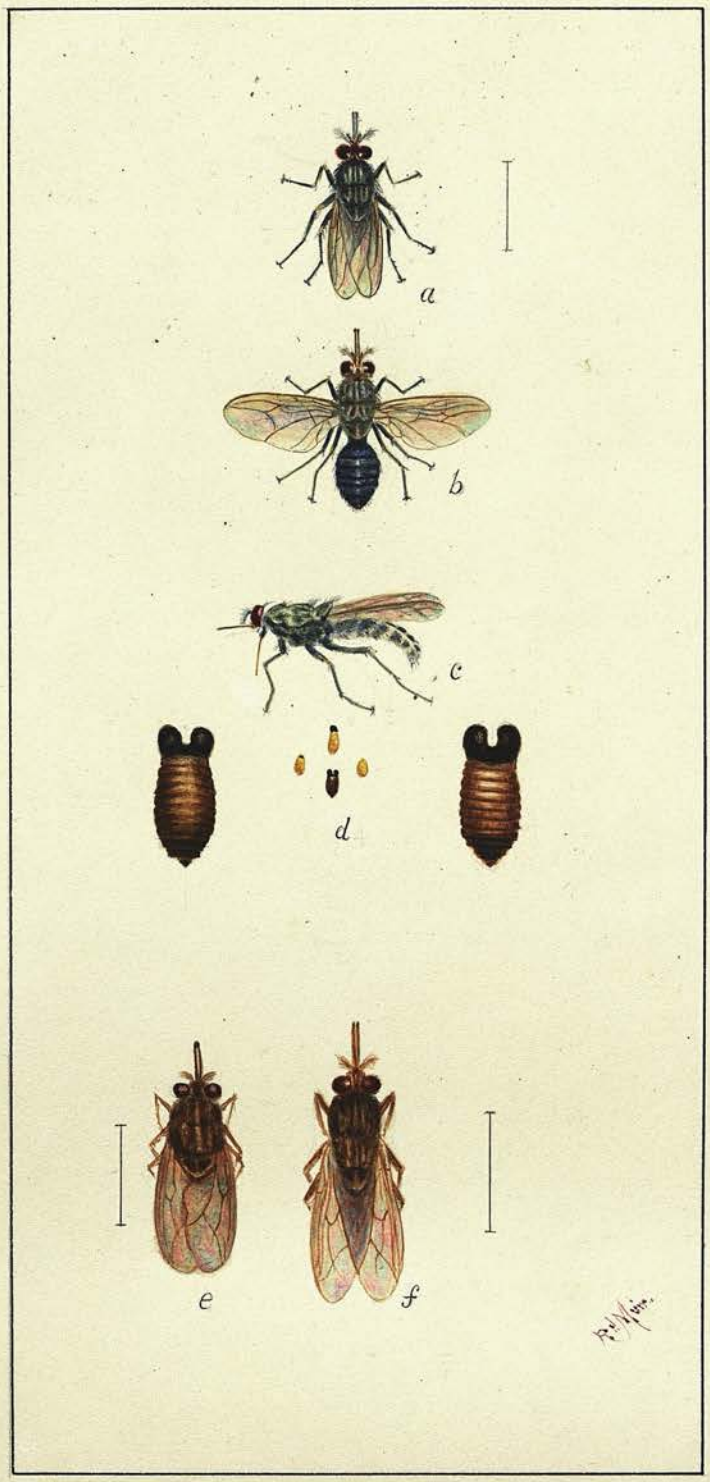


Plate 5.Fig A.Glossina palpalis, the wings folded in characteristic manner, the well marked proboscis is seen.Fig B. Glossina palpalis, the wings separate to show body and markings. Fig C.Glossina palpalis side view. Fig D. Pupa of Glossina palpalis.Fig E.shows Glossina pallidipes. Fig F. Glossina fusca (large var)

features of the fly and pupa, as described above. The drawing is made from actual specimens, and shows Glossina palpalis in two positions, one with the wings folded in characteristic scissor like fashion and the other with the wings separate to show the markings on the body. The long proboscis is also shown. To compare with this, drawings of two other varieties of Tsetse fly, a large variety, Glossina fusca, and a small variety Glossina pallidipes are placed along side of it. It will be seen that they differ, apart from size, in the colouring. A drawing of the pupa of Glossina palpalis is also given.

The character of the country, in which the fly is found, is very typical. It is cool, shady, and the undergrowth, which is situated close to the margin of the Lake, is very thick and does not allow the sun's rays to penetrate. This was strikingly seen in following the distribution of the fly down the Nile Valley. It was found to stop, as will be seen in the map, at a point where the 4° cuts the Nile, and was not found on the banks of the Nile in the Sudan. At the above point the character of the country alters entirely. It becomes open and the sun's rays are not screened by vegetation.

Some idea of the dense character of the undergrowth and it's proximity to the water is given in the accompanying photograph of the Ripon falls, where the

fly is very abundant:-

In the Bahr-el-Ghazel Province of the Sudan, which is well to the west of the Nile, the vegetation resembles that of the great Lakes and here the Glossina morsitans is found. The fact that the fly does not extend along the banks of the Nile into the Sudan, is a matter of very great importance and satisfaction to this rapidly advancing country. The fly belt of the Bahr-el-Ghazel is, on the recommendation of the Commission, being marked out, as a precautionary measure by the Sudan Government.

The fly was shown to the natives, they at once recognised it, as the KIVU. The Prime Ministers and Regents were asked to meet the Commission and have the

matter explained to them. They were supplied with several dozen nets, killing bottles and boxes and they promised to have the distribution of the fly worked out.

A letter was also addressed to the Bishops of Uganda, who kindly promised to obtain information from their Missionaries. Every Official and Missicary in the country was then sent a specimen of the tsetse fly and the following information was asked for by letter:-

1) Is the tsetse fly found in your district?

2) In what kind of place is the fly found - marsh, banana plantation, bank of river, shore of lake bush or open place?

3) When does it bite, during the morning, midday or at night time?

4) Is it numerous?

5) What animals does it bite?

6) Does sleeping sickness occur in the same place distinguishing of course between imported cases and those which have been infected on the spot?

We also stated that the flies themselves must be caught and sent in for identification to the Laboratory, as it was no use trusting to report. If no tsetse flies occurred in the district, to send in specimens of the various biting flies or insects known to the natives. During the months of June, July and August some 500 collections of biting flies were sent in from all parts of Uganda and this was continued after, so

that a large number of facts were accumulated on these points. As each packet came in it was sorted into tsetse and other biting flies. If the parcel contained one or more tsetse flies, a red disc was stuck in the map over the locality from which the fly was sent. If no tsetse fly was found, on the other hand, a black disc was fixed over the spot. A second map was prepared at the same time, to show the distribution of the sleeping sickness. If the letter accompanying the parcel stated that sleeping sickness is prevalent a red disc was fixed over the locality, if, on the contrary, no cases of sleeping sickness were reported a black dot was affixed; when cases were reported to have been introduced from some other locality and to have died out without any spread of the disease in the neighbourhood, then a cross was made on the map.

On account of the disease having broken out on Lake Albert, it became necessary to have the fly belt there and on the Nile accurately marked out, and at the same time to determine, exactly, the distribution, not only of advanced sleeping sickness there, but also, that of human trypanosomiasis (the early stage). Accordingly in November 1904, I left Entebbe for Lake Albert. I continued the same method of recording on maps. Iexamined a number of people from Bugungu on the north east shores of Lake Albert, who were sick, and the result of the examination showed that, they were

suffering from typical sleeping sickness at all stages of the disease, and all those examined, showed the trypanosoma in their glands and cerebro-spinal fluid. The results of my investigation showed that the disease had extended along the Victoria Nile and further down, as far as, Wadelai, but at this point there were only a few early cases as yet: the fly was found on the banks of the Nile as far north as a point 30 miles south of Gondokoro. In a Memorandum to the Royal Society, I expressed the view that the disease would extend both north and south to the limit of the fly belts. The latest information shows that the disease has extended south and is found on the shores of Lake Albert Edward. The investigation of the banks of the Nile in the Sudan showed that , neither the fly nor the disease occurred there. On 21st January 1905 I reached Khartoum, and a short time was spent there arranging with the Governor-General for the marking out of the fly belt in the Bahr-el-Ghazel Province, and specimens of the Glossina palpalis were, also, sent to every Official in the Sudan. A letter, with questions similar to those mentioned above, was also sent.

The accompanying maps, p.46. which are tracings from originals, show the exact distribution in Uganda of the fly and sleeping sickness. It also shows , the results of the recent investigations on Lake Albert and the Nile basin. A study of these two maps will bring home

the fact that , the distribution of sleeping sickness and Glossina palpalis is the same. The rivers in Uganda, with the exception of the NILE, are mere papyrus swamps. The fly has been frequently sought for up these rivers, but ,although many other varieties of biting flies e.g. Stomoxys, Tabanidae. Haematopota &c are met with in large numbers, yet the tsetse fly has never been found and no sleeping sickness occurs. The next question to answer is

18 Can the Glossina palpalis carry the trypanosoma found in sleeping sickness cases to healthy animals?

The animal used by us for these experiments was the monkey. They are easily procured, easily fed and keep their health perfectly in captivity. The flies were caught on the Lake shores, placed in wooden boxes with wire gauze sides and brought to the Laboratory; in this way we got as many as 100 aday. From these wooden boxes they were transferred to the feeding boxes, these were made of a wooden frame surrounded on 4 sides with ordinary mosquito curtain, so that free access of air to the insects was obtained, and further it was only necessary to place one of the muslin sides in contact with the skin, when the flies bit readily through the gauze. The two ends of the cage were closed by glass panes, so that the operation of feeding could be watched. Itwas found that the flies fed more readily

in the dark, accordingly, we covered the box with a cloth during the act of feeding. When the fly is fully fed the abdomen becomes enormously distended with blood resembling a small cherry. In the experiments the cage was placed on a case of sleeping sickness and the flies allowed to feed, then, after varying intervals of time, was placed on monkeys: there was practically no reaction and the patients did not complain of any inconvenience. About 30 flies were, as a rule, in each cage. As the experiments are important they are given in full:-

Experiment 114.- Monkey, Cercopithecus.
(Glossina palpalis)
Feeding tsetse flies, on a healthy monkey 8 hours after they had been fed on a Sleeping Sickness patient.

Date	Number of flies fed on-		Trypanosomes.
	Patient	Monkey	
May-			
20	22.	0 .	Absent.
22	4	5	
23	11	2	
23	9	7	
24	9	6	
25	15	1	
26	10	4	
27	6	5	
28	8	7	Absent
29	5	4	
30	9	3	
31	5	1	
June-			
1	1	9	
2	6	2	
3	8	1	
4	4	2	Absent.

Ex114 (cont).

Date	Number of flies fed on-		Trypanosomes.
	Patient	Monkey	
June-			
5	4	3	
6	5	5	
7	6	0	
8	13	9	
9	8	4	
10	9	5	
11	10	6	Absent.
12	8	5	
13	9	6	
14	0	0	
15	4	12	
16	8	10	
17	2	1	
18	2	5	Absent
19	7	4	
20	5	4	
21	0	0	
22	16	2	
23	24	14	
24	31	10	
25	25	17	Absent
26	28	8	
27	17	15	
28	0	0	
29	26	26	
30	24	22	
July-			
1	28	15	Absent
2	29	16	
3	28	11	
4	27	14	
5	19	13	
6	31	16	
7	32	11	
8	23	13	
9	12	15	
10	14	0	
11	14	28	
12	28	6	
13	22	18	
14	19	12	
15	18	8	
16	17	13	
17	24	9	Absent
18	22	8	
19	22	11	
20	23	17	

Ex 114 (cont)

Date	Number of flies fed on-		Trypanosomes
	Patient	Monkey	
July-			
21	16	13	
22	17	11	
23			Present

Experiment 97. Monkey, Cercopithecus,

Feeding tsetse flies (Glossina palpalis) on a healthy monkey 24 hours after they had been fed on a sleeping sickness patient.

Date	Number of flies fed on-		Trypanosomes.
	Patient	Monkey	
May-			
15	11		Absent.
16	..	1	
17	5		
18	..	8	
19	10		
20	..	5	
21	8		Absent.
22	..	9	
23	13		
24	..	8	
25	6		
26	..	9	
27	5		Absent.
28	..	4	
29	5		
30	..	7	
31	4		
June-			
1		1	
2	4		
3	..	5	
4	5		
5	..	10	
6	14		
7	..	0	
8	28		
9	..	16	
10	17		
11	..	24	Absent.
12	26		

Ex 97 (cont)

Date	Number of flies fed on-		Trypanosomes.
	Patient	Monkey	
June-			
13		20	
14	0		
15	11.		
16	..	19	
17	14		Absent
18	19		
19	..	7	
20	15		
21	..	0	
22	..	16	
23	17		
24	..	12	
25	8		Absent
26	..	9	
27	23		
28	..	9	
29	26		
30	..	56	
July-			
1			Present

Each of these experiments was repeated with the following results:-

Experiment 115. Monkey Cercopithecus.

Feeding tsetse flies on a healthy monkey 8 hours after they had been fed on a sleeping sickness patient.

The experiment was begun on May 20th and kept up to July 23 on which date trypanosomes were found in the blood.

Experiment 99 Monkey Cercopithecus

Feeding tsetse flies on a healthy monkey 24 hours after they had been fed on asleeping sickness patient.

The experiment was begun on May 15 and trypanosomes were found in the blood of the monkey On July 23

Experiment 116.- Monkey (Cercopithecus)

Feeding tsetse flies on a healthy monkey 48 hours after they had been fed on a sleeping sickness patient.

Date	Number of flies fed on-		Trypanosomes.
	Patient	Monkey	
May-			
20	10		Absent.
21			
22		10	
23			
24	9		
25			
26		5	
27			
28	9		
29			
30		6	Absent.
31			
June-			
1	6		
2			
3		7	
4			Absent
5	11		
6			
7		4	
8			
9	6		
10			
11		7	Absent
12			
13	16		
14			
15		8	
16			
17	17		
18	11		Absent.
19			
20		3	
21			
22	19		
23			
24		15	
25			Absent.
26	26		
27			
28		16	

Ex 116 (cont)

Date	Number of flies fed on-		Trypanosomes
	Patient	Monkey	
June-			
28		16	
29	9		
30			
July-			
1		49	
2			
3	51		Absent.
4			
5		29	
6			
7	40		
8			
9		20	
10			
11	25		
12			
13		26	
14			
15	25		
16			
17		16	Absent
18			
19	64		
20			
21		46	
22			
23			Present
24			

From these 5 experiments it may be considered proved that Glossina palpalis can carry trypanosomes from sleeping sickness cases to healthy monkeys, and the after history of the monkeys so infected is exactly similar to that of monkeys injected with cerebro-spinal fluid from a case of sleeping sickness.

Another point of great importance to settle was

19. Can Freshly-caught Glossina palpalis convey Trypanosomes to healthy animals?

Experiment 94- Monkey (Cercopithecus)

To ascertain if tsetse flies, freshly caught in the vicinity of Entebbe, are carrying trypanosomes.

May 13 1903. Blood examined. No trypanosomes.
13 Fed 31 flies freshly caught near
15 ,, 15, ,, Entebbe.
18 ,, 10 ,,
19 ,, 20 ,,
20 ,, 13 ,,
21 ,, 16 ,,
Blood examined. Trypanosomes absent.
May 22 Fed 20 Flies
23 ,, 25 ,,
24 ,, 17 ,,
25 ,, 31 ,,
26 ,, 18 ,,
27
Blood examined. Trypanosomes present.

Experiment 130- Monkey (Cercopithecus)

To note the effect of feeding freshly caught tsetse flies on a healthy monkey.

June 10 1903 Fed 60 flies.
11 ,, 23 ,,
Blood examined. Trypanosomes absent.
June 12 ,,12 ,,
13 ,, 26 ,,
14 ,, 20 ,,
17 ,, 25 ,,
18 ,, 10 ,,
Blood examined. Trypanosomes absent.
June 19 Fed 9 flies
20 .. 10 ..
21 .. 30 ..
22 .. 7 ..
23 .. 74 ..
24 .. 31 ..
25 .. 28 ..
Blood examined. Trypanosomes absent.
June 26 Fed 83 flies.
27 .. 64 ..
28 .. 27 ..
29 .. 38 ..
30 .. 62

Ex 130 (cont)

July 1 Fed 62 flies
Blood examined. Trypanosomes absent
July2 Fed140 flies.
3 .. 35 ..
4 .. 34 ..
5 .. 23 ..
6 .. 44 ..
7 .. 14 ..
8 .. 34 ..
9
Blood examined. Trypanosomes. present

Experiment 131 . Monkey. Cercopithecus

Feeding freshly caught tsetse flies on ahealthy monkey.

June 17 Fed 5 flies
18 .. 3 ..
19 .. 7 ..
20 .. 17 ..
Blood examined. Trypanosomes absent.
June 21 .. 23 ..
22 .. 7 ..
23 .. 28 ..
24 .. 39 ..
25 .. 13 ..
Blood examined. Trypanosomes absent.
June 26 ..53 ..
27 ..47 ..
28 .. 5..
29 .. 17..
30 ..108..
July 1 .. 36
Blood examined. Trypanosomes absent.
July 2 .. 98 ..
3 .. 45 ..
4 .. 28 ..
6 .. 38 ..
7 .. 17 ..
8 .. 36 ..
9 .. 57 ..
10 .. 30 ..
Blood examined. Trypanosomes Present.

The monkeys infected in this way have been kept under observation and they have presented exactly the same signs as monkeys injected with cerebro-spinal fluid, and further experiments show that this trypanosona is

the trypanosoma of sleeping sickness. The flies were caught near the Hut-Tax labourers camp, and as, we have already seen, about one in three of these men had the trypanosoma in his blood.

20. Can other biting flies convey the trypanosoma of sleeping sickness from the sick to the healthy animals.

From a study of the maps showing the distribution of the fly and sleeping sickness, it will be seen, that, although biting flies in certain places are very numerous and although cases of sleeping sickness have been imported among them, no spread of the disease has occurred.

A series of experiments were, also, undertaken to see if a common variety of biting fly, Stomoxys, would convey the parasite. The experiments were conducted in exactly the same manner as the above mentioned, except that a sick monkey was used instead of the patient. The experiments were maintained for several months, thus giving the fly every chance of infecting the monkey, but we were unable to convey the parasite by this species of biting fly. These experiments strongly suggest, that the universal carrier in nature of the trypanosoma of sleeping sickness in Uganda is the tsetse fly.

21. Can Glossina palpalis convey other varieties of trypanosomes from the sick to the healthy?

As we have seen other varieties of trypanosomes occur amongst the animals in Uganda, it became a matter of importance to determine, whether the common species of tsetse fly (Glossina palpalis) is able to convey these trypanosomes or not.

The experiments were conducted in the same way as detailed above. The result of the experiments showed that the Glossina palpalis was able to transmit from the sick to the healthy animal, the Jinga, Abyssinian and Uganda mule strains of trypanosomes. These were important experiments, because they showed that the animal strains of trypanosomes with their resulting disease in animals, might be spread over a very extensive tract of country, and rational measures based on these experiments could be taken to prevent this. They were, also, important from another point of view, viz, in that they strongly suggested that, if this fly can convey other varieties of trypanosomes. other varieties of tsetse fly could convey the sleeping sickness trypanosoma. As this latter point was an extremely important one, (because, if other varieties of tsetse flies convey the trypanosoma of sleeping sickness, then the area of possible extension of the disease in Africa is greatly widened), experiments were, therefore, begun in British East Africa at Nairobi to determine whether the tsetse flies found in East Africa, viz,

Glossina pallidipes, longipennis and fusca can convey the trypanosoma of sleeping sickness from the sick to the healthy. The most recent information is that the Glossina palpalis has been found on the Zambesi.

The result of our observations showed, that when all three varieties of fly were used for the experiment, that it was possible to convey the tyrpanosoma from a sick to a healthy animal. At the present time, a further series of experiments are being tried with each variety separately, to ascertain whether, all or only one or two varieties of the fly found in the belt are able to convey the parasite. The results, however, so far got make it evident that every endeavour should be made to prevent the population from sleeping sickness areas coming into the fly belt of East Africa.

Having thus completed the account of the researches on the etiology of the disease, we are now in a position to give a short account of the main features of the disease, based on these investigations, as observed by us in the cases in Uganda

22. A general account of the signs and symptoms met with in cases of sleeping sickness in Uganda.

All ages are attacked by it. Women are on the whole less affected than men, because their work is more indoors and they are less in the fly belt, but those who work in the belt suffer equally with the men.

There is no evidence that the disease can

be transmitted from parent to offspring, but it is possible that, if the population become "salted", they may be able to transmit this protegtive power, just as the wild game do in Nagana.

As we have already seen environment has a great deal to do with this disease, as it is entirely confined to the inhabitants of the fly belts.

The white man is not immune to this disease, but , as a rule, he exposes himself much less to the bites of the fly than the native, because,he goes less into the fly belts and he is also clothed.

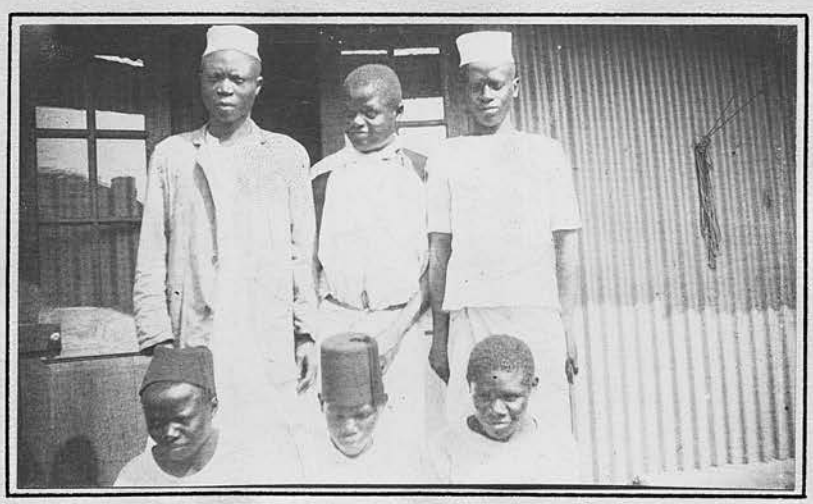
In studying the disease, it is advisable to consider it as having two distinct phases, the Early stage, in which there are no nervous symptoms, and the Late stage or Sleeping Sickness proper, in which all the classical signs are developed.

A.-What are the features of the Early Stage of Sleeping Sickness?

From 70 to80% of the population of the sleeping sickness areas of Uganda, at the present time, are in the early stage of this disease. A general enlargement of the lymphatic glands, both superficial and deep is the chief,and in fact,the only constant sign of the disease at this time. The posterior cervical glands seem to enlarge early and are readily detected, hence attention has been more particularly directed towards

them as a feature of sleeping sickness. Along with this gland enlargement, they may have occasional attacks of fever, but their temperature is for long intervals normal. The examination of the blood, at this stage, generally shows, a high lymphocytic count, both absolute and relative. but otherwise no alteration. The spleen may show some degree of enlargement, but there is usually concomitant malaria with the disease. Other signs and symptoms which are met with, not infrequently, at this stage are, rapid pulse apart from pyrexia, itchiness of the skin is also complained of, but these signs and symptoms appear when the patient is passing into the late stage of the disease, and are, probably, associated with early changes in the nervous system.

In order to give some idea of the healthy native of Uganda to compare with those suffering from Sleeping Sickness a photograph of some of the Laboratory attendants is given:-

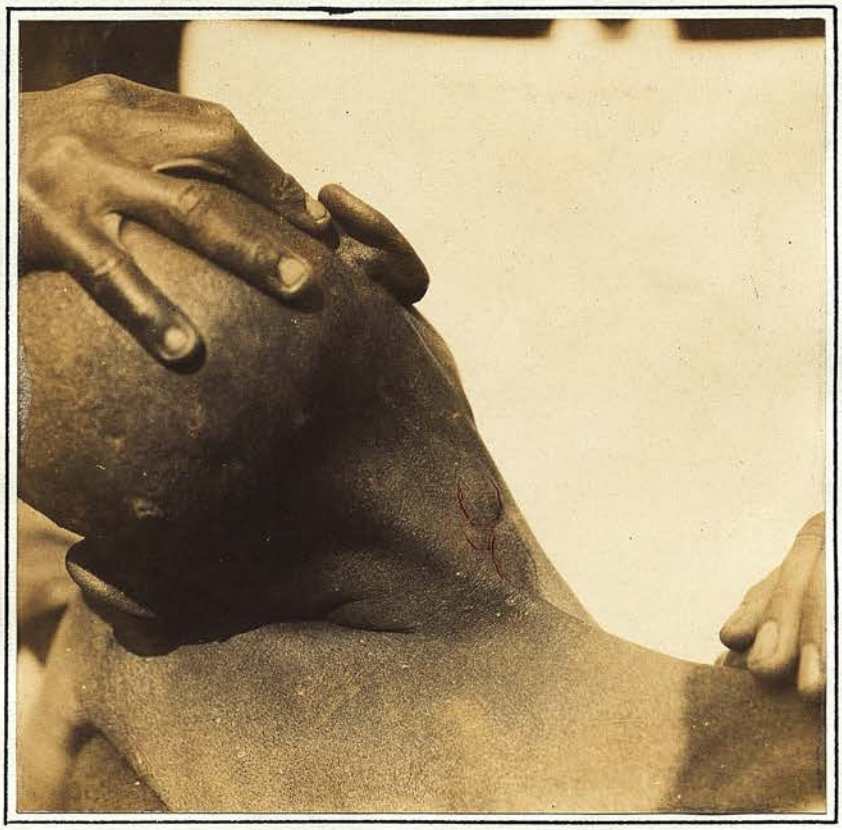


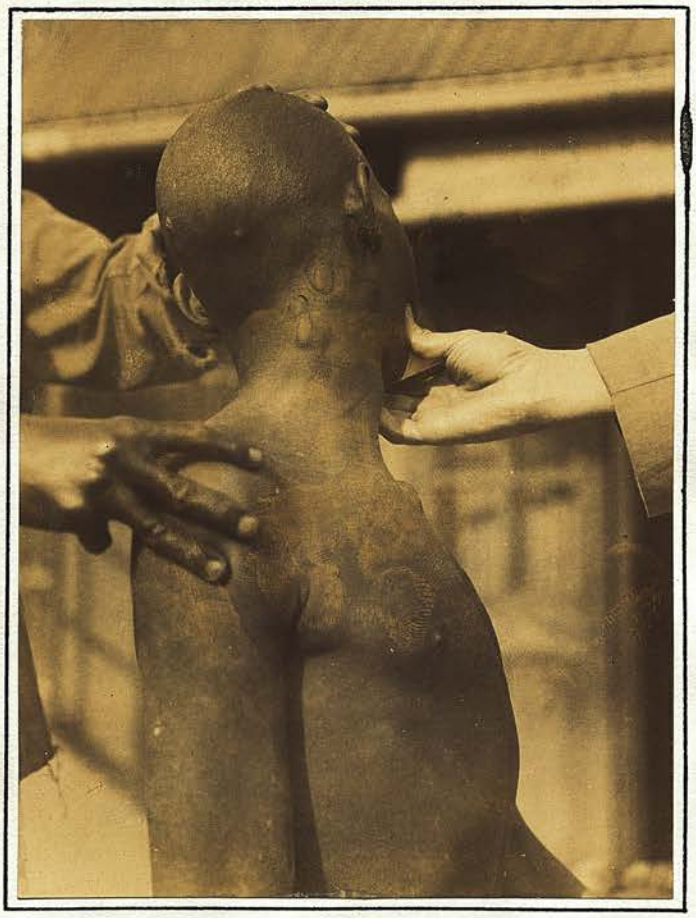
To compare with this a photograph is given of 5 prisoners in the Early Stage of Sleeping Sickness:-

On comparing the two photographs it will be seen that the early cases do not show any definite signs of illness.

The two following photographs of Case, Zururu bin Mza show the marked enlargement of the superfical lymphatic glands of the neck, which is a characteristic feature of this stage of the disease:-

Case Zururu bin Mza.





The diagnosis of the disease at this stage is by no means easy, as will be readily understood. The only practical method, is that described by us, viz, the examination of the juice from the enlarged glands in the neck. This is easily carried out; a hypodermic needle is inserted into the gland and little of the juice sucked into the needle by the syringe, this is blown out on to a slide and the drop covered with a cover slip. In this way pure lymph juice without the admixture of blood is got.. The diagnosis, by the finding of trypanosomes, can usually be made in about five minutes. In blood films, especially, when the temperature is elevated, trypanosomes may be found, but, as a rule, the examination of a simple film of blood gives negative results.

A question of great importance arises, Do any of these cases at this stage recover? The only way to give a definite answer to this question is to keep a number of these early cases under observation for a prolonged period. This is now being done in Uganda by the Medical Department on the suggestion of the Commission, and in time an answer to this important question will be given.

A further question arises, Can we destroy the parasite in the tissues of the host? Towards this end the Commission mades some investigations. It was found

that injections of Arsenic Had a distinct action on the parasite, it first causes the trypanosomes in the peripheral blood to disappear and then those in the lymphatic glands. When the Arsenic was left off, the trypanosomes, after a prolonged interval appear in the the peripheral blood. but not in the glands.

In this part of the investigation we have had the great advantage of the co-operation of Professor Ehrlich of Frankfurt. He sent out to Uganda a number of aniline dyes which he had prepared in Frankfurt and which he had tested on animals. The results, so far obtained with these substances, especially, in combination with Arsenic were encouraging and warranted a more extended investigation on these lines.

B.- What are the features of the late stage or Sleeping Sickness proper?

The later stages of the disease present a more complex clinical picture. In studying a case from the earliest stages, it is seen that there is no very abrupt change in the clinical signs, but a gradual and insidious one. The sign which attracts attention soonest is a peculiar alteration of the facial expression, it becomes heavy and dull. It is well seen in some of the photographs given below. Along with this certain signs and symptoms connected with the nervous system

appear. The most obvious being, tremors of the hands tongue and lips. As time goes on the gait and speech become wanting in coordination. He gradually passes into a tremulous and lethargic condition and becomes very thin and unable to move about much. If he does, his gait is weak and uncertain and he requires support. Finally he becomes quite unable to walk and for a few weeks before his death he is absolutely bedridden. He is then in a semi-comatose condition, sordes collect on the teeth and gums, his motions are passed involuntarily, bedsores develope and his temperature falls below normal. For a few days before death, to a casual observer, he looks already dead.

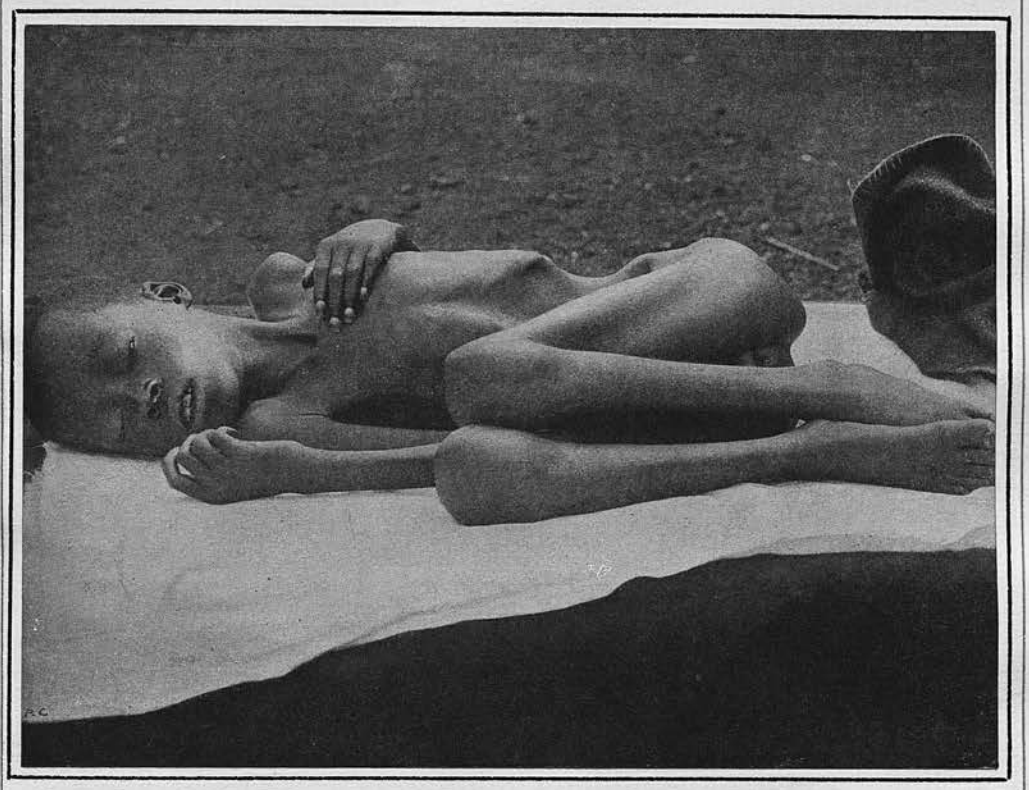
During the disease the patient does not complain of pain. The appetite is generally well maintained to the end.

When he reaches the moribund condition, it is the custom of the natives to throw him into the jungle, where the disease is sometimes shortened by the wild animals, which are always in readiness. The natives regard the disease as one which is spread by contact and the last stage is, in their opinion, the most infectious. It is extremely difficult to make, even intelligent natives, understand that disease e.g. malaria or sleeping sickness can be conveyed by biting flies.

The above is a clinical picture of a well marked case, but there are, of course, modifications

in individual cases. The duration is, on an average about 6 months.

The following photograph of one of our cases No 152 Sabiri, gives a very good idea of the patient in the very last stage:-

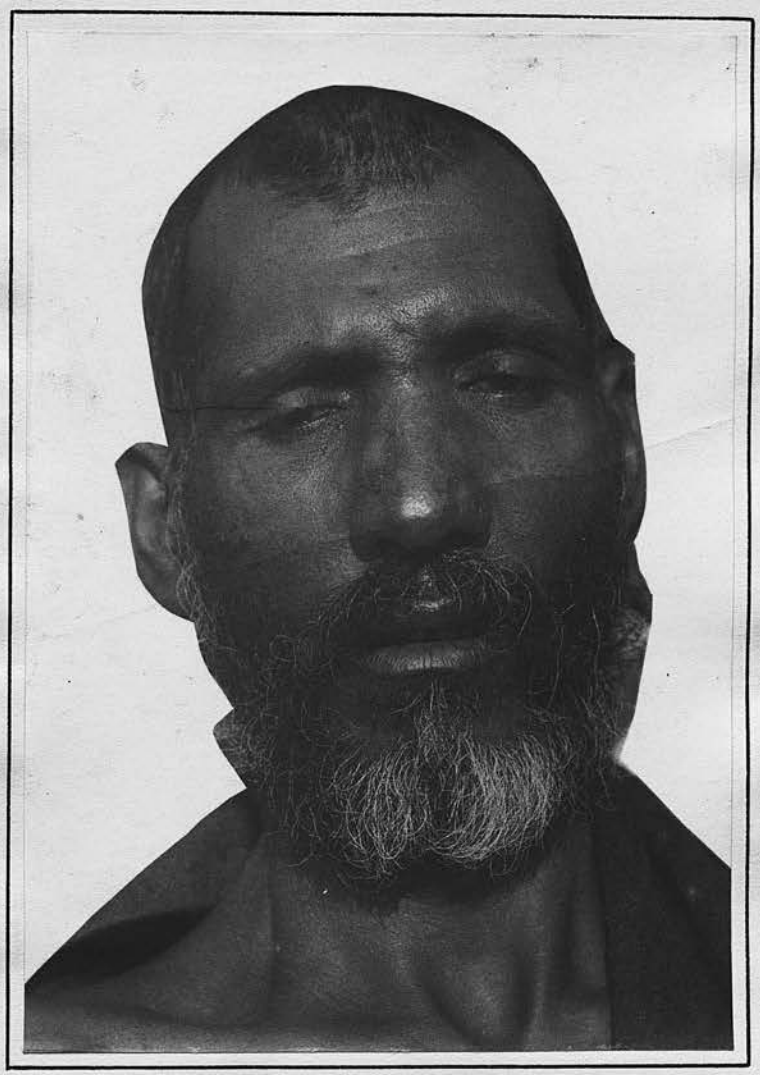


The diagnosis at this stage is, unfortunately, only too easy. The disease is invariably fatal at this stage. No treatment has been found of the slightest effect. Such is the general course of an uncomplicated case of sleeping sickness, we will consider a few of the features more in detail

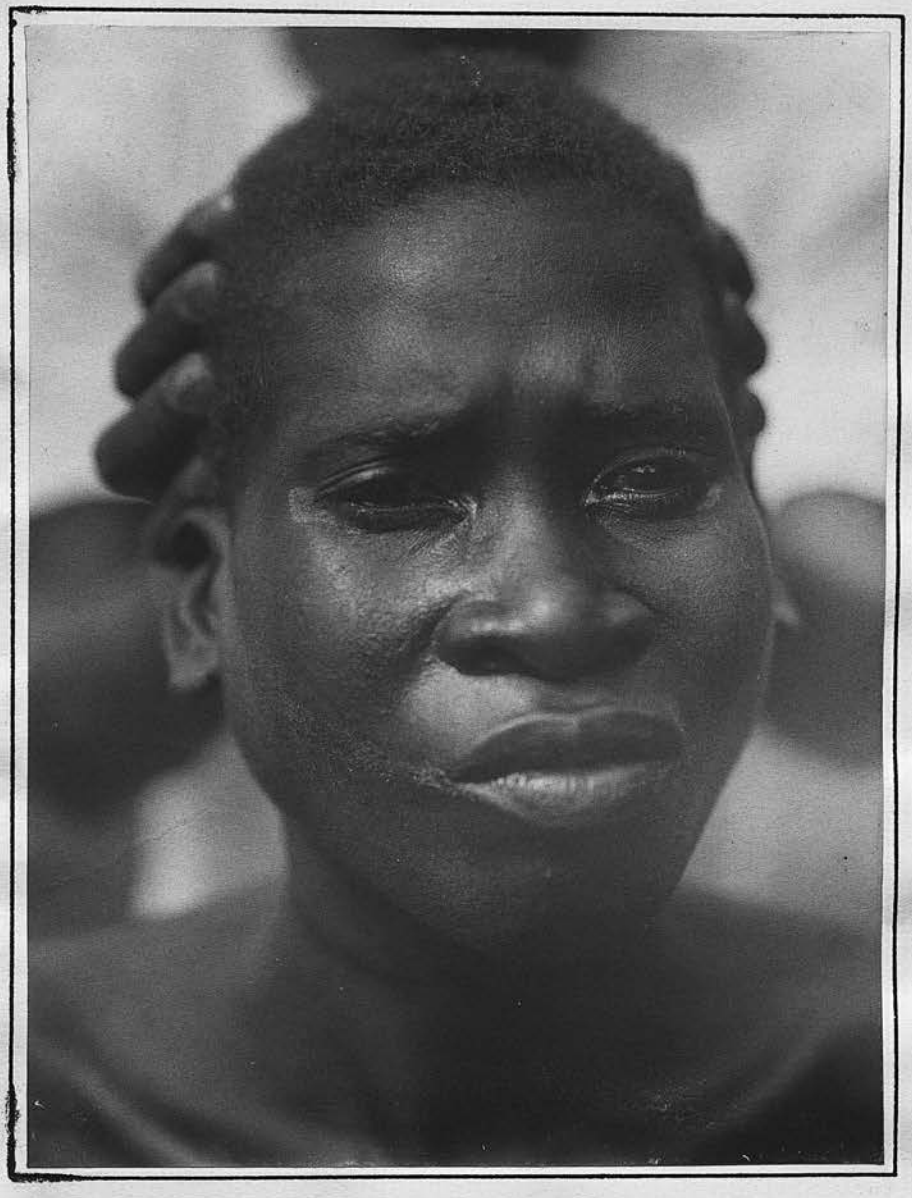
C.- Principal symptoms in detail.

General Condition.- The importance of the facial expression has already been alluded to; as it is somewhat difficult to describe, a better idea will be got from the study of a few photographs of cases of sleeping sickness:-

Case, Persian.



Case, Dreya.



In the beginning the patient may be quite well nourished, but sooner or later they begin to emaciate and in chronic cases they may be reduced to mere skin and bone.

Oedema of the lower limbs is sometimes met with, and apuffiness about the eyes is not uncommon. In one case a swelling of the abdominal wall was observed, as was shown on post-mortem examination, it was due to an infiltration of the sub-cutaneous tissues with a jelly like substance, which is so commonly seen in animals dying from Surra or Nagana.

Trophic changes may be seen in the form of bed-sores in the late stages.

Enlargement of lymphatic glands is the feature most commonly met with. All the groups of superficial glands are found to be enlarged. They may form large masses. In the neck they are frquently about the size of a bean and firm in consistence. Towards the end they may suppurate and break down.

Nervous System.- As regards Subjective symptoms; pain is sometimes complained of in the head and over the chest, but as a rule this is not a marked feature. Another symptom is itchiness of the skin and scratch marks are often seen on the bodies of cases coming up to the Hospital. As regards the disturbance of the intellectual functions, the most striking is sleep, but this must not be taken to mean that the patient is constant-

ly asleep. The condition is not one of true sleep, but rather of lethargy, towards the end this condition becomes more continuous and the patient may lie both day and night in this condition, but he can always be roused. He may lie in a semi-comatose condition for 10 days or a fortnight before death. In this condition the temperature is sub-normal throughout. In some cases the patient may, on the contrary, show marked exaltation of the mental function ; shouting, restlessness, and other signs of increased cerebration are seen at all stages of the disease. The speech becomes affected at an early stage of the disease. It becomes slow, monotonous and indistinct. The words are often slurred over. Whilst he is speaking, tremors about the lips may be observed. Sometimes speech may be reduced to a mere whisper, at other times it may be high pitched and piping. The speech is, in practically all cases, more or less affected. The intelligence is as a rule affected in these cases, but in natives it is somewhat difficult to arrive at a definite conclusion on this point, the relations, however, generally state that they have noticed that the patient's mental condition is altered. His memory, also, becomes impaired, more especially in the late stages. There is no constant and definite change in the function of any of the cranial nerves. In different cases special nerves may be picked out

with resulting impairment of function. In very chronic cases marked bulbar symptoms may be seen. Examination of the eye with the ophthalmoscope shows no deviation from normal of any part of the organ in uncomplicated cases of sleeping sickness. Nystagmus is sometimes observed. In examining the motor functions a distinct change is noticed. Tremors of the hands, tongue and lips occur at some stage in every case of sleeping sickness. They are well brought out on voluntary effort. The tremors are, as a rule, fine, but coarse tremors are , also, noted. In the last stage general tremors of the body are noticed. Choreic movement has also been noted in cases in children. Actual paralysis is not often observed until the very last stage, when practically all the bodily functions are in abeyance, but paresis and weakness of the muscles are frequently seen, especially in the lower extremities. Inco-ordination of the muscles of both upper and lower extremities is common. The muscular nutrition becomes seriouly impaired and extreme emaciation is not infrequently seen. Apart from the subjective phenomena of pain and itching the sensory functions show no noteworthy alteration. The superficial reflexes are, generally, normal. The knee jerk may be increased or diminished, there is no constancy in it's behaviour in sleeping sickness. Ankle

clonus is present in some, but not in all cases of sleeping sickness. Towards the end the patient loses control over the rectum and bladder and he passes his urine and faeces under him.

Cerebro-spinal fluid.- The examination of the Cerebro--spinal fluid taken by lumbar puncture during life shewed, as already mentioned, trypanosomes in every case, another interesting fact was obtained by the estimation of the number of cells per cmm of fluid. It was found that they rose from nil in the early stage to 300 or 400 per cmm in the last stage. The cells were all mononuclear.

Locomotory System.- With the exception of the gait this system was normal. In the late stages the patient was unable to walk entirely, but before that was reached he presented alterations from normal. There was no fixed or constant type. It was, probably, most commonly of the "reeling" or "drunken" type of gait. He is not able to walk along a straight line, and there is staggering on turning sharply.

Alimentary System.- The appetite is good and often markedly increased. In the last stages, sordes accumulate on the gums, in some cases a purulent discharge is noticed. Vomiting is, sometimes, present and blood in some cases is brought up, this is associated with a lesion which will be described later. The liver is not enlarged in uncomplicated cases. The spleen is

usually slightly enlarged, but not markedly so, if it is the condition is due to concomitant malaria.

Circulatory System.- There are, as a rule, no subjective symptoms referable to circulatory system. On palpation the apex beat may be somewhat weak. Also on auscultation the heart sounds are weak, but, in uncomplicated cases, no brûit is heard. The pulse in the early stages shows an increased rate, apart from pyrexia, this sign taken along with enlargement of lymphatic glands strongly suggests sleeping sickness.

The Blood.- The estimation of the red and white corpuscles in a large number of cases at all stages of the disease was undertaken. The counts were made by the Thoma-Zeiss haemocytometer. The haemoglobin was also estimated by means of a Gowers' apparatus. Films of blood were made and stained by the Romanowsky method. The result of these observations, made on many occasions, on about 60 cases of sleeping sickness at all stages of the disease, showed, that in uncomplicated cases there was practically no diminution in the number of red cells or in the percentage of haemoglobin, just before death a rise in the number of red cells and the percentage of haemoglobin above normal was noted. This was, probably, due to a concentration of the body fluids, Owing to the fact, that whilst in the semi-comatose condition they get little or nothing to eat or drink from their relatives.

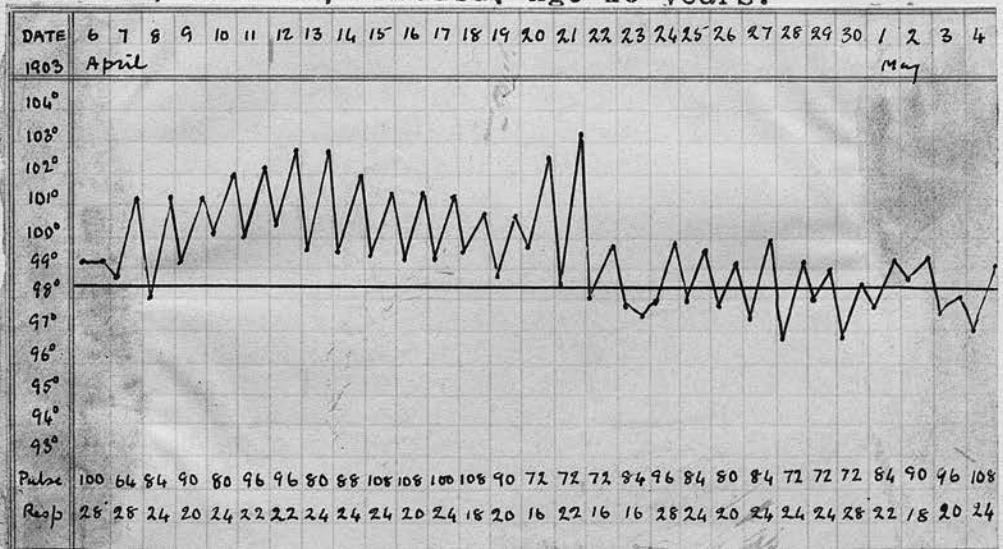
The estimation of the white corpuscles showed, that there was a marked increase in the number of the lymphocytes, both absolute and relative, apparently at the expense of the polynuclears. The presence or absence of parasites from the blood has, already, been fully discussed.

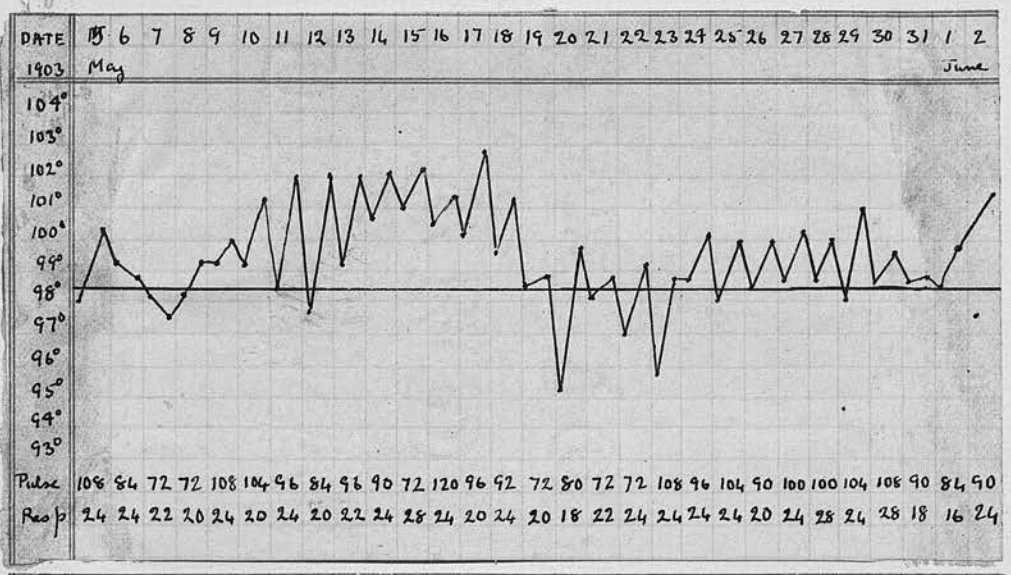
Respiratory System.- Pneumonia not infrequently complicates this disease, but, as a rule, this system is normal.

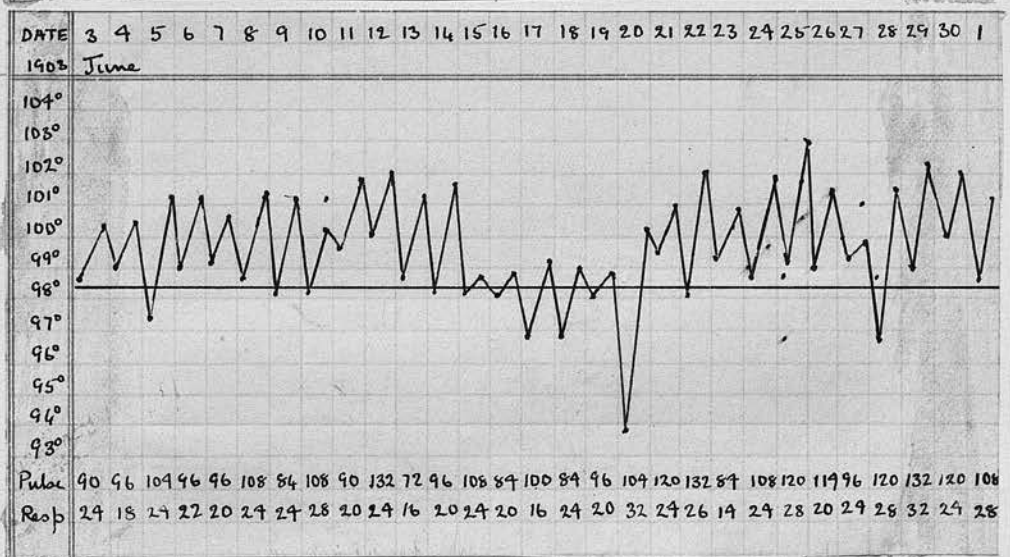
Urinary System.- This system, generally, shows no noteworthy change. The trypanosoma has never been found in the urine, although a number of samples were centrifugalised.

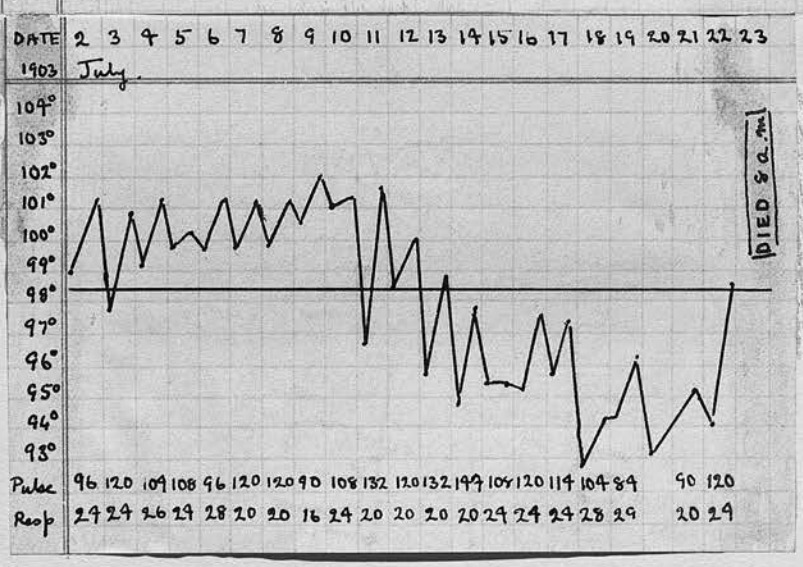
Tegumentary System.- Not infrequently a papulo-vesicular eruption is observed in cases of sleeping sickness, it is uncertain how far this is specific to this disease, as such lesions of the skin are not uncommon in natives apart from this disease.

Temperature.- The following chart represents the course of the disease in a typical case of sleeping sickness, Case 44, Nakaiba. Age 10 years.









Temperature was taken in the rectum.

It will be seen from the chart, that there is constant pyrexia, the period of more marked elevation of temperature is, generally inaugurated by an increase in the blood of the number of trypanosomes, so that they may be seen in fair numbers in an ordinary film. In the intervals the parasites cannot be found in films. Shortly before death a very marked drop in the temperature occurs. Hyperpyrexia is uncommon, but may sometimes occur.

D.- Morbid Anatomy.

External Appearances. The body is markedly emaciated. There is general enlargement of the superficial lymph glands. Bedsores and other sores are frequently present , many of these being the result of Jiggers.

Lymphatic Glands. Both superficial and deep glands are enlarged. On section, they may be red and congested, sometimes points of suppuration are seen, due to coccal infection shortly before death. The enlarged cervical glands become continuous below with the thoracic, which in turn join the abdominal, and these run down along the iliac vessels towards the femoral and inguinal glands.

Heart.- This organ may show minute petechial haemorrhages under the endo- and epicardium. The muscle wall is, frequently, flabby looking. The chambers of the heart frequently show dilatation. Occasionally a

yellow jelly like substance is seen under the epicardium towards the base of the organ. This is very commonly seen in animals dying of Nagana and Surra. Otherwise there is no specific lesion in the heart in this disease. The flabby condition of the muscle is, probably, due to the accumulation of round cells in the perivascular lymph spaces (this we shall see later is the essential lesion of this disease), which interferes with the nutrition of the cells of the organ.

Lungs,-These show no specific lesion in this disease, but Pneumonia is not uncommon.

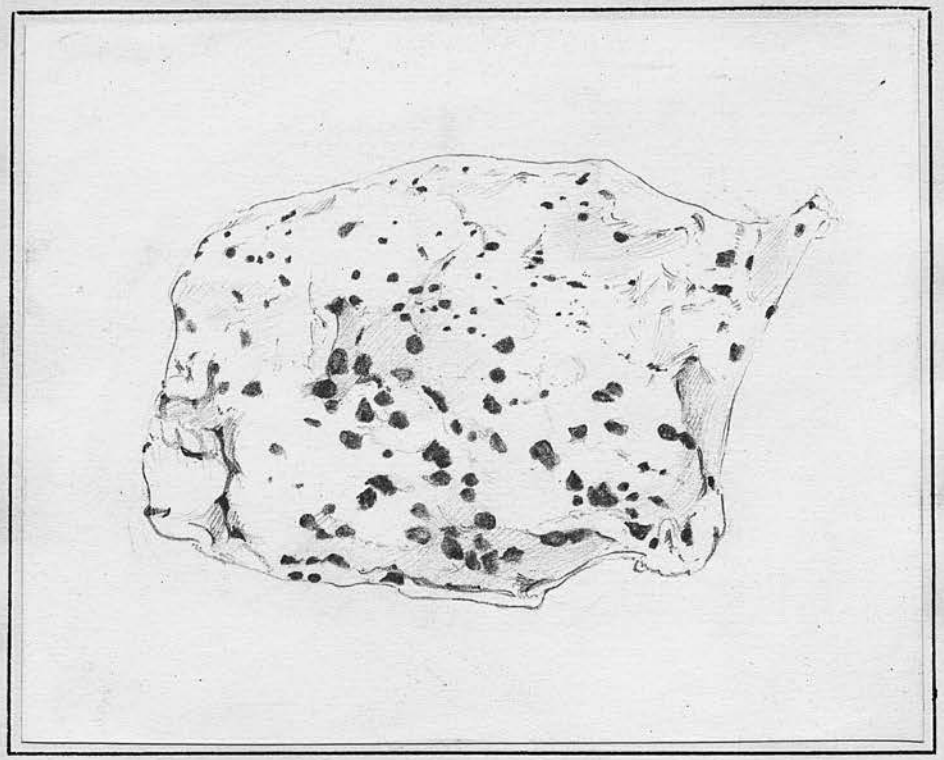
Liver.- There is often a condition of chronic venous congestion of this organ, and associated with this is some fatty change.

Spleen.-This may be slightly enlarged and show a condition of venous congestion. pigmentation and considerable enlargement is, frequently, seen post-mortem, but this is due to concomitant malaria.

Kidneys.- They not, infrequently, show advanced chronic venous congestion, at other times they are quite normal.

Stomach and Intestines.-The stomach, in all cases examined latterly by us, showed a remarkable condition. On opening the organ, it was found to contain altered blood and on removing this the mucus membrane presented a curious appearance. It was studded over with dark

areas varying in size from a pin point up to the size of a pea, they were surrounded by a line of red and were more numerous towards the pylorus. The following drawing made from the stomach of a case Gerude, shows the general appearance of the condition:-



On microscopic section these areas are seen to be small haemorhages under the mucus membrane. In the above case they, probably, occurred about 10 days before death. These haemorrhages are similar to those which take place under the endo- and epi-cardium of the heart, but under the action of the gastric juice of the stomach, they break down and give rise to the above appearance. This condition has been observed by us in

the stomach of a monkey which died, and which had been inoculated with the trypanosoma of sleeping sickness. It has , also, been noticed in animals suffering from Nagana. The finding of this condition in the stomach of cases of sleeping sickness is, therefore, very interesting, as being a pathological lesion in common with other trypanosoma infections.

Brain.- On removing the calvarium, the dura mater shows no abnormality, but, on reflecting this membrane the convolutions are seen to be flattened, the subarchnoid fluid is in excess, giving a "ground glass" appearance. The vessels, generally, are injected. On section the ventricles are dilated and contain an excess of cerebro-spinal fluid, which may be more or less turbid. In a certain proportion of cases purulent meningitis may complicate the disease. The naked eye appearances in the nervous system are not very marked.

E.- Microscopic Anatomy.- The working out of the minute anatomy was done by Dr F.W.MOTT F.R.S. London, to whom material was sent from Uganda. Mott was the first to show, some five years ago, that cases of sleeping sickness examined by him showed the same histological changes, viz, a chronic meningo-encephalo-myelitis, the leading characteristics of which is the filling of the perivascular canalicular system with large and small mononuclear leucocytes. There is, also, some

glia cell proliferation, with a certain amount of neuronic degeneration, by no means proportional to the vascular changes. Plate 3. shows this condition. It is a drawing from the section of the brain of a very chronic case of sleeping sickness, Dreya, (a photograph of this case has been given to illustrate the facial expression in sleeping sickness). The drawing is of a small vessel in the brain. The perivascular space is filled with the characteristic cell infiltration of lymphocytes and plasma cells of chronic sleeping sickness. An interesting fact indicating prolonged chronic irritation is the existence of a large number of plasma cells of Marscholko, also a number of granules the result of their disintegration. Besides these, there are a number of granule cells, which Mott states he has seldom seen in other diseases of the nervous system. Plate4 is a drawing of the cells as seen in the exudation of a case of sleeping sickness 1) Small lymphocyte 2) larger lymphocyte 3)Plasma cell 4) Granule cell 5) Granule cell disintegrating.

This is not limited to , although most marked in, the central nervous system. It affects the spinal nerve roots, the nerves, the organic viscera and the serous membranes (heart, liver, pericardium) having been examined. A further important and interesting fact is that the enlarged lymphatic glands, in which

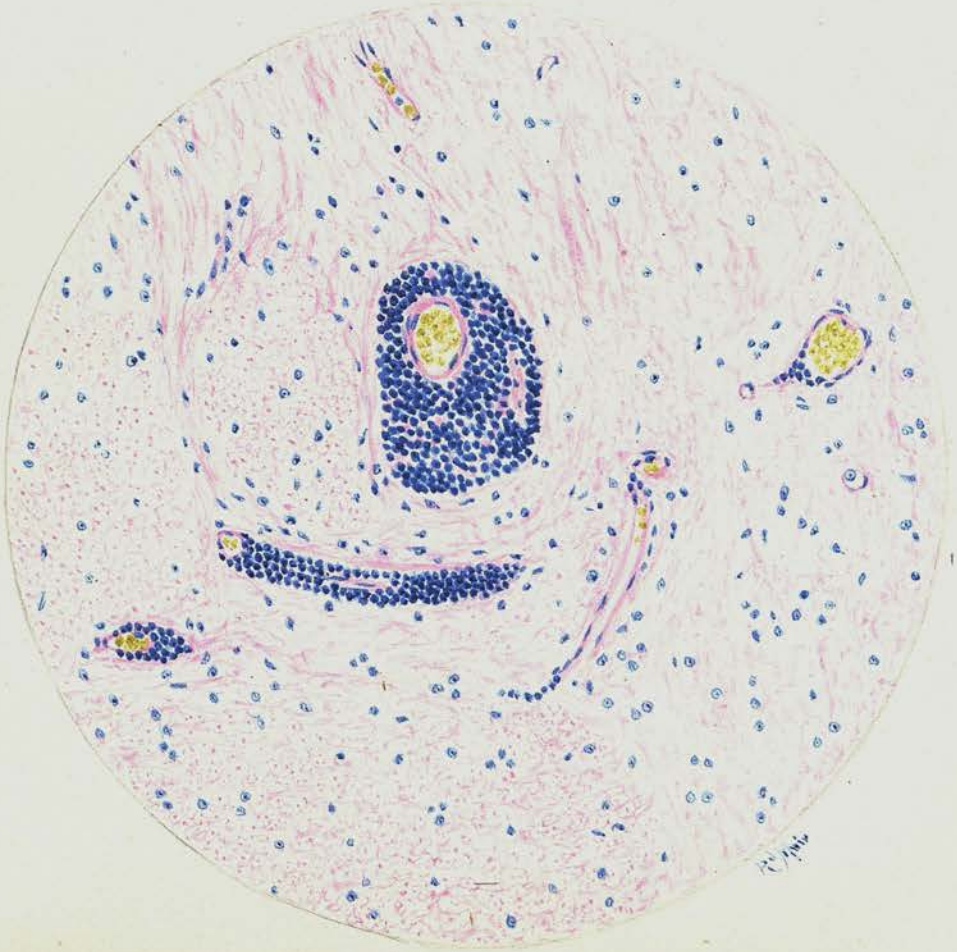


PLATE 3., Section of brain of chronic case of sleeping Sickness, Dreya,. Shows the characteristic perivascular infiltration of lymphocytes and plasma cells Stained Carbol-Thionin and Erythrosin ×300

the trypanosomes are found in number during life, show exactly the same cells, as have been depicted above. These cells are the result of chronic irritation produced by the trypanosomes. It is particularly interesting to find the Plasma cells in the gland, and Mott has been able to prove by an examination of glands sent him from Uganda, that they are derived from lymphocytes. He has been able to trace all stages from a cell consisting almost entirely of nucleus to the development of one with abundant granoplasm and the nucleus pushed up to one end of the cell; the development of the plasma cell from the lymphocyte, under chronic irritation of trypanosomal infection, is easily observed in the lymphatic glands of sleeping sickness.

F. The Pathology.- It will be of interest to consider, briefly, how the morbid changes are brought about.

In the first place let us consider a few facts about the normal cerebro-spinal fluid. It is clear like water. The specific gravity is 1,006, the reaction is slightly alkaline, and is devoid of all corpuscular elements; it contains only a trace of albumin; it becomes slightly cloudy on heating, and contains no ferments. It is a fluid sui generis. It is a true secretion. It is continually being secreted and, most authorities consider that the choroid plex-

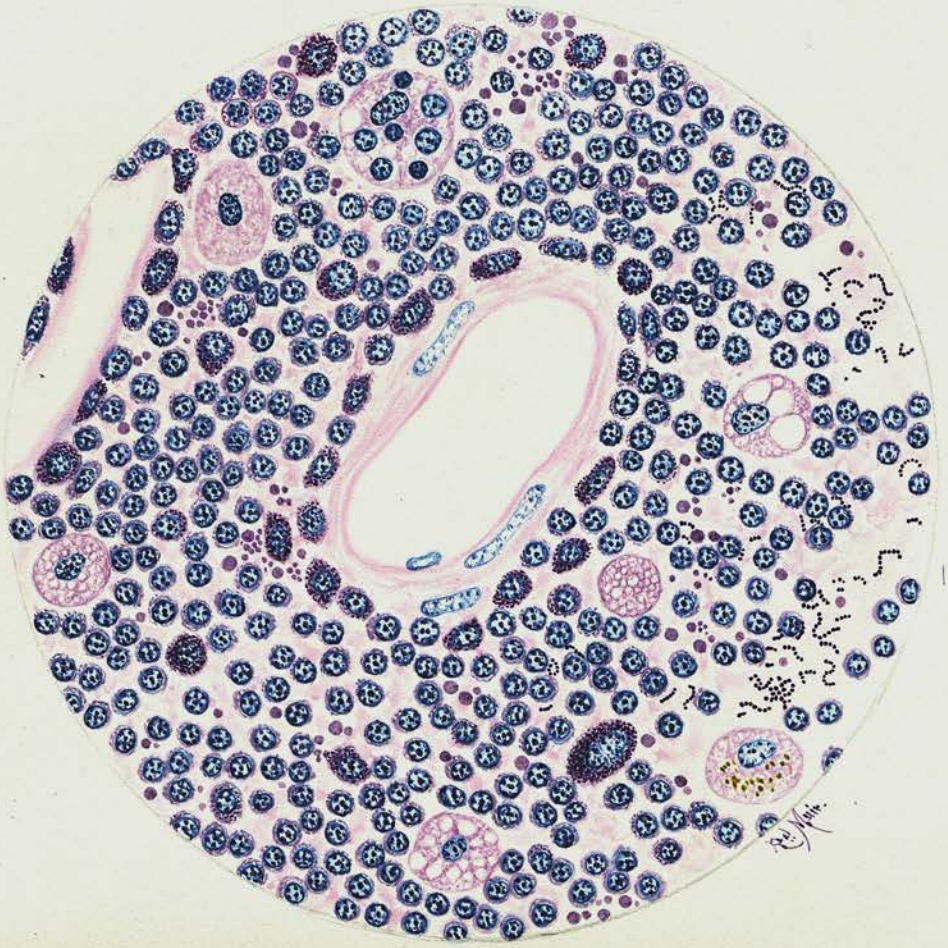


PLATE 4., Section of brain of case of Sleeping Sickness ness, Abimerika,. Shows 1) Small lymphocyte, 2) Large lymphocyte 3)Plasma cell, 4)Granule cell,5) Granules of disintegrated granule cells, 6) Diplo-streptococci. Stained Carbol-Thionin and Erythrosin. × 800

us secretes it. This fluid, which is being continually secreted, must escape in some way. According to one view it escapes along the lymphatics of the cranial and spinal nerves, through the paravertebral lymphatic glands into the receptaculum chyli and thoracic duct and eventually returning to the venous circulation. Others believe that it escapes through the longitudinal sinus, according to Cushing a free communication exists between the sub-archnoid space and the longitudinal sinus. For such a complex organisation as the cerebro-spinal axis, it is essential that it should be protected by a self-adjusting mechanism for uniform equalisation of blood pressure under rhythmical variations of circulation and respiration, and from the chemical products of it's own activity, by a fluid which can continually circulate most readily, and yet be the medium of gaseous exchange between the blood and the tissues. Does the cerebro-spinal fluid perform this function, or is there, as Sicard maintains, a perivascular sheath enclosed by the cerebro-spinal fluid? Mott from an examination of sleeping sickness cases inclines to the view that there is "What looks like a delicate sheath containing lymphocytes surrounding the vessel and outside this the canalicular space containing the cerebro-spinal fluid, across which delicate fibrils stretch, very probably fibres of neur-

oglia cells".

Let us now endeavour to explain the phenomena met with in sleeping sickness by the facts which have been brought out in this research.

In the early stages of the disease, we have enlargemant of lymphatic glands, and examination of these glands shows a constant lesion, and this is brought about by chronic irritation, and is exactly similar to the lesion which is found in the brain at a later stage. Associated with this change in the glands is the presence,in number, of trypanosomes. The glands by a rapid multiplication of their cells are able to keep the disease localised. That they are destroying the parasite is seen in the many degenerate forms of trypanosomes met with in the gland juice during life, and further that the glands are active is seen in the increased numbers of lymphocytes found in the peripheral blood. So long as the disease is confined to the glands there are no nervous symptoms ... that is,that the characteristic lesion of the nervous system has not yet been produced. Trypanosomes are never found in the cerebro-spinal fluid at this stage. When the trypanosomes begin to be found in the cerebro-spinal system the nervous symptoms develope and with this the cells appear in the fluid and these mononuclear cells increase in number until as many as 300

400 per cmm of fluid may be counted. Mott states " the characteristic symptoms of the disease are undoubtedly due and proportional to the extent and degree of the meningo-cephalo-myelitis, and it is my opinion that the lethargy is due to cerebral anaemia caused by the compression of the small vessels, by the accumulation of small lymphocytes in the perivascular spaces, and the mechanical interference thus produced in the circulation, and the obstruction to the bio-chemical changes incidental to the activity of the neurons. The tremors, paresis, fits, attacks of mania, and hyperpyrexia are, probably, the results of irritation phenomena associated with stasis in the vessels, degeneration changes in the neurons, and neuroglia proliferation. The early affection of the cerebellum, the mesencephalon, and the medulla oblongata by the lymphocytic infiltration is, very probably, connected with the noxious agent in the large collection of fluid at the base of the brain. In chronic cases, which linger to the last stage, marked bulbar symptoms may arise due to anaemia of the medulla and degenerative changes of the neurons."

It is difficult to find trypanosomes in sections of the brain. This is due to several reasons, 1) The technique is difficult, 2) We have to remember

that the patients are practically dead for some days before they actually do die. At this stage terminal bacterial invasions occur, and to these the trypanosomes are very sensitive, and which bring about some alteration in their appearance. Mott states " I have seen crowds of round bodies, measuring from 1μ to 2μ in diameter, lying about the cells of the perivascular space and sub-arachnoid space, but I am unable to differentiate any structure. I am of opinion that they are mostly disintegrating cell protoplasm, but a few might be a modified form of trypanosoma or altered nuclei or micro-nuclei of these parasites".

We see from a consideration of these facts, that the disease is essentially one of the lymphatic system. The causal agent, the trypanosoma, produces chronic irritation, this results in overactivity of the cells of this tissue, which block important food channels and in this way the cells of the various organs are starved to death, and in this way all the characteristic signs and symptoms of the disease are explained.

23. Works referred to in this Thesis.

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3. Cerebro-spinal fluid in relation to Disease of the Nervous System. Mott, B.M.J. 10th Dec 1904.

4. Johnston, Uganda Protectorate.