Thesis.

Human Trypanosomiasis.

James Dunbar Brunt"on
M. B.
Human Trypanosomiasis.

Sleeping sickness was noted for many years as a disease afflicting natives in some parts of Central and West Africa of a constantly fatal character. While the intermediate stages of the illness were not definite, the termination of the malady in unconsciousness and coma with protracted incoherent observations. In want of a better understanding of the nature of the sickness the end of the illness became the cause of its unmentionable.

This name in the native language of central Africa signifies the cause of the disease. The name that is general for this illness is "Mâlâlé." The derivation of this may be either from a corruption of the French word "maladie" as used in the Congo or still more likely from the Swahili and "lala" or sleep.

For long before the occupation of the country by Europeans, Swahili traders penetrated the country in all directions, prisoners and slaves.
ago as 1803 Winterbottom wrote that these traders used to procure slaves with large glands as they were sluggish. It is more than possible they used the Swahili word “Walalla” meaning they sleep or are sleepy. At the same time this concurrence of glandular enlargement at the course of the disease was noted then as it is now. These glands are often so large as to be visible under the skin by the eye.

This deadly disease following trade routes has gradually spread invading fresh districts and places, till it has spread into East Africa. The first effort to find out the cause of the disease was made by a Portuguese Commission who emphasized the constant presence of glandular enlargement as part of the disease. They at the same time noted that these glands had somewhat hard consistency but no evidence of suppuration. Although the blood was examined by Jorde in 1901 who found a parasite which
was named as a *trypansome* by Dutton and Todd, it was not till 1904 that 
Mott suggested that the glands should 
be examined microscopically. 
Craig 
and Gray then excited some glands 
finding *trypanosomes* in their contents. 

They also showed an easier method 
of detecting their presence by needle 
puncture, aspirating the gland juice 
rather than by excision. This was 
an important step in the progress 
of diagnosing the disease, for then not 
only could readily puncture be used 
but the very presence of the enlarged 
glands showed more than a possi-

bility that the individual so affected 
might have the disease. The exam-

ination of individuals by palpation 
of glands became a general means 
of detecting the disease. The 
parasite found first in the blood 
then the glands, and finally by 
Castellani in the cerebro spinal 
fluid, was shown by Bruce in the 
present misery case of sleeping sickness.
When it became known that the parasite caused the disease, Bruce who had been working at an allied disease in animals suggested a tsetse fly was the carrier of the cause of sleeping sickness in human beings. The tsetse fly distinguished by colour and habitat and known entomologically as Glossina palpalis was found in every district where the illness was. Many experiments by several investigators were made to determine whether the disease was exclusively carried by this fly. This at once opened up a wide field of research amongst many biting insects. It is now known that the carrier of this disease to human beings is &Glossina palpalis only. Without this fly in a locality, human beings are not infected with sleeping sickness even in places where G. morsitans is exceedingly plentiful. And again it is quite usual to find villages in similar streams the one heavily infected with sleeping
Sickness while the other is free a few miles away. Where the disease is, the fly is there. Similarly, by converse if a number of natives are examined by gland palpation and are found to have bilateral enlargement of cervical or other glands, of even small size, it may be surmised with certainty that they have lived in the proximity of a cow been bitten by S. Palpaliis, even though no acute cases of the disease were seen. In my own work in connection with this disease I have never known this action fail.

"Bilateral enlarged glands mean S. Palpaliis." If many natives in a village have these glands the stream is examined and the fly found. In contra I have palpated villages in which S. monocarsa swarmed biting savagely, and found not one case of enlarged glands. The question whether this fly may convey the disease is practically decided in the negative.

Its habitat is never the same.
its breeding grounds, as S. Palpatus. This will be discussed later. I am personally of the opinion that S. mosquitans will not carry the infective human trypanosomiasis. This is also the opinion of Dr. Pearson who has had much experience in the Congo Free State. I have stated that the presence of bilateral enlarged glands indicates trypanosome infection. Snyth and Colloch say in a report of the sleeping sickness commission to the Royal Society: "The very fact of the enlargement of the glands of the neck presenting ... glands smooth separable movable and soft with consistency of grape damson ... may thus be taken to be itself almost sufficient proof of trypanosomal infection if it occurs in inhabitants of a sleeping sickness area."

I go further and say that glands having this character are never found unless there has been trypanosome infection. The native so affected may be a
Solitary case who has taken up his residence in what is known as a "clean" area; that is free from sleeping sickness. Nevertheless, he has lived at one time in a locality where S. palpalis exists. Even if his glands are hard and small and pea-like, yet bilaterally enlarged, the presumption is that the man has been bitten and injected by the fly. This enlargement of gland varies according to the amount of trypanosoma infection, individual resistance and period grimmer. Thus enlarged prostatic or enlarged glands will be found where fly is plentiful than in another locality where the S. palpalis is more scarce. The individual resistance is not easy to gauge. Many seemingly strong and powerful individuals rapidly decline and die after infection while others of poorer physique will linger for years. I have noticed in examining villages infected by proximity to fly that pro-

-larged glands are more difficult to find during the rainy season even
though at that time the flies are most numerous. The same village during the dry season will produce many more cases of enlarged glands. The only reason I can give for this variance is that in Africa the rainy season is the time for harvest and plenty of food, so that all are well fed thus increasing bodily resistance with possible diminution of the parasites and its products.

During the long dry season with a hot sun and constant wind there is but little green food, and the principal diet is cassava or other flour eaten with dried fish or meat if they can get it. Many villages are on short rations at this period of the year as the natives are very mis provident. Thus the people suffer a deterioration in physical strength and well being. With the lowered bodily strength there is less resistance to the trypanosome tsetse with corresponding symptomatic enlargement. It is not easy to perform this by the microscope as numerous blood examinations may be negative.
ni result. This is especially the case where the disease is advanced, the trypanosomes concentrating in brain or spinal cord and difficult to find in the peripheral circulation. For purposes of classification certain symbols have been adopted. Indicate the size of the glands found on palpation in this disease. Large soft glands are designated in reports as +. Medium glands as ++ and small hard glands as +++ and absent -- (minus).

+ glands are puncturable and contain trypanosomes.
++ glands are puncturable but smaller and frequently negative on puncture.
+++ glands small hard unpuncturable.
--- glands none.

The + -- glands are often seen in the last stage of the illness where the cell elements have been absorbed and only the thickened capsule left. The large + gland is found during the period gastric invasion. The median during the course of the illness when the trypanosomes are usually found in ithe
circulation rather than in the lymphatics.

Dutton and Dooler noted that the glands diminish as the case advances. In visiting villages a certain number of cases must escape the medical officer under the gland palpation which is the only means used by the medical officers for the detection of sleeping sickness on these occasions. It is not possible to examine the blood of many individuals in an infected village who may have the disease and yet have no glands from不认识. It is only the + 1 + - glands that are segregated.

There may be advanced cases which are hidden in the huts by the villagers or even carried out into the bush till the visiting medical officer has taken his departure. These deaths are never known of or reported. Yet another difficulty in getting cases to segregate is the fact that natives who have small glands will run away or hide so as not to be seen on a further visit. The people
Knew that sleeping sickness means segregation in camp away from the village
prevalent of all sorts so affected. To illustrate this: I may mention one town where
I had examined all the people as I thought. Yet a few weeks later on
examining a number of men presenting themselves in labour from
the same town I got two cases of
plague who were promptly
taken into my camp.

The natives will be seen examining
their own stools weekly for plague
in villages so well have they learnt
the lesson that plague palpatore
means.

Knighton and
Montgomery who went through
this district previous to my appoint-
ment did as resident (former
district) dispute the accuracy that
plague mean trypanosoma vi-
pection always. My experience
in examining some 8,000 natives
is that bilaterally enlarged gland
means if not actually trypanosome,
in the individual, at least the presence of *Physalia physalis* in the district. In no cases have I found these bilaterally enlarged glands in villages away from this fly. Any individual so affected will be found to be infected cases, men who have been infected districts or those bitten. I look upon all such having those glands as suspects.

**Prevention of the Disease**

Human dengue fever is primarily produced by the bite of *A. aegypti*. whereby the parasite it harbours is introduced into the person so bitten. It is not every fly that harbours the parasite. Again, there is no doubt that it may take many bites. But infect some individuals while others are infected at once whereby the fly in filling itself with blood introduces the parasite. So prevent this infection by measures and the spread of the disease and measures are ni
general use in infested areas.
(a) Compulsory Removal of natives and villages from fly-infested localities.
(b) Endeavoring to clear the fly away by attacking its habitat.

(a) Removal of natives

The African native is very apathetic where the general good is concerned and very philosophical in accepting evils as sent by Providence and therefore beyond control. This makes it a hard task for Europeans to persuade them to undertake or carry out measures for the general safety. Men who catch fish in fly-infested waters will go on using the same waters even though they see & know that the fly is killing them. If removed at a distance the villagers will steal back to these waters till their cause is broken up.

The observations made on the habitat of S. palpalis show that not only
is it very conservative in keeping up certain hams to, but that it will not be found many yards away. In searching for it, it is frequently necessary to beat the bushes before one is seen while at other times they will come out into a meadow or lake after a boat. Similarly, they will not cross a clearing a few hundred yards wide even though a village is there.

When introduced men this distance into a village it is by attacking themselves and not the victim. This dislike of the fly to cross a clearing or any distance has been taken advantage of in the removal of villages to a safe distance. Infected cases are put into a special segregation camp. Thus the village being removed the fly can get no more victims so with the segregation of actual cases the safe guarding remains.

is made more certain.
B. attacking the habitat of the fly.

Cerania Balpallis is never found except near running water or clean lake water. This has given a useful fact to work upon to those who are endeavouring to combat its spread. Not only is it found only in certain specific places but others where one might expect to find it are free. Also if a stream is clear of marshy imp bush and shade the fly will not be found, though it has been found on Lake Tanganyika on another shore. The fact that S. Balpallis does not shade has been noted upon in cleaning away all trees and bushes in fly-haunted localities which the hope that it will clear them away.

In this district (Lake Kivu) this has succeeded very well. Two years ago several places on the Shire (N.S.R. Ride) were heavily overgrown with scrub and sheltered large
Members of S. palpalis. In a year past wherever near a village or plantation all these infected parts have been cleared of tree trash and burnt clean, and no flies are found afterwards. This of course has been followed by a lessened number of infected cases. This can be shown by the following table from my book showing the census of a village before and after clearing away the habitat of the fly.

<table>
<thead>
<tr>
<th></th>
<th>Before Oct 07</th>
<th>after July 08</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mao village</td>
<td>0 4 26 290</td>
<td>0 0 4 282</td>
</tr>
<tr>
<td>Lake Murum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The value of clearing has been confirmed in other parts of Africa where the disease exists.

This is the case where no want of a suitable site the village must remain and then an area at least 200 yards in all directions is made clean which the fly will not cross. It is possible that a dragon fly eats them when they venture out from the shade. Also direct heat from the sun kills their purpose which
are always found on my shaded banks near the water. It is difficult to know what is the ordinary food of these fish. Many places where they are very numerous are never visited by men or animals with the exception of the hippopotamus and the crocodile. I have examined the blood of the hippopotamus several times as a possible host for trypanosomes but with negative results. Water snails and the small water fowl which inhabits marshes are not bitten by the fly when shoot up together in the same bottle. Her 12 other bloods show anything. I have noticed that where T. petechialis is found a very large red & black beetle is also common on all the bushes. I have not succeeded in isolating its laws.

The Diagnosis and Treatment of Human Trypanosomiasis.

The diagnosis of this disease is for obvious reasons not usually made till late. In not only 20 many of the
natives who are suffering from sleeping sickness show no signs or symptoms but actually express themselves as fit for work and strong as well. This state of good health may exist for a year or even more depending on the amount of Trypanosomes in the blood seemingly rather than on the physique of the man himself. A strong infection or slight infection are my relative terms. I would say there is one vast infection and that according to the rapidly increase of the Trypanosome intravascularly, so is the case seriously ill in the disease prolonged in its course. As to the increase of the parasite Schaudinn has it that it is done by prions. I am doubting of this though admitting its possibility. I think it is by spores though no microsome has yet shown this. If the increase is by prions what is there to prevent a man dying within a few days of the disease through the compound multiplication of these parasites which phylogensis can't
injury? Its slower course favours any theory of spirulation. For these espèces can be attacked in the blood and many destroyed. We know clinically that the increase of the parasite in the blood is not always going on. It is often difficult to find one in a case that at other times shows plenty and that apart from inhibitory influence of drugs. G. Martin and Debret noted that trypanosomes varied day by day in number in the gland juice. So that many die in the blood, there is no doubt.

The diagnosis is made by
(a) Physical signs. (b) Symptoms
(c) Examination of blood, gland juice in special fluid for the parasites.

(a) The presence of enlarged glands has long been noted as constant in sleeping sickness. Cases in the districts where natives die of the disease. They are painful enlargements which come no distress un at the suppuration.
There are always bilateral and may be found in the axilla, semic and above elbows as well as in the neck. In some cases they are so large as to visible as the skin is caused by them. Another sign I have noticed in advanced cases is a curious wide spread purplish raised eruption resembling pityriasis. This may be in large patches all over the body. In natives the rash noted in Europeans is not seen to distinguish. This is the well known erythema. I have seen nodes on other swellings as have been described.

6) Symptoms. These in early cases may be entirely absent but most cases have severe headaches. There are invariable when the disease is advancing and the pain is wide spread over the cranium. Others complaining of weakness and lassitude, one symptom is nearly general and that is loss of sexual power. This is not simply loss but loss of sexual desire, as he is nothing if not for his amorousness. This might be there
is a valuable symptom in suspecting hypertensive infection together with the enlarged glands. Eye symptoms such as iritis, retinitis, and photophobia are seen in advanced cases. They may be due to intraocular lesions as much as local eye changes. They have been present also on the eyelid in a few cases.

The nervous symptoms are very varied, according to the progress of the disease. Fatigue and headache are usual, with rest and restlessness. The most common cause is often present. Excitement and shortness of breath at any stage of the disease are common. Numbness and tingling of the skin, as well as some dryness of the mouth, are frequent. The reflexes of the legs and ankles are variable. They may be very increased or absent in similar cases.
I have seen cases where the reflexes were increased on one side the right generally while diminished on the other.

In several cases before death any patients complained of giddiness with a marked deviation and falling away of the left on attempting to walk. One case while complaining of this giddiness had intense pains in both legs almost approaching neuritis. His head aches were severe & he lost all power of expression & in articulately ten days before his death. He never became comatose but died suddenly on attempting to walk.

Deep hyperaesthesia was observed first by Herandol. This is a state of the times where a slight knock, blow, prick is followed in a short time by an excessive pain out of proportion to the amount of injury. It does not last long. "It is a symptom pathognomonic of typhus-malaria" (ibid)

By microscopical examination gland juices or blood in other body fluid
In a suspected case of sleeping sickness, by means of this examination we have a certain means of finding the parasite if present. As soon as the trypanosomes are found, the case is put under treatment as an certain case of sleeping sickness. Till the trypanosomes are found, no treatment is given that frequent observations of those are made.

If the glands are palpable, puncturing them is the best means of finding trypanosomes. This is done by picking up the gland between thumb and finger of the left hand. A sterilized needle, having its tip sharp, is then steadily pushed through the skin, gland capsule till the point is felt just at the side of the gland. The syringe is then attached and a small drop of the gland juice is injected and ejected over a slide or cover glass put over it. If a good specimen with many gland cells the parasite should be found on examination. The fresh blood is examined the same way from
ear or finger. It may be necessary to centrifugate blood before the parasite is found. The spinal fluid is aspirated in the lumbar region. Martin and DeBoer got 88 percent of successes in suspected cases by centrifugation of the blood and this method seems to be the best.

Treatment of cases.

I have already said that all cases or suspects are put into a special isolation camp for observation and treatment. These natives are well treated, have their wives and children with them and all is done to make the detention as comfortable as possible for them. If necessary all with the cured and return home. Even if they have no trypanosomes they are kept rather than that they should become possible sources of the spread of the disease. Koch noted that the uninfected men died of the disease though not bitten by the fly. He said that
was caused by inoculation of the parents through coitus. He did not observe that there is any gytes in sleeping sickness. There is a much more likely source of direct spread that is through the blood. All sleeping sickness patients are specially liable to be attacked by jiggers. There are cut out by the man's wife who will use the same knife immediately afterwards smeared with blood stained to cut out a jigger from her own foot. Thus we may have a bilateral unsuspected source gneculation.

(c) Special treatment. Many drugs have been tried to cure the disease. The one that up to now has proven the best result is the soluble salt of sodiun arseniate. This is administered in various doses by injection into the body tissues. It is found that combined with necessary by the patient the best results are obtained. Either drug per se seems to have no great
Power to destroy the trypanosome or scene the patient. The method adopted by the medical officers in K. Rhodesia is the following.

One gramme of atoxyl is dissolved in 5 cc distilled water. This equals a 20% solution. As this does not keep only enough is made as required. Of this, a dose of 0.5 gramme equal to 2 1/2 c.c. is given subcutaneously every 10th day. At the same time 2i of the oil Hy. Perrin, (1g88 - 3i) is given by the mouth three times daily till saturation takes place. The atoxyl is discontinued when trypanosomes disappear from blood and blood. The disappearance occurs under this treatment is very rapid physically. At the same time sexual power frequently returns.

During the treatment the trypanosomes are very hard to find. It is possible that the drug cause not so much semicidal effect.
in the parasites but within a vigorous leucocytosis. If the disease is increased by multiplication of the parasites then we have the sudden betterment under treatment. The fact that the phagocytes can devour the spores does not prevent increase. It has been noted that the parasites are sluggish after a dose so would thus fall victims to their destroyers. Experiments made in vitro with trypansomes and leucocytes have given negative results. Other drugs which have been used in the treatment of the disease such as tartar emetic I have no experience of. My treatment in all cases beings the combined drugs: mercury. I experimented with sulphides of mercury. In some cases I administered 10-20 pence daily. In more cases this treatment was administered to a man who had large glands and trypansomes for 20 months. During this period he had no trypanosomes.
The gland cells were stained green by the sulphur but showed no diminution in size. I cannot say that his health improved under this treatment. At the end of the third month I put him on the combined treatment when the glands shrank at once. This man came away from the camp shortly afterwards to the Camp. He was quite well at the end of a year afterwards as he was seen reported.

Conclusions

Much has been done, and is done by numerous investigators to further the complete knowledge of human diphtheria. The greatest difficulty is to find the original work of the diphtheria. The source from which greenia paralysæ acquire it to pass it to human beings. For though many epidemics have arisen from this bane, none became infected with the sleep-sickness.
patients or rather individuals suffering from the disease, neither epidemics nor fliers have started it when no human infection can be traced. Again we have a river which contains swarms of Glossina palpalis like the Kalinguini River with a resident population of 2000-3000 people on the banks where no sleeping sickness cases have ever occurred.

It is certain that the normal food of these fliers dwelling as they do in thick bush close to water cannot be human blood. I have gone down the broad Luapula River in a canoe for 60 miles Nothing particularly. Here it abounds in swarms, yet there are no dwellings on the banks or human habitations. There are a few fishermen and travellers in canoes who use this waterway so that only one fly in a thousand could get a
meal of human blood. Yet they increase.

The body juice of some creature is necessary to the development of the larva in ventro matrix. Before it is extruded. I have examined the fresh blood of horses several times with negative results. I have shut up hungry flies in gauge stoppered bottles with the small water frog which lives beside the fly. But have only used one tentative assault upon the web by the very fly. The pop punctured away. Stails collected from the bottle the flies have amongst one not touched. Rock has sus-
ppected crocodiles but it is dif-
ficult to see how a fly could draw blood from a crocodile even while asleep on a bank with open mouth. The mucous membrane is extraordinarily hard. It is true that crocodiles are frequently numerous where the "fly" exists yet we have
the distance above seizure of the Kalumpurisi River where 20 crocodiles have been seen on one day. Yet the flies are not repelled.

I have not been able to verify another theory that the trypanosome is acquired by the fly from the "long fish." This is very doubtful to me here in the Kalumpurisi River as well as the crocodiles.

My opinion is that the fly feeds on a large grub in a cave. I have noticed that where the fly occurs generally at the same place there are numbers of a large red and black camphort beetle two inches long which crawl about the clefts and branches among which the fly hides. These beetles are most numerous among termites as are the flies. I have not been able to find the larvae as yet.

J. faurei as produced in culture loses membrane of tegument
They are not sterile. I have suggested to the London School of Hygiene Medicine that there was a parasitic device to simulate the movement of normal blood at blood heat, the motion might stimulate the non-motile trypanosomes into becoming flagellate and motile again. Then further investigation could be pursued as to their increase whether as Schaudinn says by trophic but more likely by spores. We plan a sexual cycle to the malarial organism. The binucleated trypanosome is much higher organism in the microvascular world.

We use gland palpation as a means of detection. This as I have stated is the usual means relied on for the detection of sleeping sickness when examining villages. All these places are punctured and if clearing up trypanosomes in their guise or in the blood the individuals are not suspected. But every now and again cases are punctured...
and instead of Trypanosomes filaria, vestiges is found in the glands. The blood is usually at the cause.

In these cases the glands are never symmetrical as in sleeping sickness, and are irregularly distributed.

James Dunbar-Bretton MD

November 1909
Kwamaubwa
W. Rhodesia