On Trypanosomiasis in Man; with special reference to Sleeping Sickness and the so called Trypanosoma Fever of Equatorial Africa.

With a comprehensive Bibliography.

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— Preface —

In submitting this paper, I would call attention —

Firstly, to its attempted scope. The term Trypanosomiasis in man must in fact, in recognition of the researches made during the last two and a half years, embrace the the whole subject of "Sleeping Sickness" and also of course include in its compass the allied subject of the so-called "Trypanosoma Fever", the latter being now regarded by the majority of observers as the first stage of Sleeping Sickness proper.

Had this paper been written a few months ago, it could by rights have been strictly confined to the above subject; but it happens that during this short interval of time, Rogers of Calcutta has, out of the Cunningham-Leishman-Donovan bodies of one form of Tropical Splenomegaly, succeeded in cultivating a Trypanosome.

This achievement would immediately bring the whole range of Tropical Splenomegaly under the title of my paper. In view however of its difficulty,

and of its present complexity, and in view also of the unweildiness, so to speak, it would lend to the present work, I have decided to exclude it altogether from the paper, but to refer to it in the Bibliography appended.

Secondly;- In consideration of the recent and beautiful researches of Schaudinn, showing that the Halteridium of the Little Owl is but a Stage in the life cycle of a Trypanosome, and pointing to the fact that the Spirochete of Relapsing fever may be bodies of the same nature, the latter disease might well be included in the subject of Trypanosomiasis in Man. But as nothing further is known as to its true Etiology, I have, except for mentioning it in this preface, decided to ignore it altogether.

Thirdly:- This work was mostly written during February, upon facts that were to hand up to the end of 1904. I have thought it best to make this explanation here, because of the rapidity with which knowledge and observations are accumulated on a subject like the present.

R. A. B.

London. 1st March 1905.

Table of Contents.

Chap. VII

Chap VIII

Pages.

Chap XI

Chap XII

(See over)

Page.

Chap. XIII

Chap. XIV

Page.

— Chapter I. —

Synonyms.

Besides the native names the disease is known by European Observers as Sleeping Sickness; Sleeping Dropsy; Negro Lethargy; African Lethargy; Die Schlafkrankheit der Neger; Malattia de Sonno; Doencade Sonno; Enfermedad del Sueno; Maladie du Sommeil; Maladies des Dormeurs;

It is suggested by Castellani & Low that the malady might perhaps be more correctly termed African Meningo-Encephalitis, or shortly African Meningitis.

Definition.

Trypanosomiasis (Sleeping Sickness) is an infective disease due probably to a trypanosome, giving rise in man;- Firstly to a remittent fever of a chronic type, to congested areas of the skin, local oedemas, a mild anaemia, increasing frequency of pulse and respiration, sometimes enlargement of the

Spleen & general wasting and weakness;

Secondly to a slowly increasing lethargy of an acute or Chronic course, always terminating in death. —.

Historical Review of the Older Work and Literature on the Subject.

Winterbottom[1] seems to have been the first to describe Sleeping Sickness just over a hundred years ago. Then papers appeared by Clarke[2] Dangaix[3], Nicolas[4], Santelli[5] and others; papers which give the Symptoms and Coarse Morbid Anatomy of the disease.

In 1869, Dr. P. A. Guérin[6] published an excellent Thesis on Sleeping Sickness, during a period of about twelve years in Martinique, Guerin

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(1) "An account of the Native Africans in the neighbourhood of Sierra Leone" London 1803

(2) Lond. Med. Gaz Sept. 970 also Edin Monthly Journal. 1842. April.

(3) Moniteur de Hopit. 1861. No 100.

(4) Gaz. hebd. de Méd. Oct 6. 1861. - 70.

(5) Arch. de méd. nav. 1868. Apl. 311.

(6) De la Maladie du Sommeil. Par. 1869.

had an opportunity of Studying 148 Cases of the disease in negroes imported from the Congo. In Some Cases the period of incubation lasted five years or more. The disease did not spread to the black Creoles of the Antilles, nor to other Congolese who had been in the Colony Some 40 years.

In 1876 + 1877 Drs A. Corre (1) published Some very interesting papers on the Same Subject. Corre had made a Special Study of the disease in the Severely affected districts of Joal and Portudal in Senegambia. He laid Special Stress on the paludal nature of Sleeping Sickness Centres, and remarked that the disease may attach itself to a particular house or a particular group of houses. He referred to the fact that patients believed they had Contracted the disease during the rainy Season). In his first paper, Corre Conjectured that the disease may be a Kind of food poisoning analogous to ergotism and lathyrism, but

(1) Gaz. méd. de Paris 1876 Nos 46-47 + Arch. de méd. nav., 1877. Avril 2e2 Mai

later he put it down to scrofula on account of the frequent occurrence of glandular swellings. Corre gives an admirable account of the Symptoms of the disease. He noticed that in most cases, a regular evening rise is the characteristic temperature; he also noticed the opacity of the Cornea in Some cases.

Other writers were Ogle;[1] Abbart[2] Forbes,[3] Cook,[4] Hodges;[5] all of whom recorded their African observations; whilst Manson[6] in 1900 gave a Complete description of the cases of the two Congo natives brought over to England for Study. In addition in 1890 Mackenzie[7] published the record of a case which was under his care in the London Hospital.

The pathology of these later cases was fully worked out by Mott.

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(1) Med. Times & Gaz. 1873 July 6 (information by MacArthur)
(2) Arch. de méd. nav. 1883, Dec., 456.
(3) Lancet. May 1894. p. 1185
(4) Jour. of Trop. Med. July 1901 p. 229.
(5) Ibid. Oct. 1902 p. 293.
(6) Ibid. Dec. 1898 p 121; also Tropical diseases London 1898; also Trans. Path. Soc. 1900.
(7) Clin. Soc. Trans. 1890 XXIV

Many theories have been brought forward from time to time as to the causation of the disease, all of which have now been abandoned. They will be mentioned and some of them discussed later.

More recent work comprises the discovery of the Trypanosome in animals and in man, the labours of the Portuguese Commission (the discoverers of the diplococcus); of the two Royal Society Expeditions to Uganda, and the works of Castellani Bruce Nabarro, Christy and Reig; the various Expeditions of the Liverpool School of Tropical Medicine to West Africa, and the chiefly confirmatory results obtained by Dutton, Todd, Christy, Annett and others.

Much attention has been paid to the disease in Senegambia by Marchoux and Dantig; in the Congo district by Brodin & Brumpt; in Uganda amongst others by Cook, Moffat, Hodges & Baker. Also there were the important independant and quite recent researches and observations by many workers,

that have been carried out here in England & America, and on the Continent, as to various points in relation to the parasite incriminated. These will also be referred to in their proper places in the course of this paper.

The Mortality and Importance of the Disease.

No reliable statistics exist giving the number of deaths from this cause, but all reports point to the fogure being very high indeed. The dread of the natives of this disease is very great. When Sleeping Sickness appears amongst them they sometimes abandon whole villages and districts in the endeavour to escape from the deadly scourge. Nabarro (1) states that no fewer than 50,000 natives died in 1903 on the Shores of the Victoria Nyanza and in Usoga in East Central Africa. Bruce (2) said in 1904 that more than 100,000

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(1) The Lancet 23/1/04 p. 232

(2) Report of a lecture – Lancet 20/2/04 p. 543.

natives of Uganda had died from it, and some parts of the country had become almost depopulated.

In West Africa, in the district of Wathen (Congo) for instance, 4000 people died from this cause in 1902 according to the statement of a Baptist missionary.

Near Bundundu again, at the confluence of the Kwango and Kassai rivers a Government official informed the members of the Liverpool Expedition that actual depopulation of the country was feared.

The Portuguese Commission[1] reports that in Rinces Island in Portuguese West Africa out of 821 blacks who died in the year, 148 deaths were owing to Sleeping Sickness but this proportion is probably much too low, the causes of death being carelessly tabulated.

In animals again, Trypano-somiasis in one form or other is of the greatest importance. In some countries it is the cause of a heavy mortality amongst horses, cattle, &c., entailing large

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(1) The Lancet 29/9/02 p. 886.

monetary losses. The recent histories of Mauritius and of the Philippine Islands furnish examples of the economic problems that have been raised by the ravages of the disease. "The introduction of some Surra infected animals into the former country started the malady. The disease was very virulent and spread with extraordinary rapidity, and had not the Governor at an enormous cost supplied mechanical traction to take the place of that lost by the death of draft animals the island would have been completely ruined." The development of many parts of Africa must depend largely on the presence or absence of ~~the~~ trypanosomes in the horses or cattle of those areas.

The importance of the disease therefore need not be further particularised. All that need be stated is, that Trypanosomiasis in man in the districts in which it does exist, seems to rival and even surpass Malaria in its worst phases and habitats, taking into consideration the number of deaths it brings about.

Chapter II

The Geographical Distribution and Spread; and the Epidemiology

The Geographical Distribution and Spread.

So far as we are aware Sleeping Sickness is at the present time quite peculiar to the African Continent, where it has been known to European observers, at least from the beginning of last century. Before that period records do not carry us, and it is possible that judging from its still strictly defined distribution, it existed there from time immemorial.

The geographical distribution was at one time confined to that part of West Africa, which lies between the mouth of the Senegal to the North and Benguella province in Portuguese West Africa to the South; and including various islands in the Gulf of Guinea; roughly speaking between the latitudes of 15° North & 15° South.

"At times it caused considerable losses to the Slave traders of West Africa, notwithstanding the careful isolation of the sick, and the weeding out of all such as presented glandular swellings about the neck.
When any of the slaves showed symptoms of the disease on transport ships, they were mercilessly thrown overboard, Some developed the malady long after transportation, and died of it in the plantations of the Antilles; but the disease never spread in the places to which it was imported and therefore it did not give rise to serious apprehension."

Within the last few years, possibly in consequence of the great commercial stir which the advent of the White man has created amongst the native tribes of Tropical Africa, Sleeping Sickness has begun to spread very widely and has assumed a fearful importance in the Pathology of the Dark Continent.

It has spread to many districts hitherto quite immune as various observers concur in asserting."

To the South it has spread throughout the Province of

Angola + Princes Island in Portuguese West Africa. According to the Portuguese Commissioners[1] Sleeping Sickness is supposed to have been imported from the Gaboon by the slaves who were brought from that country to the regions above mentioned, and who by their marriage with the people of Angola originated the inhabitants of Princes Island.

Before 1887 there were but a few cases of the disease and the increase of it in the last few years is doubtless due to the great importation of Coolies from the infected parts of the West African Coast.

Up the Gambia Dutton + Todd[2] found in 1903 that the disease extended practically from the mouth of the River to the end of British territory, practically Some 250 miles up stream. How far it extended into the interior they were unable to say.

Up the Niger Cases have been reported from as far north as Timbuctoo

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(1) Report of the Portuguese Commission on Sleeping Sickness. Dated Loanda 10th Aug. 1901

(2) Researches on Trypanosomiasis in West Africa Brit. Med. Jour. 19/9/03 p. 650

and along the river of that name, the extension of the disease of late years has been important and rapid. In the districts about Boma and Leopoldville according to the Liverpool Commissioners[1] the disease was found very prevalent. From the latter town to Bumba, cases of Sleeping Sickness were present in practically every town visited. After Basoko and up to the Falls only imported cases were seen in a few of the towns. In the inland towns examined, cases of Sleeping Sickness were very rarely seen. Nearly all all of them were in the riverine districts.

From the expeditions own observations and from information collected by it, it is obvious that Sleeping Sickness has spread up the Congo in recent years along the lines of communication, that is, along the rivers. The spread has been much assisted by the practice of taking large bodies of natives, soldiers and labourers, from one part of the Free state to another.

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[1] Report dated Stanley Falls. 20/9/04.

From this region and proceeding along the new track routes which are being rapidly opened out by Europeans, the Scourge has appeared in East Central Africa invading the Shores of the Victoria Nyanza lake.

According to Dr Moffat[1] the first cases of Sleeping Sickness in Uganda were reported by the Dr. book of the Medical Mission, Mengo, in April 1901. The cases came from Busoga where the disease has become epidemic having been introduced probably by Emin Pashas Soudanese who were accompanied by a multitude of Slaves from the Congo.

The disease is now widely spread along the Northern Shores of the Victoria Nyanza. It extends from the mouth of the Katonga River, through Uganda, Kome Island, Busaga Buvuma, Kavirondo, Kisumu, Lumbwa Homa, Kasagunga, Lusunga Island, and down the Eastern Shores of the Lake to the South of the boundary river Gori even into German territory.

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(1) Reports of the Sleep. Sick. Commiss. Royal. Soc. Further Reports. p. 51.

Dr. Cuthbert Christy[1] who travelled nine months in that country says that the infection does not occur in the Upper Nile or along any of its tributaries and that "the infective area shows no tendency to spread for more than a mile or two northwards down the Nile or along any of its tributaries, nor along any of the Caravan routes or roads."

Natives date the beginning of the epidemic at 1896[2], but the fact that they in Uganda, were not acquainted with it is no proof that former epidemics have not occurred.

It is possible that the disease is endemic in certain spots, and becomes epidemic only under conditions favourable to it, which may sometimes occur after long intervals.

In the general endemic area places exist which are quite free from the disease. Except for sporadic cases for instance in Sierra Leone[3] and its hinterland, the disease is not known.

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(1) Christy - Brit. Med. Jour. 19/9/03 p. 648
(2) Hodges. - Lancet. 30/9/04 p. 290
(3) Renner - Jour. of Trop. Med. 15/11/04 p. 349.

Visitations come and go.
Manson[1] states "After decimating a village it may disappear for a time, migrating temporarily, as it were to some neighbouring village.....
.... It is an endemic area which is liable to epidemic outbursts".

"Whilst only to be acquired in certain places, its symptoms may appear in another country and many years (up to seven the negroes say) after the endemic area is quitted".

"In days of the slave trade Sleeping Sickness was frequently seen among the negroes of the West Indies; it was never seen in negroes who had never visited Africa. Thus the cause of the disease must be endemic."

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[1] Mansons "Tropical Diseases" London 1903.

Epidemiology.

Influence of water soil forest & plain.

If we study the local distribution in the localities where the point has been thoroughly worked out, as it has for instance along the northern Shores of the lake Victoria Nyanza, we are at once Struck by the fact that the infective area consists of a narrow strip of the Coastline, at its widest not more than ten miles Stretching along the Shores of that Sheet of water. (Christy)[1] The affected area also includes all the islands along these Shores. It was noticed in this tract of Coastline that the Sleeping Sickness did not affect the inhabitants of all places alike. "The disease was most prevalent amongst the inhabitants of low lying shambas (banana and potatoe plantations), in places along the Shore of the lake, or in wooded districts not far from the water. But even in these districts natives who lived in

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[1] Reports of the Sleep Sick Commis. Royal. Soc. No. III

villages, particularly if they were situated on high ground were much less affected than those living in the Shambas; and those living in large compact villages encircled by the usual high cane structures, were less seriously affected than the occupants of scattered villages in which the huts were surrounded by bananas or forest growth. People inhabiting populous centres, such as for instance, Kampala and Entebbe, were practically exempt, whilst those living in open grass plains were quite free from the disease."

Dutton & Todd[1] in speaking of the local distribution, say, that there is no evidence to indicate that there is one type of locality particularly subject to the disease, neither do they find that there are zones or belts of territory in which the malady occurs. "For instance although we found three cases out of thirty five people examined in one village situated amongst the mangrove swamps, still we have examined many other similarly situated villages,

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(1) Brit. Med. Jour. 19/9/03 p. 650.

in a far more thorough way, without seeing a single parasite. We have seen cases in low lying riverside villages, in towns placed on high ground, on the sea coast far from mangrove swamp or river, and in the upper river at Talotenda.....
The neighbouring country is very flat and extends in a sparsely wooded plain broken only by a fresh water marsh or two on all sides for a distance." These observations do not seem to carry much weight for they are not bourne out by other observers in other parts of Africa, nor by the writers themselves in their Congo expedition made later.

The marked peculiarity of this disease is its close connection with water. Corré many years ago laid special stress on the paludal nature of the centres of this infection at Joal & Portudal in Senegambia.

In the Congo, M. E. Brumpt also notices this peculiar characteristic of the local distribution. He instances a case to the point[1]. At

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(1) The Lancet. 29/8/03 p. 636.

Banamia close to Boquilhaville, there exists a mission worked by Belgian Trappists about twenty minutes walk from the Congo. On the banks of the river Some years ago there used to live Some 3000 Lolo fishermen. At the present time these fishermen number about 300, all the rest having succumbed to Sleeping Sickness. On the other hand, close to the Mission buildings there was a village of Cultivators who rarely went down to the river and who drank spring water. Among these Cultivators Sleeping Sickness is extremly rare.

Another Singularity about the disease is, that it clings to particular villages, even to particular houses or to groups of houses.

What is the reason for this peculiar distribution? The Subject will be considered when we come to speak of the Tsetse fly as the probable Carrier of the disease.

Influence of Sex. The disease attacks both Sexes in equal proportion.

Age has no influence. Christy Saw many Children affected

Some eighteen months or two years old. He remarks that it is probable children may contract the disease at a very early age, but owing to the long incubation period they do not exhibit symptoms until they are older.

Occupation. The influence of this factor is important. The large majority of cases occur amongst agriculturists and residents in the shambas. Bruce remarks that "it is on the densely wooded shores of the lake that the half naked natives of the mainland and of the islands meet in thousands to trade in fish bananas, earthenware &c . . . .

Social Status "Chiefs and the majority of the better class natives live in villages and consequently are less affected by the disease." (1)

Heredity. has no influence.

Race. Contrary to former belief, it appears that race is no obstacle to the contraction of the disease. Many cases have now been collected where trypanosomiasis

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(1) Reports of the Sleep. Sick. Com. Royal. Soc. No III p. 21.

has been observed in Europeans. One case is known in a Persian another in a Moor and still others in Mulattoes. Manson's case of trypanosomiasis displayed undoubted Sleeping Sickness Symptoms before she died.

The comparative immunity of the European is probably explainable by the fact that, according to the generally accepted theory, it is only through the bite of some insect that the disease can be contracted. Europeans expose a much less area of their bodies to the bite of such insects, at the same time they live in situations where the flies incriminated as the carriers of the disease are not commonly to be found.

Seasons. Christy could not find any evidence as to whether the disease was prevalent more at one time of the year than at another. The difficulty of settling a question such as this is obvious, when one considers that the duration of the cases extend over many months.

Influence of Climate. A high mean temperature in itself seems

to have nothing to do with the Causation. The Climate at Entebbe in Uganda, although only ten miles from the Equator is much like that of an English Summer.

Food. There is no article used in the infective area which is peculiar to it. The Staple articles of diet are milk, butter, millet and any kind of meat or fish, also bananas. "Fish have been Suspected by the medical officers of the Uganda Protectorate as well as by the natives as the Cause of the disease because of the close association of the latter with the Shores of the lake. If fish eating were the Cause, the province of Budhu would not be exempt."

Drinking Water. Many inhabitants of the infected area get their Supply from the Victoria Nyanza. Many natives, on the other hand draw water from Streams ponds and Springs. The fact that the infection prevails equally would Seem to indicate that the water Supply has no relation to the S/read of the disease.

In Entebbe, which is practically

Surrounded by the lake, both the Europeans and the natives use the lake water for all purposes, yet the disease is not to be found in the town itself.

On the Prevalence of Trypanosomiasis in the General Population

Reports on this subject are meagre and not satisfactory. It is true that from East Central Africa the information is fairly full, but the same thing cannot be said of the other districts where the disease is also rife. The following are those that can be traced.

In Portuguese West Africa.

The report of the Portuguese Commission states that sleeping sickness attacks 2½% of the negroes in the infected stations. Nothing is ascertainable as to the percentage rate of the presence of Trypanosomes in the blood and in the Cerebro Spinal fluid of the general population in the districts where the disease is endemic and in those where it is not.

In the Gambia. Dutton & Todd (1)

(1) Brit. Med. Jour. 19/9/03 p. 650.

Chapter III

On the Prevalence of Trypanosomiasis in the General Population.

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In the Gambia. Dutton & Todd (1)

(1) Brit. Med. Jour. 19/9/03 p. 650.

saw Six cases of Trypanosomiasis in the native and once in a white man (Quadroon). Over 1000 persons in the Stanbrain district had their blood examined.

These figures they themselves mention, should not be taken as exact both because the number investigated is too small, and because those who were examined, were only those individuals who could be persuaded by small bribes to be pricked. The Commissioners think that they are justified in assuming the disease to be much more common than the numbers seem to indicate.

In the Congo district.

Messrs Dutton Todd & Christy in their report dated April 1904[1], state "out of a total of 465 natives coming from all parts of the Congo as well as the districts round Leopoldville, where they were examined, 54 were found to have trypanosomes in their blood. and out of 707 examined at Boma Matadi & in the Cataract region of the Lower Congo, 49 were

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[1] 2nd Prog. Rep. of the Liv. School of Trop. Med. Exped. to the Congo. 1903.

found to be infected with them.

In Uganda & the districts round about.

A. Incidence of Trypanosomes in the blood of the General population.(1)

1. In Sleeping Sickness areas.

Out of 81 examined 23 were found affected

2. In Non Sleeping Sickness areas.

In Uganda

66 people examined none found affected

In Nairobi - Brit. East Africa

50 people examined none found affected.

B. Incidence of Trypanosomes in the Cerebro Spinal fluid of the General population.(2)

Of both Endemic & free areas.

15 cases examined absent in all.

The figures from the Gambian, Congo and Portuguese districts simply give the percentage distribution of Trypanosomiasis in the populations examined.

In Uganda, on the other hand, the figures not only do this, but they point in a very definite manner to the Causation, which will be referred to later, in the paper.

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(1) Reports of the Sleep. Sick. Com. Royal. Soc. No IV pp. 14-19.

(2) Ibid. No I p. 15.

Chapter IV

On The Allied Diseases of Lower Animals.

History of Researches. The genus Trypanosoma was established by Gruby in 1843, but the haematozoa included in this division were first described by Valentin in 1841, who discovered them in the blood of a trout (Salmo Fario); and in the following year by Gulge who found them in frogs. Since then numerous species have been described in fish birds &c &c.

The first to find these parasites in mammals was Dr Timothy Lewis who found them in 1879 at Calcutta in the blood of rats. The rat trypanosome very appropriately called Tryp. Lewisi, has a world wide distribution, its prevalence however varying greatly in different localities. This trypanosome is quite non-pathogenic to rats.

Similar parasites have been found in hamsters, guinea pigs, rabbits and other rodents.

In 1880 in the Punjab Griffith Evans discovered in the blood of horses a trypanosome of a far greater pathological importance. The horses examined by Evans were suffering from Surra, a disease known to the natives of India from time immemorial, and ascribed by them to the bite of certain Tabanidae. The Surra parasite (Tryp Evansi) is not limited to horses and mules, but also attacks camels elephants, buffaloes and dogs.

Experimentally it has been conferred on monkeys rabbits rats mice & guinea pigs.

It has been found by the Germans in East Africa and recently by the Americans in the Philippine Islands, also appearing in Mauritius. Surra has a very wide distribution in Southern Asia.

Evans was favorable to the popular opinion which ascribed the transmission of the disease to certain bloodsucking flies, but subsequent authors especially Lingard considered food and drinking water to be the true vehicles of infection.

The exact method of the spread of this disease is not known, but probably it is disseminated by means of stinging flies of the Genera Stomyx and Tabanus.(1)

The fly disease of Africa has been known as long as the fly-disease of India. James Bruce in "Travels to discover the Source of the Nile". David Livingstone in his "Missionary Travels and Researches in South Africa", Dr Drysdale and numerous other Writers have contributed to our knowledge of the African disease. These authors describe very accurately the Symptoms of "Nagana", its Coarse Anatomical lesions, its peculiar distribution, the immunity of local wild animals, and the structure distribution and life habits of its Carrier, the Tsetse fly. At last in 1895 Lt. Col. David Bruce was sent to Zululand to investigate Nagana and found that the specific parasite of the African horse disease was a trypanosome similar to the one found by Evans in Surra, fifteen years previously.

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(1) Rogers. L, Brit. Med. Jour. 26/11/04 p. 1454 + Proc. Roy. Soc. Lond. LXVIII

Durham, Kanthack, Blanford Plummer and Bradford made a more complete study of the parasite, and the latter two investigators named it the Tryp. Brucei. Then followed other observations by Laveran and Mesnil, by Koch, and by Rabinowitsch and Kempner.

Another trypanosome infection which exists in horses & peculiar to Southern Europe and right round the Mediterranean basin, has been known since the beginning of the 19th Century under the name of "Dourine" or the "Maladie du Coit." The parasite Tryp Equiperdum was first discovered in 1892 by Chauvrat.

America also has its trypanosome disease the "Maldecaderas." It is chiefly dangerous to horses but behaves otherwise like Tsetse fly disease and Surra. The trypanosome was distinguished in 1901 by Elmassian and is called Tryp. Equinum.

To complete the list of pathogenic trypanosomes so far discovered in the domestic mammals, one must mention the large organism found by Theiler in 1903 in the so called Gall Sickness of South African cattle, and named

by Bruce; Tryp. Theileri. This parasite is peculiar in being twice the size of any of the above. It is confined to cattle, all other domestic animals being immune. There is not much known about it. The disease is not fatal to cattle.

Lately Navarro enumerated other trypanosomata which he had found in Uganda, in dogs, mules and cattle; and Dutton Todd and Christy also mention their having come across some in the blood of cattle &c whilst on their Congo Expedition. Nothing is known about them and their significance is not determined.

Symptoms & Signs in Animals.

It would take too long to enter into any details of the various diseases of the animals. It must suffice to present the salient features of one or two; sufficient in fact to help us later in the elucidation of the real character of Sleeping Sickness in Man.

The account is taken chiefly from Manson's description.(1)

(1) Tropical Diseases London 1903.

Surra, Nagana & Mal de Caderas, these diseases seem to be identical, though they occur in different parts of the world.

(1) Nagana.

The Carrier of this affection was proved by Bruce[1] to be the Tsétsé fly Glossina Morsitans

The Animals liable. Excepting man and certain kinds of donkeys and goats, all domesticated animals and many wild animals, except the large game of South africa, antelopes &c (in whom the parasite exists but is not pathogenic), can acquire Nagana by inoculation. Birds are not susceptible to either Nagana or Surra.

Results of Inoculation

The general result is, that in two or three days trypanosomes appear in the blood of the animal and persist till death, which is inevitable in most species.

In rats and mice the trypanosomes are fairly numerous. In Rabbits and Guinea pigs they are very scanty but can be proved to exist, by

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(1) "Further Reports on the Tsetse fly disease" Ubombo 1896.

inoculation experiments.

The resistance varies widely in individuals and species, as will be seen from the following:—

Rats & Mice	death ensues in	about 2-3 days
Rabbits	"	" 5-12 "
Guinea pigs	"	" 50 "
Dogs	"	" 22-26 "
Monkeys	"	" 15 "
Horses & Donkeys	"	1 week to 3 months.
Cattle	"	1 week to 6 months

a portion of the last recovering, when immunity is found to be established.

Goats & Sheep. death occurs in several months.

In animals where death occurs in a few days, the parasites are very numerous and after one or two oscillations of temperature, death is sudden.

When death is delayed there appears a Chronic Cachexia. There is a peculiar Chronic Relapsing fever with numbers of parasites in the blood, greatest at times of the febrile accessions. A form Oedema from infiltration of Coagulable lymph shows itself in the Connective tissues of the neck, the abdomen, the Sheath of the penis, and the genitals and limbs. There is

intense anaemia, wasting, some skin eruptions and often blindness.

The Post Mortem examination shows a large spleen, ecchymosis in various viscera; and swollen lymphatic glands corresponding to the part where the inoculation was made

2. Dourine

Tryp. Equiperdum resembles Tryp. Brucei and is the cause of Dourine or Maladie du bort, a disease of stallions, broodmares, and donkeys in Southern Europe, Northern Africa, and in Chili.

Symptoms within 10 to 20 days, there sets in, in Stallions, oedema of the penis and a discharge from the urethra; in mares, oedema of the labia and vaginitis. There is oedema of the limbs and abdominal walls; a progressive anaemia, weakness and skin eruptions. The appetite remains good. Fever rarely reaches over 39° C. The duration of the disease is from four to ten months. Death results from paraplegia due to softening of the cord.

The trypanosomes are found to be very scanty in the blood,

but an abundance of them is made out in the oedematous tissues, skin lesions and the various discharges.

The organism is feebly pathogenic to rats and mice (a contrast to Tryp. Brucei). In the rabbit and dog it behaves as in the horse and is communicable by Coitus. The disease is more prolonged than Nagana.

Monkeys Sheep, goats and bovines are insusceptible. These differences in susceptibilities point to specific differences to Nagana.

It is said that Dourine can be communicated by the agency of insects especially fleas (Rabinowitsch and Kempner (1)) as well as by the act of Coitus.

The Question of Specific differences.

The question now arises, as to whether the above named variously described diseases are specifically separate, and whether the causative agents are distinct entities or otherwise.

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(1) Centralb. f. Bakteriol. Bd XXXIV No 8.

For the differentiation of Species we must consider the following factors:—

(1.) Their Morphological Characters

As we have already noticed the Tryp. Theileri (of the Gall sickness of South African Cattle) can be distinguished by its large size. It should not be forgotten however, that the same Trypanosome can present different dimensions in different host Species. Thus Tryp. Brucei which measures about 26 μ. in the Rat, attains a length of from 28 to 33 μ. in the horse.

As to the trypanosomes of Surra Nagana and Dourine it is not not possible to distinguish them morphologically. Dourine Seems to differ somewhat Symptomatically from Surra and Nagana. Dogs may recover from its attacks and the animals which have acquired immunity against dourine, are not immune to Surra and Nagana.

Surra and Nagana are strikingly alike. Their identity suggested by Koch, Musgrave and others, Seems therefore quite possible. Laveran & Mesnil are however opposed to this View.

(2) The Results of Animal Inoculations and the production of Immunity.

These have been disappointing. Different investigators have obtained opposite results. The frequent fallacy of such experiments need to be bourne in mind. Different species of oxen, horses or dogs may exhibit a very different degree of susceptibility. Then again, the passage of the parasite through certain animals may greatly alter its virulence, and even modify its aptitude for its original host.

These difficulties have caused distinguished observers such as Koch and Laveran and Mesnil to give diametrically opposite views, and as nothing has been definitely settled, it will not be profitable to enter further into the subject in this place.

Suffice it to say that cattle have been rendered immune to the Tsetse fly stock (Koch and others), but it was found that in these animals, though immune themselves, the parasites continued to exist; and therefore they formed permanent sources of infection to other cattle;

a fact which proved, that it was not advisable to combat tsetse fly disease by the method of artificial immunisation hitherto practised.(1)

(3) The Cultivation Characteristics

This method might in the future be used to distinguish between the different species of the parasite; but unfortunately Cultivation has been successful in only three of the forms, - Tryp Lewisi, Tryp. Brucei & Tryp. Evansi.(2)

Tryp. Lewisi. First cultivated successfully by Novy and MacNeal, the experiments were lately repeated and the results confirmed by Smedley. The medium employed was a mixture of agar and defibrinated blood,

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(1) Rob. Koch. Brit. Med. Jour. 26/11/04.

(2) a. Novy & MacNeal. On the Cultiv. of the T. Brucei. Jour. of the Amer. Med. Assoc. Chicago. p. 1266-1268.

b. Novy & MacNeil. On the Culiv. of Tryp. Brucei. Jour. of Infect. Dis. Chicago. 1904. Vol. I page 1.

c. Novy, MacNeal, & Hare. The Culiv. of the Surra Tryp. of the Philippines. Jour. of the Amer. Med. Assoc. Chicago 1904 Vol XLII p 1413.

d. R. D. Smedley. Jour. of Hyg. Jan. 1905

usually of the rabbit, obtained with aseptic precautions. The haemoglobin seems to be an important constituent. A special technique is used. The material is inoculated with the affected blood. Incubated at 37° C., growth is apparent but rapidly degenerates. At 20°–25° or kept in the dark at room temperature, growth is shown in numerous colonies at the end of three weeks and remains alive for several months. Novy and MacNeal report that they have cultivated for 26 generations during a period of two years.

Tryp. Brucei. The same workers were successful in cultivating this organism by the same method but with much greater difficulty. Novy and MacNeal cultivated through 27 generations in eight months.

Tryp. Evansi. has also been cultivated.

Chapter V

On The Etiology.

Older theories of causation

It would be idle to discuss some of the various theories put forward by the older writers to account for this formidable disease.

Some believed it to be a kind of nostralgia, intensified by the ill treatment suffered at the hands of slave dealers and planters. Others considered it due to Malaria; to Sunstroke; to Amenorrhoea; to Inanition; to the immoderate drinking of Palm wine; to the eating of raw manioc, or to the smoking of Indian hemp.

More recent theories have connected Sleeping Sickness with an intoxication of food; animal parasites; and with bacteria.

The Food Intoxication theory, suggested first by Corre then again by Pereira do Nascimento and Calmette[1], was revived

[1] Arch. de Méd. nav. 1888, Nov. 321

lately by Ziemann[1] who ascribed Sleeping Sickness to the eating of raw or unsuitably prepared Manioc, in fact, that the disease was a food intoxication analogous to Pellagra.

Against this theory of Ziemanns, is the fact that in Uganda, Sleeping Sickness has appeared only of late years and no change of food whatever has taken place (Low & Castellani). Another reason against the Manioc theory is the occurrence of Sleeping Sickness amongst negroes far and long removed from the endemic centres of the disease, such for instance as the manifestations of the affection in Europe or in the West Indies.

The Parasitic theories. The best known of these was originated by Manson. While examining the blood of a case of Sleeping Sickness under the care of Dr. Stephen Mackenzie at the London Hospital, Manson discovered the larvae of a new filaria which he named Fil. Perstans. Subsequently he found the same larvae in films of blood from cases of Sleeping Sickness on the Congo. In 1898 he again

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(1) Jour. of Trop. Med. Oct. 1902 p. 309.

noticed them in the two cases of the disease brought over from the Congo for study in England.

Struck by the constant presence of these blood worms in cases of Sleeping Sickness and also by the singular correspondence which seemed to exist between the geographical distribution of the disease and that of Fil. Perstans; and paralleling the long incubation period of the affection with the fact that Fil. Perstans can remain alive within the body of its host years after the infective area has been quitted, Manson formulated the theory that this organism might be the cause of Sleeping Sickness.

This theory has been disproved by the observations of Low (1) and others who have shown that in British Guinea where this parasite is common, there is no Sleeping Sickness; and vice versa, in Kavirondo (East Central Africa) where the latter disease is rife there are no filariae.

Other parasitic worms that have been incriminated are the Rhabdonema Strongyloides and the

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(1) Reports of the Sleep. Sick. Com., Royal Soc., No II pp 6 et seq.

Ankylestoma Duodenale. The embryo of the former was considered by Forbes on very insufficient grounds to be the cause of Sleeping Sickness. This parasite according to Tessier penetrates the mucous membranes of the intestines and reaches the general circulation & is then retained in the Cerebral Vessels.

Fergusson on the other hand, considered the Ankylestomum Duodenale as the cause of the disease. In Uganda this parasite is met with very frequently in Sleeping Sickness but it cannot be considered the cause, as the administration of Anthelmintic Remedies frees the patient from it and sometimes improves the general condition for a few days, but the fatal course of the disease is not checked.

Bacterial Theories. Many writers have favored a bacterial origin, and the most different germs have been described as the true cause. In 1897 Cagigal + Lapierre (1) found a bacillus in the blood of a case of Sleeping Sickness imported from Angola, and claimed that it was the cause of the disease. They stated that by inoculating rabbits with cultures of this bacterium, they produced a disease resembling Sleeping Sickness.

These results were not confirmed by

(1) Coimbra Medica, 1897, Nº 30-31

Brault and Lapin[1]

In 1899, Marchoux[2] suggested that Fraenkel's diplococcus might be the long sought for cause. He performed the autopsy of one case of the disease at St Louis (Senegal), and found a diplococcus in the pericardium but was unable to detect its presence in the Cerebro Spinal system. Pneumonia was very prevalent at the time. In a second case complicated by a Chronic Rhinitis and Suppuration in the Sinus Frontalis, the secretion of the nose showed the same microorganism.

Later still (1901), Broden of the bacteriological laboratory at Leopoldville (Congo), examined several cases of Sleeping Sickness and found in the blood and in the Cerebro-Spinal fluid, (post mortem) a bacillus which grew abundantly on potatoes. This bacillus was not agglutinated by the blood of patients suffering from Sleeping Sickness.

In the same year Dr. Bettencourt and his Colleagues of the Portuguese Commission, dispatched to Angola to investigate the Etiology

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(2) Ann. de. l'Inst. Past., 1899 No 3 - 193 -

(1) Arch. de Parasitol. 1898, 1, No 3, 361.

of the disease, described a diplostreptococcus which they stated they had found constantly in the Cerebro Spinal fluid & at the Postmortem examination of their Cases. This Organism will be referred to more fully in the next Chapter.

The Predisposing Causes.

The influences of race, sex age &c &c have already been entered into. "As important predisposing Causes, Clarke mentions disorders of Circulation, mental depression; and bad and insufficient food. It may also be that parasites like Fil. Perstans, Ankylostoma Duodenale &c. So Common in natives, impairing the natural forces of resistance, may play a certain role in the Etiology of the disease". (Low & Castellani)(1)

The Exciting Causes (see the following Chapters) The two organisms which have been most studied in connection with Sleeping Sickness are (1) The Diplo-streptococcus (2) The Trypanosome.

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(1) Reports of the Sleep. Sick. Com., Royal Soc., No II p. 18.

Chapter VI

The Diplostreptococcus.

History of Discovery. As mentioned in the last Chapter this organism was first observed and described by the Portuguese Commission to Angola in 1901, as occurring Constantly in the Cerebro Spinal fluid in the post-mortem examination of their Cases.

In their orginal report dated Loanda 10/8/01[1], they said that lumbar puncture was performed nine times, and in Six Cases the organism was found. On three occasions Glands were extracted during life, and in two of them the bacterium was present. In the blood of one case out of four examined, it was also observed. In the Meningeal exudation of the dead body, this organism was detected in all of the thirteen subjects examined.

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(1) Abst. in "Lancet" 27/9/02 p. 885.

In this report they describe the organism, its cultivation characters etc., points which will be gone into more fully further on in the paper. They called the bacterium a Diplostreptococcus, because it resembled Fraenkel's Diplococcus and also the Streptococcus, but could not be identified with either of these groups, to which however they considered it closely allied. Later on, the Commissioners had occasion to modify some of their descriptions and conclusions especially in the matter of the cultivation characteristics of the organism.(1)

Independantly of the Portuguese observers, Castellani, whilst working with Uganda cases, also found a Streptococcus in non-complicated cases of the disease. At the time, he thought that in it he had come across the true causative factor of the malady. This opinion he modified later.

These observations were again further confirmed by the researches of Mott and others whilst working at the Pathological Anatomy of Sleeping Sickness.

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(1) a Brit. Med. Jour 18/4/03 p 908.
b. La Maladie du Sommeil. Lisbon. 1903.

The Discription of the Organism.

The following description is taken chiefly from Castellani.(1)

"The microscopic appearance is very variable depending on the different media on which the germ has been cultivated &c., all transitional forms from long chains to typical diplococci being seen. The form and size of individuals are also within certain limits variable. Frequently about the chain and the diplococcus forms, well defined mucoid capsules are seen, and in hanging drop preparations, the short chains and the diplococci forms show a well marked Brownian movement.

The Staining properties. It is easily stained with the ordinary solutions of the various aniline dyes. Gram is positive.

The Cultivation Characteristics. Castellanis remarks on this subject vary somewhat in his earlier and later reports. In the latter he gives

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(1) "Researches in in Etiology of Sleep. Sickness." Jour. of Trop. Med. 1/6/03 p. 167.

the following characters.

On Gelatin growth occurs very well at a temperature of 22°C. and also much below. In a stab culture the stab is generally thread shaped, although sometimes it may appear a little granular. The surface growth is very slight. In streak cultures the colonies may coalese forming a mass with a fine granular surface and sometimes wavy borders.

In some very few cases, after five or six days, was noticed a very slight liquefaction of the gelatine.

The Portuguese commissioners in their original report stated that gelatine cultures were not successful. Later they modified their statement and said that their coccus also grew well in this medium.

On Agar. In a stab culture growth takes place luxuriantly along the stab, the surface growth being generally more delicate.
In streak cultures in most cases the growth is very vigorous, the colonies not remaining separate but coalesing into a whitish mass with granular surface and wavy borders. Still, in rare cases, especially if the agar

is old, the growth may be much more delicate and the colonies may remain separate. The water of condensation shows as a rule, a slight whitish deposit.

Glycerin-Agar. The growth is the same as on Agar, but rather more delicate.

Sugar Agar. There is no gas formation.

Litmus Agar. The color of the medium does not change.

Potatoes. A slight growth becomes manifest.

Bouillon. The appearance of a bouillon culture varies greatly. In the majority of cases the bouillon remains clear, and there is a flocculent and sometimes sandy sediment. In these cultures one generally finds long chains on microscopic examination. In some cases the bouillon is cloudy with little or no sediment, and in cultures of such an appearance, microscopic examination will often show the cocci arranged in pairs and in short chains. The same strain of germ will sometimes make the bouillon cloudy, and sometimes not.

Serum. There is good growth, but more delicate than in Agar.

Milk. There is generally no coagulation.

Relation to Oxygen. The micro-organism is a facultative anaërobe.

Vitality. It is more resistant than other varieties of Streptococci.

Virulence. Very few experiments have been made. In monkeys ½ c.c. of bouillon culture inoculated under the dura mater gave rise to a general septicaemia, the animals dying in about two or three days.

The Distribution within the Body and the percentage of cases in which it is found.

(1) Castellanis results[1]. Out of 39 cases he has grown this variety of Streptococcus from the blood of the heart in 32, and from the liquid of the Lateral Ventricles in 30.

He states that the germ does not seem to be frequently present in the organs, although he found it a few times in microscopic sections of the

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(1) Jour. of Trop. Med. p. 167 et seq.

brain and the spleen.

Three punctures of the Spleen during life all gave negative results.

The examination of the enlarged lymphatic glands removed during life was also negative.

Out of 3 cases of peripheral blood examined bacteriologically, only One gave a positive result.

The Cerebrospinal fluid obtained by lumbar puncture in 28 cases gave positive results in 5.

In 6 bacteriological examinations of the urine, he grew the germ once.

(2) The Portuguese investigators[1] observed the diplostreptococcus in Vessels of the pia-mater, in the Cerebral and medullary Capillaries, in the lymphatic Sheaths of the Vessels, in the intracellular nerve Substance, in the Cerebrospinal fluid and in meningeal exudations. Also in bronchial and other lymphatic glands and in the peripheral blood of one Case.

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(1) The Lancet. 27/9/02 p. 887 et seq.

(3) Second Royal Society Commission

Dr. Navarro[1] states that the Commission carried out many post mortem examinations and looked for the Streptococcus and found it in several cases, but not in all.

(4) Greig and Gray[2] report that in fifteen cases of Sleeping Sickness the lymphatic glands were examined for streptococci, both by staining and by culture, but in every case they were found to be sterile.

(5) Dr. Bullock in London examined glands and blood of two cases. Nothing was found.

(6) Low + Mott.[3] The post-mortem examination of Manson's case of Trypanosoma fever in a lady from the Congo, who died later with symptoms of Sleeping Sickness, showed diplococci "in all parts of the Central Nervous System, indeed in all the organs and tissues" — including Lymphatic glands Lungs, Liver, Bone marrow, Spleen and Heart. None however were demonstrated in the Kidney.

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(1) The Lancet 23/1/04 p. 228.
(2) Ibid. 4/6/04 p. 1570.
(3) Brit. Med. Jour. 30/4/04 p. 1000 + 10/12/04 p. 1559.

The Period of the Disease at which it can be demonstrated. Castellani found it in the last stages only of the disease. The Portuguese are of opinion that the organism could be distinguished much earlier if looked for carefully enough. In some cases it is never found at all.

The Experimental Inoculation of Animals. Very little work has been done on this subject. It has not produced in the animals inoculated, symptoms at all resembling Sleeping Sickness; but it causes death from acute Septicaemia in two to four days in Rabbits and other small animals, and in from one to three weeks in the monkey (Cercopithecus).

Is the Organism of the Portuguese the same as the one described by Castellani? Probably the organisms are identical. It is true that the Portuguese first stated that their diplococcus grew very poorly on the ordinary culture media, and that they had never succeeded in obtaining a culture on gelatine. After Castellani's

publication however, they modified their statement and affirmed that their Streptococcus grew very well in gelatine (1).

Agglutination reactions - Nothing satisfactory can be traced on this subject.

The Mode of Entrance into the Body. It is surmised that it finds an entrance at the same time as, and with the trypanosome, - but nothing is known.

The Identity of the Organism. From the Streptococcus pyogenes it is differentiated by the more vigorous growth on Agar, by the tendency of its colonies to coalese and by the non-Coagulation of milk.

Differences between it and other diplococci can also be distinguished by their cultural reactions.

The Relation of the Streptococcus to the Disease. It is not convenient to enter into this subject here.

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(1) Brit. Med. Jour. 18/4/03 p. 908.

Immunisation experiments.
No work can be traced.

Chapter VII

The Trypanosome
(Fig I & II pp 231–238)

Classification. The trypanosome belongs to the Protozoa.

Salmon and Stiles give the following classification:—

Class. Mastigophora.
Subclass. Flagellata.
Order. Monadida.
Family. Trypanosomidae.
Genus. Trypanosoma.
Species. Tryp. Gambiense. Tryp. Evansi.

Calkins in his book[1] gives the following characters.

Class Mastigophora. Are protozoa of definite or indefinite form, naked or provided with a well defined membrane. The nutrition is holozoic, parasitic, holophytic or saprophytic. The motile organs are flagellae which may vary in number from one to many. Mouth contractile, vacuole and

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(1) The Protozoa. New York, Macmillan. 1901 p 137

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(Fig. 1 to 6 pp. 236-238)

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(1) The Protozoa. New York, Macmillan. 1901 p137.

nucleus are usually present. They are usually small forms with a widespread tendency to colony formation.

Subclass Flagellida. Are small organisms possessing usually a sharply defined mono-nucleated body, with a definite anterior end in which are inserted one or more flagellae. They are actively motile during the greater period of life, but all have the power of encystment. Reproduction occurs by longitudinal division usually during the flagellated stage, although it may take place during resting phases. Nutrition is holophytic, holozoic parasitic or saprophytic.

The History of Discovery in Man. — Vespret (1) seems to have been the first to find this parasite whilst studying malarial blood in Algeria in 1890. Trypanosomes were found in seven cases of which six were those of Malaria. Although there is little doubt that he did see a trypanosome, yet his descriptions

(1) Comptes. rend. et mem. de la Soc. de Biol. 1898 p. 1072.

were very vague and his drawings too crude for much credit to attach to him for his discovery.

Heleri (1891 + 1892) and Barron (1894) reported very doubtful cases of trypanosome like forms in human beings.

The first case authenticated, was observed by Forde and Dutton in Gambia, in 1901. The former, while examining the blood of an European patient suffering from an anomalous form of fever, discovered some small, worm like, actively moving bodies the nature of which he was unable to ascertain. Dutton saw the case, first in Liverpool where he found nothing in the blood, then once more at Bathurst where he now succeeded in detecting the parasite, and recognising it to be a trypanosome, he named it the Tryp. Gambiense.

The description was published first by Dutton[1], then by Forde.[2]

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(1) "Prelim. Note on a Tryp found in the blood of man". Thomp. Yates Labor. Repts. May 1902 Vol IV. pt II p 155 + "Note on a Tryp &c" Brit. Med. Jour. 1902 Vol II p 881.

(2) "Some Clin. Notes on a Europ. patient in whose blood a tryp. was observed". Journ Trop. Med. 1/9/02 & "The Discov. of the Human Tryp" Brit. Med Jour 29/11/02

To Forde belongs the credit of having first observed the parasite and to Dutton the greater credit for having recognised what he saw.

The next Step was taken by Manson, who, having previously had an opportunity of examining Forde's case in Liverpool, when consulted about a Congo lady suffering from the same peculiar Symptoms, had his suspicions aroused; and on further investigating the case, Daniels on the 29th Oct. 1902. Confirmed them, by finding in the patients blood, the trypanosome.

Other cases soon came to light. One by Manson, his patient returning to Africa and remaining well ever since. One was notified by Le Moal in Brazzaville, one by Brumpt in Bourmba and two by Broden in Leopoldville. Meanwhile Drs Dutton and Todd had been despatched as a Commission to the Gambia, by the Liverpool School of Tropical Medicine, to Ascertain the Extent and prevalence of the disease in that Colony. They examined over 1000 persons in the Gambia and found the parasite in

Six natives and one white man. (1)
(Quadroon).

Thus the occurrence of Trypanosomes in the human body was firmly established, and the disease to which they gave rise was termed "Trypanosoma fever" or "Gambra fever".

In rapid sequel the researches regarding the Etiology of this tropical disease experienced a further advance; for it became known that Castellani who had been sent with Low and Christy to Uganda by the Royal Society, to study the distribution of Sleeping Sickness, had observed on the 12th November 1902, in the Cerebro Spinal fluid obtained by lumbar puncture of a well marked case of Sleeping Sickness, a living trypanosome. (2)

Up to March 16th 1903 the date of the arrival of Bruce and Nabarro at Entebbe, he had found the parasite in five out of fifteen cases examined. Dr Castellani remained in Entebbe three weeks after the arrival of the new Commission, and during this time

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(1) Brit. Med. Jour. 19/9/03 p. 650.
(2) Reports of the Sleep. Sick. Com. Royal Soc. No 1. p. 1.

he examined 29 further cases for trypanosomes, with the result that 70% were found to contain the parasites. (1)

None were found in twelve control cases, three of which it must be mentioned were cases of the trypanosoma fever as described by Forde and Dutton, and Manson and Daniells; and these of course had the parasites in their blood.

Basing an opinion on his discovery, Castellani formulated the theory that the trypanosome was the cause of Sleeping Sickness, and that the Streptococcus previously described by him was merely a secondary factor in the causation. The trypanosome he named the Tryp. Ugandense.

His discoveries were confirmed by Bruce and Nabarro, by the various Liverpool expeditions, by the Portuguese Commission and by others. It was suggested subsequently that although Castellani actually discovered the trypanosomes in the Cerebro-Spinal fluid, he did not realise the full significance of his find until it was

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(1) Reports of the Sleep. Sick. Com., Royal Soc., No I p. 12.

pointed out to him by Navarro and Bruce. The matter is still one of Controversy and cannot be further discussed here.

Method of Examination of the Cerebro Spinal Fluid.

The Operation of Lumbar puncture

The method is well described by Christy.(1) "The patient is placed on his right side, on a table if possible, with his knees drawn up to his face. After thoroughly cleansing his back with soap and water and again with alcohol or ether, Cocaine is injected with a short strong needle if the patient is a black man, both subcutaneously and deep into the muscles over the interspace above the last lumbar vertebra. This interspace is on a straight line between the two Iliac crests, and the needle should be passed half an inch to the left of the middle line, not midway between the two ~~inter~~spinous processes, but slightly nearer the upper one. The next lower space between the Sacrum and the last lumbar vertebra

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(1) Christy. "The Cerebro-Spinal fluid in Sleep. Sick. (Trypanosomiasis) Brit. Med Jour 20/8/04 p 373 et seq.

can be selected, if for any reason it is desirable, but owing to the flattening of the Canal in this situation, the operation is not quite so easy to perform without drawing blood. After waiting a few minutes for complete Cocainisation, the knees are adjusted so as to be exactly opposite each other, and whilst the assistant secures the position of extreme flexion, the tips of the fingers of the left hand are placed firmly upon the Iliac Crests, leaving the thumb to indicate by practice, not only the interspace, but the exact spot and direction as well.

The puncture needle is then passed through the skin, the precise direction again gauged, and the needle passed on slightly upwards and toward the middle line. If the spot and direction have been well chosen, no bone is encountered and the passage of the needle point into the Canal can easily be felt, and the clear fluid at once appears drop by drop.

With a little practice and a docile patient, no operation is easier, and I have performed it on the floor in native huts, in the open bush, in my tent and in a canoe.

"Having learnt the exact spot and the direction, the only difficulty is to gauge the depth to which the needle should be passed, for if the point is allowed to prick the cord or the membranes opposite, blood immediately appears, and the result of the operation is valueless for statistical purposes.

The needle selected should be as fine as possible consistent with sufficient strength to withstand the grip of the back muscles, if in the early stage of the disease the patient is restless or insufficiently cocainised."

"The careful sterilisation of all instruments is of coarse necessary"

In Churstys opinion no introduction of septic matter has resulted from the operation, but he adds, that it would probably be wisest after cocaine has been injected to cauterise the site of the puncture with some small cautery made for the purpose.

With regard to the anaesthetic, according to the same observer, Cocaine is the best, cases of excitement or mania necessitate Chloroform, but it is inadvisable to give the latter in advanced cases if it can be avoided. for, at all events in two cases, the

struggle and subsequent exhaustion have, he believes, hastened a fatal issue.

The cases of Septic Meningitis noticed in some of the cases, in Christy's opinion were not due to the lumbar puncture, for in some, pus was also found in the ethmoidal and other sinuses, and in others, symptoms of meningitis antedated the punctures.

The method of Examination of the Fluid is the one elaborated by Castellani(1)

"Ten c.c. of the Cerebro Spinal fluid is taken by lumbar puncture. The fluid is centrifuged for a quarter of an hour and the whole of it poured away, except the little which clings to the sides and bottom of the tube. The Sediment is stirred up in this and examined under a low power 150 to 200 diametres of the microscope. Zeiss 16 mm. apochromatic objective & No 8 or 12 eyepiece will do well.

The trypanosomes are never very numerous. In some cases one is found only after looking through several slides in others two or three may be seen

(1) Reports of the Sleep. Sick. Com., Royal Soc., No I p. 12.

in one field.

The Cerebro spinal fluid in Sleeping Sickness differs slightly from that found in healthy persons. It usually has a very slight tinge of yellow due to the presence of a few blood corpuscles, and also it has more cellular elements (lymphocytes) in suspension. The healthy Cerebro-spinal fluid on the other hand, is as clear and limpid as distilled water and contains no sediment."

Being in small numbers one examination will not always decide the presence or absence of the Trypanosomes.

The method of examination of the Blood, in no way differs from the ordinary.

Being parasites of the blood plasma and always free in the liquor sanguinis, they must be looked for in that situation.

So far as we know at present, at least so far as it concerns this stage of the life history of the trypanosomes, they are never to be seen in the red blood corpuscles themselves. Future researches however, conducted on the lines laid down by Schaudinn may alter our views.

Being very scanty in the peripheral blood, Manson

suggests (1) that it is probably best to make the examination when the body temperature is high, possibly Centrifuging the blood previously. The trypanosomes accumulate in the leucocyte layer, above the red corpuscles. He also suggests that dehaemoglobinising thick films by dipping them a short time in water, and then fixing with alcohol and ~~then~~ staining, or the method described by Ross for weak Malarial infections, might be of some service.

The Staining Reactions. For staining the parasite many observers are agreed that Leishmans modification of Romanowsky's method, gives very good results. Staining in this way the Macronucleus, the Micronucleus and the flagellum appear red, the protoplasm blue, while the undulating membrane remains almost unstained.

Methylene blue or Thionine on fixed films also gives good results.

Nocard uses three solutions: -

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(1) Manson, Pat. Discussion on Trypanosomiasis Brit. Med. Jour. 19/9/03 p. 646.

Soln. A. Chlor. hydrate of methylene blue ½ gramme
Carbolic acid ½% 100 c.c.
Soln B. Rosin extra B.A. max, 1 gramme
Water 4000

Fix the film in absolute alcohol, take one drop of A. 12 drops of B., mix, allow to remain for half or one hour, wash in water. Stain for 30 seconds with C. Tannin Orange, Unna & Gubler.

The Description of the Parasite

In the beginning two descriptions were given; one of the parasite found in the blood of the so-called Trypanosoma Fever (Gambia Fever) cases, the Tryp. Gambiense (Dutton); — the other of the form found in the Cerebro Spinal fluid of Sleeping Sickness cases, the Tryp. Ugandense (Castellani) or the Tryp. Castellani (Kruse).

The two discriptions do not differ in any material detail, and as later researches have tended to show that the parasites are identical, only one form will be fully described; the supposed differences between the one and the other, being also shortly noted.

A. In fresh preparations[1] "the parasite has the usual general outline of the other trypanosomes, It has a worm like shape, and one observes in it, one end terminating in a flagellum, the other more or less bluntly conical though sometimes it may be quite pointed, an undulating membrane, and a vacuole.

The protoplasm does not appear to have quite a uniform structure, but rather an alveolar one as described by Plimmer & Bradford in Tryp. Brucei, although apparently far from being so well marked.

At first the parasite moves fairly actively, but on observing the preparation for some time, the movements by and bye become more sluggish, until they stop altogether. Frequently the trypanosome stops near a leucocyte which by degrees engulphs it. In other instances, after having slowed down very much in their movements the parasites stop far from any leucocytes and disappear suddenly as if they had been dissolved by the liquid.

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(1) Reports of the Sleep. Sick. Comm., Royal Soc., No ii p. 9.

On several occasions one sees in fresh specimens, trypanosomes with apparently two well marked flagellae; they certainly are parasites in longitudinal division".

Locomotion. Castellani states that his trypanosome (Trypl Ugandense), moves always with the so called posterior (blunted end) in front, whereas other known trypanosomes move generally with anterior end (flagellum) in front. The Tryp Gambiense, (Dutton) he continues is usually described as progressing with flagellum (anterior end) in front, unless there is some insurmountable obstruction, when at times it shoots backwards for a short distance with the blunt end in front.

This difference in the type of locomotion seems to have been held to constitute an argument against the identity of the two parasites. But really it is not so at all. For, considering the comparitive morphology of various flagellates, it is found that instead of the free flagellum end of the parasite being the anterior one (as the authors of various publications seem to think), it is in reality the posterior end. The flagellum arises really from

the anterior blunt end of the parasite is folded back upon itself to constitute the free edge of the undulating membrane, and is then continued free from the posterior end. The undulating membrane is nothing more than a flagellum linked with the body for a certain part of its length.

If now the usual mode of motion in flagellates be considered, it is found that the flagellum is placed at the front during motion, and that it drags the body towards it.

In any case it can be stated, that the argument as to the method of progression is not very sound, for although a parasite may move more rapidly and more frequently with the flagellum end first, it is quite possible that it may also, under certain conditions, move with the opposite end placed anteriorly.

Vitality of the Parasite outside the Body.

"The trypanosomes may remain alive in fresh specimens of blood ringed with Vaseline for from four to six hours. The vitality seems to be longer in Cerebro spinal fluid, where they may remain alive for from fifteen to eighteen hours. At this time the number of parasites is very

much decreased and the movements of the few left are very slow. After twenty hours none are visible. Differences in temperature, at least to a considerable degree, do not seem to affect much the vitality of the parasites. For this purpose some tubes of the Cerebro-Spinal fluid were kept at the temperature of the room (28°C) others incubated at blood heat, and still others at 18°C. The results were alike for all tubes; viz, some parasites still alive after 18 hours and ~~no~~ more ~~parasites~~ present after 20 hours.

B. In Stained Films. As mentioned above, after staining by Leishman's modification of Romanowsky's stain, the macronucleus, micronucleus and flagellum appear red, the protoplasm blue, whilst the undulant membrane remains unstained.

The following is Castellani's description.

"The nucleus is generally large and of variable shape. It is as a rule situated in the posterior half of the parasite. The micronucleus (Plimmer & Bradford) or the Centrosome (Laveran & Mesnil) does not show apparently any structure. It stains red but of a much more vivid colour than the nucleus.

It is situated very near the posterior (really the anterior) end of the parasite and generally outside the vacuole.

The vacuole is oval and of rather large size. It is situated anterior (really posterior) to the micronucleus.

The flagellum takes origin apparently from the micronucleus; then following the external edge of the undulating membrane reaches the anterior (really the posterior) extremity, where it becomes free. The free portion of this trypanosome is usually longer than that of other trypanosomes (?).

The protoplasm does not stain evenly and not very deeply; it shows some chromatic granules.

The total length of the parasite is from 16 to 24 μ. The width is from 2 to 2·5 μ. "

Morphologically there does not seem to be much difference between Castellani's trypanosome and that described as Tryp. Gambiense (Dutton) = Tryp. Ugandense (Castellani). Average length 21·7 μ. Chromatic dots 20%. Distance of micronucleus from posterior (really anterior) end 0·47 μ.

Tryp Gambiense (Dutton). Average length 24·3 μ. Chromatic dots 47%. Distance of.

micronucleus from posterior (really anterior) end 1·5 μ.(1)

From his observations, Castellani states that in his trypanosome the micronucleus lies nearer the extremity and the vacuole is apparently larger; besides, the movements are not so active; but he does not seem certain of his points, nor does he lay any stress upon them.

Bruce and Nabarro(2) state that the trypanosomes found in cases of Sleeping Sickness are shorter, have chromatic dots more frequently, and the micro-nucleus is situated nearer the end than in the other. They also appear uncertain as to whether these differences actually exist, and whether they have any importance whatever in deciding the question of identity or specific difference.

In a later report the same observers(3) say that "an observation had been made which would seem to do away with any significance the above differences in size and shape may seem to have.

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(1) Reports of the Sleep. Sick. Com. Royal Soc., No I. pp 24-25.

(2) Ibid. " p. 25.

(3) Ibid. No IV p. 20.

It is, that trypanosomes from the Cerebro Spinal fluid injected into the blood of monkeys became quite as long as the trypanosomes found in the blood of man. "This would go to show that the parasites merely find the cerebrospinal fluid not as favourable to their growth as the blood, and on this account are stunted".

C. Atypical Adult Forms.

Besides the above forms, Castellani has met in the blood as well as in the Cerebro Spinal fluid, with other rare forms with different shapes. "The parasite has lost its slender outline and has become thickened, in fact almost sausage shaped. The posterior (really anterior) end is much more rounded and the free portion of the flagellum is shorter. The vacuole may take greater dimensions. The protoplasm is less well stained. Round the nucleus there may be several points where the Chromatin collects." Castellani thinks that these are parasites which are preparing for division.

In addition to the above, he notices others, supposedly in the stage of division. The division begins probably at the micronucleus. From this point

it spreads posteriorly. The nucleus and the protoplasm apparently divide last.

D. Developmental forms. The same observer meets with, in addition, rounded bodies of 10–14 μ. in diametre possessing very finely granular protoplasm with one or more vacuoles.

These bodies may slowly change their shape from a rounded to an oval form.

If stained by the Leishman Romanowsky method, they show two or more points, where the chromatin collects, and sometimes very fine flagellae. Rabinowitsch & Kempner described similar bodies in Tryp. Lewisi. Castellani thinks they are developmental stages.

Yet other bodies are described by the latter, pear shaped and oval, which he thinks are amoeboid forms noticed by Plimmer and Bradford in Tryp. Brucei.

Multiplication in the Blood.

The characteristic mode is by longitudinal fission and it takes place in the actively motile stage. Rabinowitsch

and Kempner[1] declare that this method of division in the long axis does not exclude transverse fission; they have also seen the rapid formation of rosettes by multiple division. In this mode of multiplication however, the mother cell is no longer recognised as such.

The fission seems invariably to be preceded by division of the centrosome, followed successively by the flagellum, nucleus, and protoplasm. These fission forms are rarely to be seen in the peripheral blood, occasionally however they are met with; and two flagellae with no signs of division in the centrosome and nucleus are also encountered.

The above remarks refer especially to the rat trypanosome (Tryp. Lewisi), and no doubt also apply to the human species.

Cultivation. Excepting Tryp. Lewisi Tryp. Brucii and perhaps Tryp. Evansi none have been successfully cultivated.

Agglutination – Nothing is known on this subject as regards the human parasite, the experiments so far being unsatisfactory.

(1) Centralb. f. Bakteriol. Bd XXXIV No 8 and Jour. of Trop. Med. 15/12/03 p. 389.

Is Tryp. Ugandense (Castellani) of the same biological species as Tryp. Gambiense (Dutton)?

Before proceeding with the discussion of this subject, it must be remembered that it is quite possible to get different species of the genus Trypanosoma, infesting the same host. eg. In horses there are:

1. Tryp. Evansi the cause of Surra.
2. Tryp. Brucei the cause of Nagana.
3. Tryp. Equiperdum the cause of Dourine.

The question involves the consideration of the following factors:—

1. Their Comparitive Morphology. This has already been referred to, (p84-86) with the result that no distinctive stigmata could be discovered, distinguishing the one from the other.

2. The method of Locomotion. This point has also been criticised (p81-82); and the conclusion was drawn, that to decide the question on this basis was, to say the least, not desirable.

3. Animal inoculations. The results of these will be referred to later. Suffice it to say, that there seem to be no specific differences in the reactions of animals to the trypanosomes of the blood and to those of the Cerebro-Spinal fluid.

5. Symptomatology in Man.

When first discovered it was said that the trypanosome of the blood (Tryp. Gambiense) may not seriously affect the health of its host, whilst the organism of the Cerebro spinal fluid (Tryp. Ugandense) occasioned a grave malady invariably terminating in death.

The argument of non identity based upon the above mentioned supposed fact is fallacious; for, it is quite possible that when confined to one part of the organism (the blood) a given parasite may occasion one set of symptoms, whilst if the same parasite invades another part (say the Cerebro Spinal fluid), a totally different set of consequences may accrue.

6. Immunisation Experiments.

On this point as yet we have no certain knowledge, the subject not having been worked Scientifically. Plimmer however basing his Statement on the results of experiments, is of opinion that the two forms are quite distinct. So far, details of his experiments could not be obtained.

Nabarro on the other

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(1) oral communication.

hand states,[1] that whilst working in Uganda, he and Capt Greig immunised certain monkeys against the blood and the cerebrospinal fluid trypanosoma, and found that the animals were then immune against the cerebrospinal fluid and the blood trypanosoma respectively, though not against the animal trypanosomata they met with in Uganda.

Laveran[2] bears out Nabarro's observation.

7. Agglutination. As mentioned already, no facts as to this point are to hand on which a definite conclusion can be based.

The general opinion on the subject, an opinion in which one is inclined to fully concur, is, that the parasites are identical.

The Distribution of the Parasite within the Body.-

Up to the present the organism has been encountered in the cerebro-spinal fluid; very few (doubtful degenerated forms)

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(1) Discussion on Trypanosomiasis. Brit. Med. Jour. 20/8/04 p. 398.

(2) The Lancet. 30/4/04 p. 1240.

in the blood vessels and perivascular spaces of the central nervous system; in the peripheral blood; in fluids obtained by punctures made during life into lymphatic glands (Greig and Gray)[1]; in the fluid of hydroceles (Dutton Todd & Christy)[2]; in the pericardial pleural and peritoneal fluids when examined fresh after death.[3] Very few (doubtful forms) have been detected in sections of organs.

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(1) Greig & Gray. The Lancet. 4/6/04 p. 1570.

(2) Dutton Todd & Christy. Brit. Med. Jour. 20/8/04 p 371 et seq.

(3) Ibid.

Chapter VIII

On the Experimental Inoculation of Animals.

The experiments as yet performed resolve themselves mainly into two separate classes.

1. Those intended to show whether the disease can be communicated to the lower animals; to prove the identity or otherwise of Tryp. Gambiense with Tryp. Ugandense; the production of immunity &c.

2. Those intended to give us information as to the carrier or carriers of the infection.

In this Chapter it is proposed to study only the first set of experiments.

A. In Uganda.(1)

The Materials employed were

(1) Cerebro spinal fluid of Sleeping Sickness cases where the trypanosomes were found in the fluid.

(2) Blood from cases of the so-called

(1) Reports of the Sleep. Sick Com. Royal Soc Nos I + IV

Trypanosoma fever, in whom the trypanosomes were present in the peripheral blood.

The Sites of Inoculation were

(1) Subcutaneous.

(2) The Vertebral Canal.

(3) Through the Foramen magnum into the brain cavity

The Animals used were Monkeys, Chiefly Macacus Rhesus and Cercopithecus.

These, former animals showed the greatest susceptibility and exhibited Symptoms (according to Bruce), resembling those of sleeping Sickness, no matter whether inoculated with material, blood or Cerebrospinal fluid, of either Sleeping Sickness or Trypanosoma Fever cases.

Of Cases of inoculation described as typical, the two following might be cited:—

Experiment 34. Monkey (male) (Macacus Rhesus).

April 8th 1903. Injected 1 c.c. of Cerebrospinal fluid containing trypanosomes, of a case of sleeping sickness, into the Spinal Canal of this monkey.

April 30th. Trypanosomes appeared in the blood today, 19 days after inoculation. The temperature shows no signs of the invasion.

May. 21st. Trypanosomes are numerous in the blood. Temperature 106·4° F.

Aug. 28th. This monkey is beginning to show the usual symptoms of the disease in the monkey. He sits most of the day with his head fallen on his chest, evidently asleep, and his temperature has become very irregular.

Commissioners' remarks — "Four months after inoculation this monkey begins to show signs of Sleeping Sickness".

At the foot of the same page of the report, a paragraph tells us — "Capt. Greig writes us on the 10th Sept. that No 34 has died. The post mortem appearances were pretty typical of an ordinary Sleeping Sickness Case. Trypanosomes were found living in the Cerebro Spinal fluid of the brain."

Experiment 60. Monkey (Macacus Rhesus).

Apl. 15th 1903. Injected subcutaneously 2 c.c. of blood containing trypanosomes.

May 7th Trypanosomes appeared in the blood for the first time, 22 days after injection.

May 14th. The Haematozoa are noted as being very numerous. Temperature is so far normal.

July 2nd. Appears listless and less energetic. Henceforward and until

death the temperature varies from 95° to 103° F.

July 15th For the last fortnight the animal has presented a picture of Sleeping Sickness. He sits about all day with his head sunk on his chest evidently asleep. Death occurred on the 16th July.

Post mortem examination shows the typical Sleeping Sickness appearence as seen in man.

Other experiments were performed showing that trypanosomes can disappear entirely from the blood of monkeys inoculated, the animals remaining in perfect health without any symptoms of trouble.

Other animals employed. Beside the monkey only the dog, the rat and the jackal were found susceptible to the trypanosome. The other animals inoculated viz, the guinea pig, Sheep, goat, donkey and ox failed to show the parasites in the blood.

The susceptible animals in cases where death is recorded, generally died from other causes apparently than trypanosomiasis.

Conclusions derived from the above experiments:—

Bruce attempts to prove chiefly two points:-

1st That the trypanosome of the blood of fever cases, is the same as the trypanosome of the Cerebro Spinal fluid of Sleeping Sickness Cases.

This proposition is one which we cannot attempt to disprove. All workers are generally agreed on the subject and all the facts tend to point to the same conclusion.

2nd That the inoculation of various materials produced at least in some of the monkeys, symptoms and post mortem appearances identical with Sleeping Sickness, and inferring therefore, that in these instances at any rate, Sleeping Sickness was transmitted to monkeys.

This proposition is generally not acceptable: —

Firstly, It is denied that the symptoms exhibited by the monkeys were those of Sleeping Sickness at all. If a monkey is ill from any cause whatever, it generally assumes the attitude described by Bruce as that of the monkey Sleeping-Sickness attitude.

Secondly, The specimens of brain te sent over from Africa, as representing typical examples of the inoculated disease,

do not seem to present, in the opinion of competent authorities,[1] those appearances which have been described as pathognomonic of Sleeping Sickness.

Nabarro[2] makes some interesting observations as to these experiments. He states - "in the case of monkeys very curiously, a few weeks after inoculation trypanosomata appeared in the blood, and in some instances became quite numerous; but after a short time - perhaps a month -, they began to disappear" and when he left Africa all the monkeys failed to show the parasites in their blood, and were nearly all in a perfect state of health. "One of the monkeys died from tuberculosis, and three others also died, but whether from sleeping sickness or not, it is difficult to say.

The same observer also states that after the trypanosomes had disappeared from the blood of the infected monkeys, he reinjected them with the same trypanosoma, but they did not reappear, as the animal had become to a

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(1) Mott "The Cerebro Spinal fluid." Brit. Med. Jour. 10/12/04 p 1559.

(2) Dav. Nabarro, "The Lancet" 23/1/04 p. 230

certain extent immune. He then injected the other trypanosoma (from the blood or the cerebro spinal fluid as the case may be) and when he left the country the trypanosomes had not reappeared in the monkeys thus re inoculated. This seemed to show that the two trypanosomata were identical.

These observations on immunity are not fully confirmed by those of Wolferton Thomas and Linton. (see later)

B. Mansons Congo Case (1). The inoculations of blood from this case were carried out by Prof. Stewlett, into rats, mice, guinea pigs, one rabbit, one dog, two monkeys, one pony and one pig.

Although these animals were kept under observation for a considerable time — some of them for several months — after inoculation, none of them showed any evidence either Clinical or microscopic, that the inoculation had succeeded.

Of this case it may be remarked that,

(1) Manson & Daniels. "A case of Trypanosomiasis" Brit. Med. Jour. 30/5/03 p. 1251.

for some unascertained reason, the experiments did not prove successful.

C. Congo Experiments (1)

Messrs Dutton Todd & Christy worked with Cerebro Spinal fluid and blood of Sleeping Sickness and Trypanosoma fever cases respectively, with identical results.

These observers came to the conclusion that judging from the very slight insusceptibility of laboratory animals to infection with Trypanosomes found in Man in the Congo; the great chronicity of the infection produced when inoculation has been successful; and the periodicity with which parasites have appeared in the peripheral blood of the experimental animals; they think that these are points which greatly resemble the animal reactions of the Tryp. Gambiense. "During the eight or nine weeks ~~when~~ the animals were under observation, none of them ever manifested any gross signs of disease."

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(1) Dutton Todd & Christy. First progress report of the Exped. of the Liver. School of Trop. Med to the Congo. & Brit. Med. Jour. 23/1/04 p. 186-188.

D. The Experiments of H. Wolferstan Thomas and S. F. Linton in Liverpool.(1)

These observers worked with the following material:- Strains of:-

a. Cerebro spinal fluid of Uganda Sleeping Sickness cases.

b. Cerebro spinal fluid of Congo Free State Sleeping Sickness Cases.

c. Blood of Uganda Trypanosoma Fever Case.

d. Blood of Congo free State Trypanosoma Fever case.

e. Trypanosoma Gambiense from the Gambia.

They found that

1. These were all identical both in animal reactions & in morphology.

2. There seemed to be no acquired immunity against infection.

3. There was no transmission of immunity to offspring.

4. An animal which seemed to have recovered many months, may later show parasites once more, apparently as the result of lowered vitality.

In greater detail, they say:-

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(1) Johnston & Yates. Labor. Reports + The Lancet 14/5/04 p 1337.

"In rats and mice - the same chronic disease, periodicity in appearence of parasites, and absence of symptoms are in all cases observed as were described by Dutton and Todd. M. Brumpt, M. Wurtz[1] have described very marked symptoms in mice and rats inoculated from Congo Sleeping Sickness cases, eg. progressive emaciation, intermittent paralysis of the posterior quarters, oedema of the perineum, and sometimes acute nervous affections. We have observed none of these symptoms. Occasionally we have noted slight oedema postmortem but never in sufficient degree to detect before death.

In guinea pigs, there is with all strains the same lengthy incubation period. In those infected up to the present there is the same more or less chronic disease, characterised by loss of weight and constant presence of parasites in the blood.

In rabbits we have produced with all strains the same chronic disease with fairly constant presence of parasites,

(1) Maladie due Sour. Experimentale. Comptes rend. de la Soc. de biol., tome LVI 1904 No 12., Avril, 569-73.

"loss of weight and anaemia.

In cats the disease is the same with all strains, with rise of temperature on appearence of parasites; fairly constant presence of parasites, and absence of other symptoms so far as we have yet observed.

In dogs and puppies there are no differences to be noted. Incubation periods are the same, and whatever strains be used, there is the same constant presence of parasites in the blood, with loss of weight and anaemia.

In goats and donkeys, no differences have been observed between the strains used.

In monkeys. Infection is readily produced with all strains, even with very small doses, and parasites are fairly constantly present in the blood, often in considerable numbers.

Similar symptoms are observed with the different strains, viz. Slight loss in weight, anaemia, rise in temperature, especially with the first appearence of parasites in the blood, and occasionally localised oedema.

We have observed no marked tendency to sleep in our monkeys. When a monkey is ill, it sits on

"its haunches with its head between its knees. This position which has been termed the Sleeping Sickness position is not characteristic of trypanosomiasis or Sleeping Sickness; it is the position assumed by any sick monkey from whatever disease it may be suffering.

We have noted no nervous symptoms at all"

Stained specimens of parasites from the systems of inoculated animals.

The same observers state that they have not observed any differences between the trypanosomes of Uganda and Congo Sleeping Sickness Cases on the one hand, and Tryp. Gambiense (Dutton) on the other. "In the same species of animals and at corresponding stages of the infection, the size and appearance of the former trypanosome is precisely the same as those of the latter as described by Dutton and Todd and since observed by us"

Passage through various animals seems to vary the size and form of the parasites, but these variations are the same for each species of animal and for all the different sources of inoculative material.

Pathological Lesions. Summarized they were :-

1. Enlargement of the spleen in all animals.

2. The glands very little enlarged. Petichial haemorrhages were rarely seen.

3. No macroscopic changes were observed in the nervous system.

4. No trypanosomes were ever found in the Cerebro spinal fluid after death, nor did any animals inoculated with this fluid ever become infected.

Causes of Death. The observers were "unable to say definitely that trypanosomiasis was the sole cause of death. Very frequently an intercurrent affection has occurred which, the animal's vitality having been impaired, has caused death."

Natural Immunity. "There is a certain amount of natural immunity or resistance to the human trypanosome met with, in individual rats and other animals." "Guinea pigs show considerable resistance to infection".

"Baboons (Cynocephalus Sphinx) have up to the present been absolutely refactory"

Authors Conclusions derived from the results of Animal experiments.

It is considered

1st That it is very probable that Tryp. Gambiense (Dutton) of the blood is identical with the Tryp. Ugandense (Castellani) of the Cerebro Spinal fluid. It follows therefore, that by right of priority of discovery and description, only the former name - Tryp. Gambiense - ought to be retained in the nomenclature.

2nd That it has not been proved that Sleeping Sickness can be communicated to lower animals, and it cannot be stated that deaths after inoculation have been due directly to the parasites:

It has also been shown that animals may recover entirely from the results of inoculation.

3rd That the question of the production of immunity in the lower animals has not yet been decided.

Chapter IX

On the Mode of Infection.

The analogy of the Trypanosome diseases of other animals.

In the Chapter on the local distribution of Sleeping Sickness, it was noticed how very peculiar it was, its connection with water; its patchy distribution; its predilection for forest and plantations, and its avoidance of open lands. We have seen that the infection could not have anything to do with the food supply, or the water supply, and we had reason for supposing that it was not communicable directly from individual to individual.

When these facts became known, the questions occurred to many:—

(1) Is it possible that Sleeping Sickness is transmitted through the agency of a blood sucking insect?

(2) If so, then does the distribution of the disease coincide with that of any

one of them?

Observers had before them the analogies of Nagana and of the other trypanosome diseases of the lower animals. Bruce had proved in 1894 that the Tsetse fly, Glossina morsitans was capable of carrying this infection from animal to animal. In 1898 Haslam had found the living trypanosomes in the stomach of two species of Stomoxys.

In Surra various Tabanidae had been incriminated by Rogers and others. Lignières had found the trypanosomes in the stomach of Stomoxys calcitrans, and Sworc and Lécler had stated that they had allowed sound horses to be bitten by these flies and obtained positive results.

Other analogies were also to hand, and it is not surprising that these put the workers in Uganda at once upon the correct path of investigation, and as soon as the enquiries were persued a little further, they found that the distribution of the Tsetse fly (Glossina Palpalis) corresponded with the local distribution of the disease.

The comparitive distributions of the Tsetse fly and of Sleeping Sickness.

A In Uganda &c. The investigation was undertaken by Navarro Bruce and Christy of the Royal Society Sleeping Sickness Commission, and they came to the conclusion that the distribution of the fly and of the disease exactly corresponded. Along the the wooded portion of the lake shore of Victoria Nyanza, as well as in Uganda and Busoga provinces, the Glossina Palpalis was found; the disease and the fly being limited to the shores of the lake and to the islands.

Two maps[1] are given in the Reports of the investigators, illustrating the exact areas in which the observations were made and giving the results obtained from them.

"On Comparing the two maps the similarity of the distribution of Sleeping Sickness and Glossina Palpalis is self evident. The disease and the fly are limited to the shores of the lake + to the islands", except in Busoga

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(1) Reports of the Sleep. Sick. Com:, Royal Soc., No IV opp. p. 54. + and end of this paper p239. Fig. 7.

where both the fly and the disease are found a little inland. "The fly is also seen to pass up the Nile". "The other Uganda rivers are merely swamps full of papyrus". "The fly does not proceed up the swampy river valleys; even on the coast behind papyrus swamps, it is also absent."

In the Entebbe district "the fly is only found on the shore of the lake where there is forest. This forest is thick jungle with high trees and dense undergrowth. The fly is never found in open sandy beaches backed by grass plains, even although there may be some small scrub near the waters edge. It is never found in the grass of the grassy plains" nor "in banana plantations, nor at any time far from the lake shore."

In the whole of Utonga the same observations hold good.

These remarks are important for it is in these densely wooded shores of the lake where the fly frequents, that the half naked natives of the islands and of the mainland meet in thousands to trade in fish, &c.

In addition, it seems that the Tsetse fly avoids the neighbourhood

of villages and populous centres.

Comparing the information above given, with the described local distribution of the disease itself, it is evident that it is in just those situations where the tsetse fly abounds that the disease is epidemic; a fact which although pointing to the fly being the possible carrier, yet does not absolutely settle the question.

Turning now to other parts of Equatorial Africa, we find that in no other place, have the comparitive distributions been investigated with such precision as in Uganda and neighbouring districts.

B. From Senegambia and Angola we have no information

C. In the Congo districts we are informed by messrs Dutton Todd and Christy (1) that "the tsetse fly was incessantly present from Stanley Pool to Basoko. After Basoko was passed there were very few flies, and just after the expedition left

(1) Dutton. Todd & Christy Brit. Med. Jour, 26/11/04 p 1482.

the mouth of the Lomami river, the last one was seen on the steamer. Although the natives in the towns at which we stopped recognised the fly none were found in the neighbouring bush. It was noted that where there were many Tsetse flies there was much Sleeping Sickness; but where these flies were scanty, cases were rarely seen"

The common species noticed was the Glossina Palpalis.

Brumpt[1] also observed the same series of facts in the Congo district.

The Glossina Palpalis

Short description of the fly. Mr. Ernest E. Austin[2] in his monograph of the Tsetse flies (Genus Glossina, Westwood), based on the collection in the British Museum, recognises seven species of Glossina.

"Glossina Palpalis, the carrier of the trypanosome of Sleeping Sickness; dark brown; thorax usually paler with

(1) Brumpt. The Lancet 29/8/03 p 636.
(2) Austin - Monograph of the Tsetse flies. Longmans & Co. London. 1903.

dark brown marking on a greyish ground; abdomen generally with at least an indication of a pale longitudinal median stripe, with pale lateral triangular markings, and usually the hind margins of the segments narrowly pale. Legs (except the hind tarsi and last two joints of the front and middle pairs) sometimes entirely buff coloured. (var. Tachinoides, Westw.); usually the femora for the most part are entirely dark brown, in well preserved specimens clothed with greyish dust, and the tibiae yellowish."

Habits (1) "The glossinae are never found on mountains, they are seldom seen above 3000 ft.; they are absent from extensive plains or other open spaces, and rarely found in cultivated patches. Their habitat is always in the neighbourhood of water, along the banks of rivers, round the coasts of lakes, or low riverine islands in swamps and meres, especially at the foot of mountains.

They are most numerous along the water's edge; they become scarcer and scarcer, as one advances inland,

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(1) The Lancet 23/1/04 p. 229.

and they disappear entirely within a few miles of the water.

The places they occupy are sharply defined and permanently established. These places or stations are called "fly belts" and the natives know their limits precisely". "The flybelts may extend for hundreds of miles, varying greatly in width according to the nature of the country. In such cases however, tsetse flies are not found at every point, throughout the belt, but in particular patches the area of which may be quite small."

According to Bains, "the fly is extremely local, and extensive districts in which it prevails may be passed through with the aid of guides who know the 'patches' of fly, just as a pilot knows the shoals of an estuary." "These fly patches are confined to reed swamps, to banana bushes, or to patches of mossani or mimosa forest."

The essential condition seems to be the presence of water and of a loose fragmentary soil.

Austin states that the tsetse flies are more active during the

hottest hours of the day, whilst Bruces' opinion is that they bite preferably at sunset.

The limitation of these fly belts has its attempted explanation in various theories.

Austin says". The limitation of the tsetse flies to belts is not as remarkable as may at first sight appear. There can be little doubt that it is due to a characteristic social tendency of the order to which these insects belong; which, though frequently overlooked is exhibited by the majority of species of diptera, and has attracted special attention in the case of the tsetse owing to their blood thirsty nature and the fatal consequences of their bites."

Bauron thinks that this patch distribution is not explainable on social grounds but rather has reference to the food habits of the insect. He suggests that it may feed on the blood of some air-breathing mudfishes of Equatorial Africa, a large proportion of which are known to have trypanosomes in their blood; these parasites being remarkably like those of mammals.

He infers therefrom, that this habit might possibly explain the source from which the fly originally obtains the parasites.

Another point in the history of the tsetse fly, which might in the near future, turn out to be more important than it is at present, is, that the genus glossina do not lay eggs as do the majority of the diptera, but extrude yellow colored larvae nearly as large as the abdomen of the mother. Immediately on being born this larva creeps about with activity, finding a resting place in some hole or cover. After a few hours it turns into a jet black hard pupa or nympha.

(1) Contrary to what has been found to be the case with regard to Glossina Morsitans in South Africa, Glossina Palpalis does not appear to be dependant upon big game; and in Uganda at any rate, the members of the Sleeping Sickness Commission seem to have come to the conclusion, that this species of

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(1) Austin – Supplementary notes on the Tsetse fly. – Brit. Med. Jour. 17/9/04 p. 660.

Tsetse fly subsists largely upon human blood."

Writing to Dr Navarro from Wadelai, Wyndham observes that the fly cannot depend for its existence upon game, as in most of the places in which he found it, there is none or next to none.

Can the Glossina Palpalis carry the trypanosome found in Sleeping Sickness Cases, from Animal to Animal? Experiments have as yet been few, nor have the results of them been particularly satisfactory.

Two sources of information are available.

1st " Experiments by Dutton Todd and Christy in Senegambia and in the Congo district.(1) These were not successful and will not be referred to further.

2nd " The experiments of Bruce, Navarro and Greig in Uganda(2)

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(1) "Human Trypanosomiasis & its relation to Congo Sleep. Sick". 2nd Prog. report of the Liv. Exped. to the Congo 1903; also abstract in Brit. Med Jour. 20/8/04 p. 372 et seq.

(2) Reports of the Sleep. Sick. Com., Royal Soc., No I p. 37 et seq.; No IV p. 56, et seq.

Uganda Experiments. "The animal chosen to carry out these experiments was the monkey. They were chosen because they were easily procured, easily fed and kept their health perfectly on captivity."

"Two sets of experiments were performed.

The 1st Method used was simply to "feed tsetse flies on a Sleeping Sickness case, and at varying intervals of time to place the same cage of flies on the monkey. The sleeping sickness patient did not seem to feel the bites of the flies and they made no complaint or other signs of inconvenience. There was as a rule about 30 flies in each cage, but only those which filled themselves were reckoned to have fed".

The flies were put on the monkeys at varying intervals, i.e., some eight hours, others twenty four hours, and yet again, some forty eight hours after feeding off the Sleeping Sickness patients.

Hundreds of flies were used in each experiment, and they were used every day in batches of 10 to 140 at a time, on the same individual monkey, until a positive result

was obtained.

Some weeks generally elapsed (usually two months) between the commencement of the experiments and the dates at which the trypanosomes were found in the monkeys' blood.

Five experiments were performed and in each one a positive result was obtained.

As a result the commissioners came to the conclusion "that Glossina Palpalis can convey trypanosomes from Sleeping Sickness cases to healthy monkeys up to at least 148 hours after feeding"

The 2nd series was made to find out if the ordinary wild tsetse flies, fresh caught and placed on healthy monkeys without any artificial feeding, would give rise to the disease.

The flies were caught on the shore of the Victoria Nyanza, in the vicinity of the hut tax labourers' Camp near Entebbe; the latter living in rudely built grass huts near the shores of the lake about a mile from the town.

After the flies were caught they were brought to the laboratory and immediately placed on healthy monkeys.

In the three experiments performed the result was positive in all, the trypanosomes appearing in the blood of the infected monkeys as early as 14, 29 and 23 days respectively after the first feedings.

The Conclusions of the Commissioners.

The experiments made by the Commissioners with tsetse flies collected at Entebbe and fed on monkeys, were (at the time they were published) accepted by themselves and by some others as proving:—

1st. That the trypanosomes of Sleeping Sickness are transmitted from the Sick to the healthy by Glossina Palpalis.

2nd. That the flies collected in the vicinity of Entebbe were actually carrying the trypanosomes of Sleeping Sickness at the time they were captured.

Objections to the Experiments.

But really, the experiments performed do not prove what is claimed for them, and the objections to them are:—

1st The flies were not reared in the laboratory for one or more generations as they should have been, before the experiments were performed.

It is known for certain,

that some of the flies freshly caught, already carried trypanosomes, and therefore it is not at all proved in the first set of experiments that the monkeys were inoculated from the sleeping sickness cases; for they might have been infected by the trypanosomes the flies themselves were previously carrying.

In this connection might be pointed out the peculiar discrepancy between the periods of incubation in the first and in the second set of experiments. In the first set where the flies were previously fed on sleeping sickness cases, the period was about two months; in the second, where the flies were directly set on the animals, it only averaged three weeks or thereabouts. What is the reason for this?

In Sambon's opinion the difference is explained by the fact, that in the first set of experiments, the flies when put upon the sleeping sickness cases, actually parted with some of the infection they were already carrying, therefore leaving comparatively little for the monkeys on which they were subsequently fed. In the second set obviously, the

full measure of infection was conveyable to the animals; thus explaining why the period of incubation in the latter was so much shorter than in the former.

Nabarro[1] however explains the discrepancy on different grounds. He states that whereas in the first set of experiments the flies were overfed, and consequently did not bite the monkeys freely; in the second series the flies were freshly caught and by biting ravenously conveyed the infection in a much more virulent manner.

2nd "; It is not proved that the flies caught were carrying Trypanosomes of Sleeping Sickness at all. It is only shown that some kind of Trypanosomes were carried, which might or might not be the human species, and that the monkeys were susceptible to them.

It is stated by the Commissioners themselves (Nabarro & Greig[2]) that they

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(1) Discussion on Sleep. Sickness. Epidemiological Soc., The Lancet 23/1/04 p 231.

(2) Discussion on Sleep. Sickness. Brit. Med. Assoc meeting; Brit Med Jour. 20/8/04 p. 398.

examined various other animals and found trypanosomes; in cattle, oxen, in the dog and in the mule.

3rd ". The monkeys experimented upon were kept in the open and therefore quite liable to sources of infection other than those of the flies provided for them.

It is evident therefore, that on the whole, these experiments of the second Commission of the Royal Society are comparitively of little value, and that they will need to be repeated with much greater scientific precautions and exactitude.

The Dissection of the Flies.

"The dissection flies", states Navarro[1], "at varying intervals after a feed yielded interesting results which may be summarised as follows. The trypanosome of sleeping sickness was found actively motile in the stomach contents of the fly 7½ hours after the feed."

As against this observation regarding the human trypanosome, he mentions that in the same species of fly he found:-

(1) a cattle trypanosome 100 hours after feeding.
(2) a Dog. Do 5½ do. do
(3) a Mule Do 20 do. Do.

He adds that though motile

(1) Brit. Med. Jour. 20/8/04 p 379.

so long after the feed, the trypanosomes stain badly after a time.

It is also said that trypanosomes have been found in the proboscides of the flies on dissection by Bruce. No particulars as to this have been given out. It must however be borne in mind that the mere presence of living trypanosomes in the probscis or midgut of a blood sucking fly, by no means proves that the latter is capable of transmitting the disease. Any bloodsucking arthropod feeding upon the blood of a trypanosome infected animal would naturally suck up some of the parasites with the blood.

Further observations are required.

Conclusions based upon information as yet received.

The probability is, that the Glossina Palpalis is the carrier (or at least one of the carriers) of the Sleeping Sickness organism; but no definite scientific proof has as yet been advanced.

The great arguments in favor of the supposition are; the analogy of Nagana and of the allied

diseases of the lower animals, and, the comparitive distributions of the Tsetse fly and of the disease. But it should not be overlooked that this distribution has been definitely traced in only a very limited portion of the area affected by the malady, and it may quite well turn out in the future, that the supposed co-incidence is not so close as it is now considered ~~supposed~~ to be.

It may be added that it is well known that Sleeping Sickness when imported into Countries where the tsetse fly does not exist, exhibits no tendency whatever to spread; and this fact in a negative kind of way, may be held to be an additional argument in favor of that fly being the Carrier.

Chapter X

The Mode of Infection (Cont.)

Is Glossina Palpalis the only Carrier? The Analogy of the Trypanosome diseases of Animals. The following is taken chiefly from Rogers' account.(1)

Speaking of the Carriers of trypanosome affections generally, he continues:—

"In 1902 Schilling(2) in Togo proved that at least two species of flies can transmit the infection in dogs; while Curry(3) in Manilla found that Stomoxys Calcitrans was the principal agent in the transmission of the disease among horses &c, active trypanosomes being found in in the proboscis and Stomach 24 hours after feeding them on infected blood.

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(1) Leon. Rogers. Brit. Med. Jour 26/11/04 p 1454.
(2) Deutsches Colonialblatt No 14, & Centralbl. f. Bakt 16, 1902.
(3) Vet. Journal. Vol LIV p 292

In the same year Sivori & Leclerc[1] in South America proved that the Musca Brava, the Stomoxys Calcitrans, and the Tavon can transmit the disease from horse to horse."

The Conclusions of Musgrave and Clegg[2] working on Surra in the Philippines, are summed up as follows: "Trypanosmiasis is essentially a wound disease, and infection takes place when the materies morbi are brought into contact with an injured surface, and in no other way.

The most common agents in bringing about this condition are biting and stinging insects, and of these, certain flies and to a less extent fleas are the most important."

Bruce[3] on the other hand is of another opinion and he maintains that there is no proof that any biting fly of a genus other than Glossina can carry the infection. He adduces the researches of Nuttall of Cambridge

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(1) Centralbl. f. allg Path. 1902 p. 963.

(2) Reports of the Biological Laboratory. Manilla. No 5 (1903)

(3) Brit. Med. Jour 20/8/04 p 368.

who experimenting on the conveyance of Nagana trypanosomes from sick to healthy animals by means of Stomoxys calcitrans, always had negative results. Greig and Gray also inform Bruce that they had tried this experiment in Uganda with Stomoxys & had also failed.

He adds that experiments on a large scale have been going on in South Africa for many years, in regard to the spread of Nagana or the Tsetse fly disease; it is only where the tsetse fly Glossina morsitans is found or one of its allied species Glossina pallipides is found, that the disease occurs. Outside that area there may be many other species of biting flies, but the disease never spreads beyond the zone of the tsetse fly.

Conclusions; and the importance of the Question.

Obviously Bruce is speaking of the one disease Nagana. Even if what he maintains be correct in the disease he instances, it does not follow that the observations of other workers in the other affections of different countries are to be excluded.

For instance, it is well known that the genus Glossina is not to be found in India, and assuming that trypanosome disease is only transmissible by the bites of certain bloodsucking insects, it follows that it must be some insect or insects in India, other than Glossina, which are able to carry the infection from one animal to another.

Again, the researches of Rogers and Chatterjee have shown, that it is possible that one of the forms of Tropical Splenomegaly found in India and in other Countries, may eventually turn out to be a trypanosome disease of man. Yet this disease can spread, even epidemically in India, without the aid of the genus glossina, which, as already stated, does not exist in that Country.

The great argument which so far as we know, only applies to a limited region of Africa, is, that the distribution of Sleeping Sickness and of the Glossina Palpalis being so alike, the spread of the disease must in some manner, depend upon the fly in question, and

not upon others; for it has been noticed that where the fly does not exist, even though other blood sucking insects be present in numbers, the disease does not spread.

On the whole it is evident that this is another of the many questions in regard to the etiology, which has not been definitely decided; and it is in reality an important issue indeed, in regard to the spread of the disease if introduced into other parts of Africa or into other countries.

If it should then appear that potential carriers other than the Glossina were actually present, then, unless suitable measures were organised this introduction of cases might prove of the greatest importance to the inhabitants of the country in question.

Does the Trypanosome pass through any metamorphosis in the body of Glos. Palpalis or does the latter act simply as a mechanical carrier?

There is a considerable divergence of opinion on this subject: —

The Arguments against Metamorphosis

1. The fly is not able to retain, or does not retain (see Uganda experiments) its infective quality for more than 48 hours. Attempts to infect a healthy animal by means of the Tsetse fly after a longer period than 48 hours has elapsed after feeding it on infective blood, have so far all failed. If any metamorphosis analogous to that which the malarial parasite undergoes in the mosquito, was undergone by the trypanosome in the tsetse fly, it would be expected that the latter would not become infective until some time had elapsed from the last period of feeding. This is not the case.

2. No signs of metamorphosis have been detected in the interior of the fly although looked for.

It does not seem however that a sufficient number of flies have been dissected for the purpose. No particulars of the researches have been given and it is just possible, that even if metamorphosis in the body of the fly did take place, the same has not yet been detected.

It may be added (verbal communication)

that it is intended to send out competant observers shortly to Africa, in order to give attention to the elucidation of this, amongst various other important problems.

The Arguments in favor of Metamorphosis

1. The analogy of Anopheles as a definitive host to the malaria parasite.

2. The researches of Schaudinn[1] on the halteridium of the Little owl. (Athene noctua); which show that the male and female forms copulate within the stomach of Culex pipiens, and give rise to male, female, and asexual trypanosome forms, which multiply within the midgut of the mosquito and subsequently pierce through the stomach wall, pass into the circulation and reach, some, the lacunoma surrounding the pumping organ, others, the ovaries.

Those which agglomerate round the pharynx, pierce the delicate membrane between the Chitinous plates, and

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(1) Fritz Schaudinn. "Change of generation and host in Trypanosoma & Spirachoete" Trans. from the German; Jour. of Trop. Med, 1/6/04 + eight following numbers.

pass into the blood of the Avian host during the feeding process of the mosquito. Those which reach the ovaries penetrate into the vitellus, and finally into the embryo, thus producing the infection of the progeny.

Schaudinn maintains that he has been able to prove that the halteridium is the sexual stage of a trypanosome, which multiplies in the Culex pipiens; and after a complicated migration through the body of the mosquito, is again introduced by its bite into the blood of the owls, where, after a period of sexual multiplication, it is transformed into the well known male and female halteridium.

With regard to the male, female and asexual trypanosome forms described by Schaudinn, L W Sambon,(1) after examining large numbers of trypanosomes of Sleeping Sickness cases, is of opinion, that there can be no further doubt as to the presence of the sexual forms. "The large stumpy macrogametes, with short flagellum, numerous dark staining

(1) "The Transmiss. of Sleep. Sick. by flies. of the G. Glossina." Brit. Med Journ. 19/3/04 p 696.

granules and sometimes vacuoles can be easily distinguished from the small hyaline, slender microgametes with large deeply staining nucleus, large micronucleus and long flagellum, and from the fars more numerous asexual forms which multiply by longitudinal division. Besides, each form exhibits peculiar nuclear changes."

This discription of Sambons', so far as one is aware has not yet been conformed:

3. The method of reproduction in the Tsetse flies, (the eggs hatching and the larva developing within the body of the mother) is in favor of the theory; chiefly in view of Schaudinns researches quoted in the previous paragraphs, and also in view of the well-known method of transmission of red-water fever by the cattle tick, by means of infection of the progeny of the latter within the body of the parent.

4. The paucity of trypanosomes in the blood of sleeping Sickness cases, furnishes another argument.

The source from which the fly derives the infection being then so limited, if metamorphosis did not

take place within the body of the insect, or if the infection was not conveyed by some means to the progeny of the flies, it is difficult to conceive how so many flies are found which are shown to be efficient in the communication of the infection.

6. Conclusions. On the whole one is inclined to the opinion that it is very likely a metamorphosis does take place in the body of the carrier.

At any rate, the present indirect evidence does not go to show that all the stages of the parasite take place in the human host. The probability of a double alternating life cycle in the history of the Tryp. Gambiense is therefore quite feasible.

The part played by the lower animals in the spread of Trypanosomiasis in Man. We have much evidence that trypanosomes exist in the blood of various animals, fish &c in the infected zones; but we have as yet, absolutely no data to guide us in expressing any opinion

as to the part that is played by them.

The trypanosomes seem to be of different species to those found in man, but nothing is definitely decided.

It is quite possible however, that some animal or fish we might in some as yet unascertained manner, serve as the fountain, so to speak, from which all infection is derived.

Chapter XI

The Pathological Anatomy.

Historical Note

The naked eye characters of the various organs in this disease had been described more or less accurately long ago, by Clark, Dangaix Guérin Gore and others.

The first detailed microscopical examination was that which Regis and Gaid published in 1898. These authors attributed the symptoms of Sleeping Sickness correctly to a meningo-encephalitis, and the ir observations referred to a single case in the region of Timbuctoo.

In 1899 and 1900, Mott[1] published a record of the changes found in the Central nervous system of two cases of the disease; these observations being confirmed by the Portuguese

(1) Mott. Brit. Med. Jour. Dec 16. p 1666. (1899)

Commissioners[1] in 1901, and by Warrington[2] in 1902.

Later researches include those of Messrs Dutton Todd Christy Brumpt and others on the west side of Equatorial Africa, and those of Bruce Castellani Navarro, Greig & Low in Uganda and neighbourhood.

These different observers all agree as to the changes found, the following is taken chiefly from the descriptions of the Commissioners of the Royal Society,[3] and is given as a good representation of the Pathological Anatomy of the disease:—

Naked Eye Anatomy

Central Nervous System. The changes are essentially those of a chronic meningo-encephalitis and a meningo-myelitis. In a large number of cases there is not much to be seen macroscopically.

"The calvarium is not thickened. The Duramater shows.

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(1) Docuco de Sonno. Lisbon 1901 and The Lancet 28/9/02 p. 885 et seq.

(2) Warrington, Brit Med. Jour Sept. 1902

(3) Reports of the Sleep. Sick. Com., Royal Soc., No II

little change; it is seldom adherent to the skull but may be to the subjacent arachnoid. (The Portuguese commission never noticed this.) The subdural fluid is not usually in excess, though in some cases it shows a marked increase. The pia-arachnoid though generally clear, is sometimes ~~centrally~~ opaque and slightly thickened. In some cases it is adherent to the brain, and on being stripped causes some erosion. The vessels in this membrane may show some congestion.

The subarachnoid fluid is usually pale straw colored and is often in excess. In a few cases it is slightly turbid, and in some, even purulent. Recent lymph in small amount may be found.

On section the substance of the brain is moderately firm and nothing abnormal is to be seen with the exception sometimes of excess of fluid in, and dilatation of the lateral ventricles.

The pituitary body, the pons, Cerebellum and medulla Oblongata show no(?) macroscopic changes.

The membranes covering the Spinal Cord show the same appearances

as those of the brain, and sections of different areas reveal nothing macroscopically."

Generally speaking the convolutions are neither flattened nor wasted. Puncta cruenta are rarely marked in the cut surface of the brain. The medulla may show to the naked eye marked congestion of the vessels.

The Heart is usually pale, flabby, and may manifest signs of myocardial changes.

The Lungs. "Congestion and oedema are nearly always seen" (Low and Castellani); "Apart from old pleuritic adhesions there was mostly nothing abnormal in the Respiratory organs." (Portuguese Commissioners).

In some cases pleuritic adhesions are noticed though effusions have not been found.

The Liver and Spleen. Both are generally enlarged and pigmented. (Causation, Malaria?).

Kidneys, Suprarenals and Pancreas are of a normal appearance.

Stomach and Intestines. The former may show a patchy congestion, the latter exhibiting a similar appearance. Of parasites,

are found, Ankylostomum duodenale Ascaris lumbricoides, ova of Bilharzia haematobia and Trichocephalus dispar in the intestines in cases of natives.

Enlarged glands are present in all cases, generally throughout the body, the retroperitoneal groups often being the most affected.

Bladder urinary and Sexual organs. These are unaffected.

Histological Anatomy.

Central Nervous system. The change described shortly, is that of a chronic meningo-encephalo-myelitis, the leading characteristic of which is the filling of the vascular Canalicular systems with large and small mononuclear leucocytes. These changes are definite and quite invariable.

In detail:—

The Cortex. A mononuclear leucocytic infiltration is always seen on the meningeal surface of the brain spreading down into the sulci, and affecting in varying degree, the perivascular spaces around the bloodvessels in the substance of the Cerebrum, pons, medulla and Cord.

Cerebro spinal fluid. The leucocytic formula of this fluid is mononuclear

Nerve Cells. The ganglionic nerve cells of the cortex and of the medulla, and to a less extent of the spinal cord show frequent pathological changes, being often altered and irregular, and partaking of the character of coagulation necrosis.

There is chromatolysis; there being loss of Nissels bodies; and diminution and atrophy of connecting fibres.

Membranes. The pia arachnoid exhibits an infiltration with large and small celled mononuclear leucocytes.

Nerve fibres. The axis cylinders and medullary sheaths of the nerves in the cord may show (marchi's method) a diffuse degeneration in some cases.

Vessels. No endarteritis is noticed. The blood contained in the vessels exhibits usually an excess of mononuclear leucocytes.

Organisms. Very few trypanosomes have ever been found in the blood vessels or perivascular spaces of the central nervous system. On the other hand, diplococci can generally/

be demonstrated often in enormous numbers in all parts of this system.

The Peripheral nerves. No changes have been noted.

Other parts of the body. There is nothing special to be described. The Liver and Spleen generally show old malarial changes.

Organisms. The trypanosome has been detected with certainty after death only in a very few instances. Peculiar forms were seen which were taken to be degenerated parasites.

The diplococci have been found in some of the organs. In one case (Manson's described by Mott and Low[1]), they were recognised in all the organs with the exception of the kidney.

The matter has already been dealt with (p. 61 + 91.).

Be it noted that the post-mortem appearances and changes in the so-called Trypanosoma Fever

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(1) Mott + Low. Brit. Med. Jour., 30/4/04 p. 1000 et seq.

as illustrated by Manson's case in a European, and of which, the anatomy was described by Mott & Low, appear to be identical with those described as occurring in Sleeping Sickness proper.

The Blood will be noticed later on. (See "Clinical features.")

The Significance of the Pathological Changes will also be gone into in a later chapter (see "Further Considerations as to Etiology and Pathology" p. 183 &)

Chapter XII

The Clinical Features and Symptomatology.

Introductory. At the outset a difficulty confronts us.

A few years ago before the trypanosome was demonstrated in the blood and cerebro-spinal fluid of man, it would have been an easy matter indeed to enumerate the various symptoms and signs encountered in the disease under discussion.

Since that period however, it has been observed that the presence of these trypanosomes in the circulation of man, may produce in him certain symptoms and signs; the combination of these passing under the title of "Trypanosoma fever" so-called.

What connection have these Trypanosoma fever cases (with parasides in the blood), with cases of Sleeping Sickness proper (with the organisms in the cerebro spinal fluid as well as in the blood.)? The question has not yet been

fully answered; but, for reasons which will be enumerated later, it is here presumed that the former is in reality but the first stage of the latter condition.

It is convenient therefore, in describing the symptomatology of the disease, to treat the subject, firstly under the heading of Trypanosoma fever and secondly under the designation of Sleeping Sickness proper.

I. Trypanosoma Fever

A. In Natives. Our present knowledge is very incomplete and the published reports are too meagre to allow of an exact account being given.

In these cases we are able neither to fix the date of the inoculation, nor to trace the history of the initial pyrexia which in most accounts seems to be one of the first signs noticed.

In Baker's Uganda Cases.(1) In the five cases fever seemed to have been the prominent feature; but as Manson remarks, it was because

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(1) Three cases of Trypanosoma fever in Entebbe, Uganda; Brit Med Jour., 30/5/03 p 1254

the patients had fever that their blood was examined. "It is quite possible therefore, the concurrence of the fever and the parasite was to some extent coincidence, and that the parasite may be present in other natives who have no fever."

Some of these cases were kept under observation. Regarding one of them:— the patient was admitted to hospital on March 12th and his disease was diagnosed as trypanosoma fever. After a few days his temperature became normal and he remained apparently in good health and did his duty as a policeman until the end of July when his temperature again became unsettled. "During all this time trypanosomes were found in his blood but it was only towards the end of June that they were noticed in the Cerebro Spinal fluid, and this corresponded fairly well with the rise of temperature." (1) The temperature curve also, seemed very suggestive of Sleeping Sickness, but no marked symptoms of the latter were manifest.

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(1) Reports of the Sleep Sick. Com., Royal Soc., No. IV p. 10.

Another case exhibited the same sequence. The remaining three had shown nothing at the time the report was penned.

About a year later however, it was announced by Bruce[1], that one of the natives was suffering from unmistakable symptoms of the disease. Also, some of the other cases of Trypanosoma fever which had been observed in Uganda in 1903 were found by Greig and Gray to be suffering from symptoms a year later, and some of these were reported as having died.

The significance of these cases will be pointed out later.

In the Congo and Gambian districts.

Dutton Todd and Christy in Reporting cases of Trypanosoma fever, also remark on the mild character of the disease in natives; but add that there are other cases which show marked symptoms of illness, and which are quite comparable to the Trypanosoma infection in the European.[2]

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(1) Bruce. Brit. Med Jour. 20/8/04 p. 367.

(2) "Human Trypanosomiasis and its relation to Congo Sleeping Sickness."
Brit. Med. Jour. 20/8/04.

B. In Europeans.

Manson's Case is taken as a type.
The patient gives a history of having resided in the Upper Congo district from August 1900 to November 1901, and her illness ~~was~~ is said to date from August of the latter year.
On about Aug. 14th she was bitten on the left leg "by some insect or other animal." The bitten part became red swollen and very painful, so much so that suppuration was apprehended. Under treatment however, the inflammation subsided. She stated that the bite may have been inflicted by a fly.

Fever. On Aug. 28th she commenced to have fever which began suddenly but without any rigor. On the eighth day the temperature fell to normal, quinine in large doses having been given in the Meanwhile.

This fever, which seemed to be the first of a long series of attacks (a constant feature of trypanosomiasis in Europeans), was not amenable to quinine nor to the usual antipyretics, and after

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(1) Manson & Daniels, "Remarks on a case of Trypanosomiasis," Brit Med. Jour. 30/9/03

Continuing for several days (8 to 10), the temperature rapidly fell to normal.

In all cases the remission has no definite character in its duration and is followed by another attack of fever, then by a subsequent remission and so on. The temperature is high in the evening and low in the morning. A characteristic is its irregularity which is of a relapsing undulant type.

In hospital the temperature of this particular patient ranged from 97°F. in the morning to 100°F. in the evening. It was never absolutely normal for 24 hours on end. Occasionally it would rise to 101° or 102°, these rises being generally succeeded by profuse night sweats, and a fall to 96° or 96·5°F. the following morning

The Relation of the Temperature to the parasites in the peripheral blood.

We have evidence (Baker, Moffat, Christy) that there does exist a connection between them. The parasites have often been observed to greatly increase in number at the periods of febrile accession, and

Sometimes to entirely disappear at the times of defervescence.

The other important features of trypanosoma fever are, — the characters of the pulse, a peculiar erythema and oedema, eye changes, anaemia, muscular weakness, breathlessness, general wasting, and sometimes a transient paralysis and thrombosis of the veins of the leg.

The Pulse is always fairly rapid and feeble due to a peculiar cardiac irritability. "During exacerbations of temperature it has mounted to 140 or even 150. and the palpitations and sometimes headache were complained of". (Mansm). In some cases, increased frequency of pulse and respiration occur regularly together. (Dutton).

Skin Lesions. The lesions of the skin preceding or sometimes subsequent to the fever are represented by a peculiar circinate erythema (Forde, Dutton, Mansm & Daniels) and accompanying oedema of the skin and subcutaneous tissues: —

The Erythema. In Mansons case this was first —

observed during the primary fever on the Congo. "The skin of the trunk face and limbs were all involved, more especially the back of the trunk, and the face. The eruption was said to have been more marked during the initial pyrexial period than subsequently. When she was in hospital, it showed itself on many occasions only as an obscure patchy mottling; at other times it was very ~~very~~ prominent."
"The patches which are of an evanescent character, varied in size and form from an inch to many inches across; from distinct rings or segments of rings, to ill defined irregular blotches shading insensibly into healthy looking skin.

One or both sides of the face and forehead often presented a flushed appearance as if from wine. "There was no pruritis or urticaria."

The Oedema. "This like the erythema was most pronounced on the back and face, especially towards the flank and sacral region. The legs were also distinctly implicated, the arms less so"

It involved the cutis as well

as the subcutaneous tissue. It fluctuated in degree from time to time and had a patchiness in distribution similar to the erythema. The oedema of the face seemed often to be combined with flushings, sunken eyes and a watery conjunctiva.

The Spleen is not found enlarged in all the cases.

The Eye Symptoms include in some cases Choroiditis, Iritis, Cyclitis and optic neuritis. (Manson).

Blood examination reveal the parasites, which have already been fully described.

Red Corpuscles. There is no marked anaemia; in Manson's Case the R.B.C. averaged 3,300000, the Haemoglobin being reduced in about the same proportion. - 36% was the lowest estimate. The reds are fairly uniform in size and there is no poikilocytosis; and very few nucleated corpuscles are apparent.

The Leucocytes are found to be slightly below the normal number, they average about 6500.

The differential count shows excess of large mononuclear elements, to two or three times their normal

proportion. The lymphocytes are not in excess. The polymorphonuclear and eosinophile cells are fewer than normal. The lymphocytic elements are not affected beyond the normal range of variation.

Mast cells are found in larger numbers than in ordinary blood. Abnormal mononuclear cells (1·5%) are found; they vary in size, have large round nuclei, and protoplasm which stains evenly with Leishman's stain. This type of cell is found in small numbers in Spleno-medullary leucocythaemia.

Progress of the Cases. No improvement in this particular patient was ever manifest. After leaving the hospital she returned home to Bristol, where for the first time, about the middle of October 1903[1], a marked tendency to drowsiness appeared. "With the exception of some twitchings of the left angle of the mouth, there were no other evidences of tremors. Emaciation however had now become extreme, and small hard glands were palpable in the posterior triangles of the neck.

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(1) Low and Mott. Brit. Med. Jour. 30/4/04 p. 1000.

She gradually became more drowsy; in the last days of life the sphincters relaxed and she died in a state of coma." The duration of the case was over two years.

It is yet much too early to say whether all patients suffering from trypanosoma fever, do eventually die with Sleeping Sickness symptoms, and the researches which have very lately (1904) been carried out in Uganda by Greig and others, should help to elucidate the problem. The European case of Forde and Dutton died without any signs of lethargy or somnolence. At least one European patient who had manifested all the Clinical Symptoms of Trypanosomiasis three and a half years ago, and in whose blood Dr Broden of Leopoldville had found a trypanosome, was believed to be quite well, in fact in better health than she had been for years, in July 1904.

II Sleeping Sickness proper.

The Latent Period. A period exists between the date of infection with the specific cause and the clinical manifestation of the disease, the duration of which is not known with any degree of certainty. But we have reasons for believing that the interval may be very prolonged and that the disease may manifest itself years after the endemic area is quitted. The natives of some places give seven years as a limit.

Many of the older writers, Guérin for example, working in the West Indies have laid stress upon the long incubation period in some instances.

A well authenticated instance is given by Manson(1). — The patient was a negro boy sent home from the Congo to be educated at a training institution in Wales. The boy arrived in this country in September 1885, and enjoyed excellent health for about two years until September 1887, when symptoms of sleeping sickness were noted. There was a

(1) Brit. Med. Jour. 19/9/03 p. 647.

dulness in his eyes, and laziness and indifference at his lessons. The memory became dull, and staggering began, — then drowsiness and somnolence on all occasions —, until eventually he died of the disease.

Thus it appears that although the malady can be acquired in certain places only, the symptoms may manifest themselves far away from and years after the patient has quitted the area where he contracted it.

Christy's opinion (1) after having had the opportunity of following the history of three cases, is, that the period may be as short as eight or as long as eighteen months.

Towards the termination of the incubation period, a gradually increasing lassitude and weakness of the limbs occur, and afterwards frontal headache which is sometimes very distressing.

General Description. As regards symptoms and signs, the disease has been arbitrarily divided into three

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(1) Reports of the Sleep. Sick. Com., Royal Soc., Vol III p 29.

stages, but it must not be imagined that these can be sharply differentiated.

Many types occur, and in the Gambia and Congo (Dutton Todd & Christy) and in Uganda (Kabarro), cases are often seen which do not exhibit the sign, lethargy, from which the disease derives its well known name.

In addition to the three stages of classical description (1) the early (2) the pronounced and (3) the somnolent or lethargic stage, there is also sometimes an intermediate stage of nerve crisis, excitement or exhilaration, which occurs usually at the beginning of the second stage, and is really a part of it.

The following is the description given by Hodges,(1) which will be taken as a type. Any differences in the symptomatology as described by him and as given by others, will be pointed out in due course.

"The Early Stage". Probably the earliest subjective symptom is a chronic persistant or intermittent headache

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(1) Hodges, A.D.P. Sleep. Sick., a Resumé. The Lancet. 30/9/04 p 791 et seq.

"with lassitude and this may be accompanied with, or replaced by vague pains in the back, chest or "all over." With regard to the objective signs, pyrexia if constantly looked for may practically always be detected.

From the first there is a general enlargement of the lymph glands, in which glands from the size of a filbert to that of a hazel nut are found in most or all of the superficial groups; those of the neck being the most constantly affected.

One of the earliest signs usually noted is an arhythmical, jerky or twitching tremor of the tongue. There may also be an alteration of mental attitude or habits, which however is often noticeable only by relatives or associates of the patient.

As none of the above symptoms, unless it be the tongue twitching when well marked, is in any way pathognomonic, it is to a combination of them that one must look for a diagnosis in the early stage. A conjunction of chronic headache or pain, with lassitude, tongue tremor, and glandular enlargement, is always

"Very suspicious in a person who has visited an epidemic area, and if there is also evidence of change in disposition, or if there is recurrent pyrexia, the diagnosis becomes almost certain.

Another early, though less early symptom is a more or less general pruritis of which there may be evidence in the form of scratch marks or small sores, but which is not definitely associated with any kind of rash. Very soon there may be some muscular weakness chiefly noticed at first in the lower limbs.

The patients appearance and demeanour are generally normal, at least while under medical examination or to ordinary observation, and diagnosis may be very difficult.

The more cases one sees, the more difficult it becomes to make a negative diagnosis in patients exhibiting symptoms of the early stage."

Second or pronounced stage.

In this stage the diagnosis becomes almost always easy and certain.

As a rule it may be dated from the characteristic alteration which begins

"to take place in the patients facial expression and general appearance, often accompanied by a change in his manner, habits or disposition.

This stage however, is not infrequently ushered in by nervous crises, such as epileptiform fits, attacks of mania, melancholia or dementia, or by a state of exhilaration during which the patient has very much the appearance of being under the influence of alcohol.

The duration of these nerve crises is generally short in relation to the duration of the disease, but they may recur or be continued into the later stages. During their continuance the patient suffers pain and may complain of sleeplessness.

Very early in this period, if not frequently before, sexual impotence occurs in males, though there is occasionally an outburst of excitement during the phase of exhilaration or mania. In women the menses cease early, often indeed before they have noticed any signs of illness, so that one is tempted in such cases to antedate the alleged time of onset of the disease, by the duration of amenorrhoea.

With the development of the

second stage, tongue twitching becomes more marked, and tremor begins to spread to the cheeks and lips and to the body generally. In some cases choreic twitchings ~~occurs~~, especially in children, occasionally general, but more often confined to the face and arms, will be observed, but they might more properly be included among the nerve crises above enumerated.

The muscles become flabby, the face begins to lose its expression, and the limbs their strength; the speech often becomes mumbling and the articulation blurred.

Fibrillary tremor becomes more evident in the tongue, facial and systemic muscles. The eyes get a vacant stolid, tired or suffering look. The vague pains about the head, trunk and limbs continue and are sometimes severe. Soon there is a disinclination to move or to speak and inability to fix the attention for any length of time. There may now be signs of muscular wasting, but this occurs late as a rule, and even then not invariably, a good deal depending on the patient's ability to obtain food.

Third or lethargic stage. At

length there is a tendency to sleep at all hours, and the patients pass surely but gradually into this last stage which has been so graphically described, and in which they eventually die, sometimes suddenly, but nearly always very slowly, so that the vital functions seem to dwindle away".

Bed sores develop, the lips swell, saliva dribbles from the mouth. The knee reflexes which had at first been somewhat exaggerated are now diminished, and the urine and motions are passed involuntarily in bed.

Drowsiness now passes into Coma from which the patients can only be roused with difficulty, the temperature falls to subnormal, in rare cases Convulsive fits occur, and the patient dies in a state of Coma.

As Occasional Symptoms of the last stage may be mentioned a movement of the thumb and finger or fingers, generally of one hand only, resembling Paralysis Agitans but not truly Rhythmical; and a conjugate deviation of the eyes, with a movement resembling

nystagmus.

Intermissions and Remissions.

These not rarely occurring in the 1st and 2nd stages of the disease, may occasionally be of considerable duration.

During these intervals symptoms may almost all disappear, so that the patient may seem to casual observation quite well. But they all sooner or later invariably die.

Chapter XIII

The Clinical Features and Symptomatology (continued) In Detail.(1)

The Temperature. In typical cases this is characterised by an evening rise and a morning fall, the range being often 4° or more. The night temperature varies from 100° to 103° F. and the morning temperature is generally about the normal, sometimes however a little over this, or often distinctly subnormal.

The regular type may go on for three or four weeks and then become distinctly irregular, sometimes almost keeping normal with the exception of a slight evening rise now and again. This condition may persist for a variable time. A week or two before death the temperature almost always becomes subnormal, and remains

(1) Reports of the Sleep Sick. Com. Royal Soc., No II p 20 et seq.

so during the whole day. The rises in temperature are not accompanied by rigor or sweating.

Variations from the type may be encountered.

1. Those showing a practically subnormal course, throughout the length of the disease.

2. Those in which the temperature remains high for several days, without any morning remissions; as a rule, these revert sooner or later to the usual type.

3. Those where intercurrent disease (chiefly malarial fever) may modify the temperature. Malarial parasites are demonstrated in the blood, and the administration of quinine, causes the temperature to revert to it's ordinary course. (p. 240, Fig. 8)

The Circulatory System.

The Pulse. The frequency is generally 90–130 per minute. The ratio to the temperature is inconstant, a very high frequency often being associated with a low temperature; but in the last stages a low frequency associated with the subnormal temperature is the rule.

The Rhythm is generally regular in time and in force till near the end, when the pulse becomes weaker and then imperceptible. Dicrotism is very uncommon but may occur when the temperature is high.

The Volume is generally very small.

Tension is remarkably low in all cases. This point is also emphasised by the Portuguese Commissioners.

Vessels walls. No abnormalities have been noticed.

Physical examination of the heart generally shows nothing abnormal. Inorganic bruits may however be present.

Subjective symptoms. are all absent.

The Respiratory System.

The Respirations regular in time and equal in force, are always increased, especially so in the evening. They correspond fairly well to the increased pulse rate, and their number per minute is generally between 20 and 30. In the last stages, Cheyne-Stokes breathing is common.

Physical examination in the earlier stages reveals nothing. In the later stages, some congestion and oedema of the bases of the lungs due no doubt to the recumbant posture in bed, are commonly met with, and pneumonic patches may appear.

Alimentary System. In some patients the appetite is slightly increased and even in advanced cases nourishment can still be taken.
The bowels are constipated.
Ulcerative stomatitis in a slight degree is sometimes seen, and the gums in rare cases become swollen and spongy.
The tongue is flabby and covered with a dirty fur. In the last stages, sordes tend to accumulate in the mouth. The breath often has an offensive odour.
Physical examination often reveals a certain amount of bulging of the abdomen. The stomach is generally normal but dilated slightly in some instances. The spleen is always enlarged, hard and not tender, but the question of antecedent malaria must be borne in mind. The Liver. The same

remarks apply to this organ.

Integumentary System

Roughness of the skin is not a constant feature of this disease.
Eruptions are not frequent (Low and Castellani); and the type when existing is similar to that seen very commonly among the healthy natives.

The most common eruption is a papulo-pustular one, the lesions being most frequently seen on the dorsum of the hands, extensor aspects of the forearm and on the back. The pustules are generally isolated and have no tendency to run together. Pruritis often accompanies this condition, and the skin as in other marasmic states, may especially in chronic cases become rough, scaly and lose its lustre. Forms of eczema and ordinary scabies are sometimes encountered.

Lymphatic System.

Enlargement of the lymphatic glands in most situations of the body has been described and laid special stress on, by most authors.

They are most commonly

noticed in the posterior and anterior triangles of the neck, the submental and submaxillary regions, Scarpa's triangle and the groins. In emaciated individuals the abdominal ones can also be felt.

Their size varies from a small bean to a hazel nut, and they are always hard and firm in consistence. They never become adherent nor do they cause ulceration of the skin.

The condition is a chronic one, though in some rare instances, suppuration may be encountered.

Low and Castellani in their paper do not seem to attach much importance to the hyperplasia of the glands, stating that many natives suffer from them, being due apparently to skin diseases, syphilis and verminous invasions generally.

Greig and Gray (1) & others are however of a different opinion. After having examined the glands of fifteen sleeping sickness cases and of five cases of trypanosoma fever in Uganda, they state that they

(1) "Note on the lymphatic glands in Sleeping Sickness" The Lancet 4/6/04 p 1570.

observed numerous active trypanosomes in every instance, and consider that Sleeping sickness is essentially a polyadenitis brought about by the arrest of the parasites in the glands.

In the analogous diseases of Nagana Surra, Dourine and Mal de Caderas, the same polyadenitis is met with, and from the earliest times this enlargement of the glands has been considered a premonitary symptom of sleeping sickness by slave traders and African natives alike.

The area of distribution of enlarged Cervical glands in Equatorial East Africa agrees with that of Sleeping Sickness (Christy)(1)

Nervous System.

The dull apathetic look is one of the most characteristic features of the disease though not a constant one. The expression is heavy and shows little emotion. There is a slight loss of intelligence, but memory is never impaired. Proper Sleep is not a symptom of the

(1) First proper Report of the Exped. of the Liv. School &c. to the Congo 1903. Brit. Med. Jour 23/1/04 p. 186.

disease as is so generally supposed. The total amount of sleep may be above the average in a few cases, but the usual feature is one of lethargy, indifference, or drowsiness; and even this in several cases is not well marked, while in other cases it may be entirely absent.

These observations are confirmed by the workers[1] on the western side of the African Continent, who have often remarked that many of the Sambrain and Congo cases do not display an unusual amount of sleep or even undue lethargy. They (Dutton Todd & Christy) state "Continued sleep or even abnormal sleep has been almost absent from many of the cases. It has been absent even in those believed to be in an advanced stage of the disease and who have ultimately died."

On the other hand, lethargy was one of the principal manifestations of the disease as met with in Portuguese West Africa. (The Portuguese Commissioners).

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(1) 1st Prog. report of the Exped. of the Liv. School &c &c. (1903). — Brit. Med. Jour 23/1/04 p 186.

Maniacal Attacks sometimes usher in the onset of the disease. Headache chiefly occipital, indefinite pains in the chest and sometimes in the joints especially in the knees and ankles, are sometimes complained of.

Sensory functions. Though at first generally normal, even early there may be some hyperaesthesia at the trigeminal points. Touching or moving the patient, especially in cases where flexure contraction or rigidity of the muscles of the neck is marked, causes pain.

General or local anaesthesias are not observed. The temperature and muscular senses seem unimpaired.

Motor functions. The motor power at first normal, deminishes towards the end. In many cases a certain degree of incoordination is distinct, and in a few cases is Romberg's sign present. The gait is a typical one and is best described as "shuffling", the feet not being raised from the ground but being pushed forward.

Muscular nutrition. The muscles often become wasted towards the end, but not necessarily so in acute rapid cases.

Abnormal muscular movements are one of the most striking features of the disease. The tremor in the tongue is very constant, and a somewhat coarser tremor is also usual in the hands and arms, purposeful movements often increasing it. In a few cases tremor is found in the muscles of the trunk and legs so excessive as to cause shaking of the bed on which the patient is lying. In a few rare instances no tremor is observed.

In the last stages rigidity is common in the muscles of the neck; and flexure contractions of the legs on the thighs, and of the thighs on the abdomen, may at this time be extreme.

Fits - of an epileptiform nature sometimes occur, either general or localised to a particular group of muscles.

Paralyses are rare.

Reflex functions. The superficial reflexes are generally normal; the deep, exaggerated at first, afterwards become lost. No clonus is ever present.

The organic reflexes are normal except towards the end, when the motions and urine are passed involuntarily. Babinsky's sign is never present.

The Cerebro Spinal fluid. This generally escapes with increased pressure. As a rule it is quite clear though in some cases it is found to be turbid. The leucocytic formula is mononuclear.

The Special Senses are all normal. No changes are seen at the back of the eye.

The Urinary System.

The weakness of the Sphincter Vesicae often noticed in the last stages of the disease has already been mentioned. The urine though alkaline (due in all probability to the Vegetable diet of the natives) is generally normal in appearance and reaction.

The Sexual System.

At first unchanged, the potency is lost later. Menstruation may remain normal for a considerable time, but disappears as a rule in advanced cases.

In the mucous secretion of the Vagina which is frequently increased and of acid reaction, is often found a form of flagellatum with three flagellae and an undulating membrane, showing very active

movements. (Trichomonas Vaginalis). (Dormé).

Faeces. Constipation is very frequent. Besides, the various appearances to be expected in the stools of those who are practically vegetarians, and ova of different parasites are always present. The commonest of these are Ankylostoma duodenale and Ascaris lumbricoides; less common is Tricocephalus dispar.

In few cases are the ova of Bilharzia haematobia present in the faeces.

Haemopoietic System.

Anaemia of varying amount is constant, the average number of red blood corpuscles being 3,500,000 or thereabout.

So many blood destroying factors are present such as Malaria and Ankylostomiasis, that it is difficult to say what part they play in producing the condition of the blood. Just before death there might be a gradual fall in the number of R.B.C. to 2,000,000, or under.

The Haemoglobin is generally reduced in relation to the amount of the Anaemia.

The leucocytic count shows no absolute increase from the normal

until just before death, when a certain number of the cases get a well marked terminal polymorphonuclear leucocytosis. Relatively the large mono-nuclear elements are increased, but Malaria must again be taken into account in considering this.

Especially in young subjects, a relative increase in the number of eosinophile cells is often met with; this is probably due to the helminthiasis.

The main features of the blood may be summed up as follows:— Anaemia of varying degrees with a relative increase of the large mononuclear leucocytes; malarial parasites, and pigmented leucocytes indicating malarial complications are frequently met with.

Relation of the Appearance of the Parasites to the Symptomatology.

A. In the Peripheral Blood. The conclusions of Dutton Todd and Christy[1] who paid especial attention to this point in their Expedition to the Congo, are as follows:—

(1) Second prog. report of the Exped. of the Liv. School &c + Brit. Med. Jour 20/5/04 p 37. 1903

1. The parasites may be absent from the peripheral blood for varying periods. The frequency with which it is obviously present bears no relation to the symptoms.

2. The number of parasites seen in ordinary fresh Cover slip preparations is generally small, but in some cases large numbers have been recorded. In two cases a large increase occurred in the few days immediately preceding death. (Say two to a cover to twenty on the day of death in one case.).

3. The parasites may gradually increase from small to fairly large numbers (twenty to a Coverslip or more), and then suddenly disappear on the day their acme is reached.

4. With regard to the symptoms associated with the presence of these parasites in the blood, these observers cannot make out any definite relation between the temperature and pulse, and the appearance of the parasites in the peripheral Circulation.

B. In the Cerebro Spinal fluid. The provisional conclusions of Cuthbert Christy (1)

(1) Brit. Med. Jour. 20/8/04 p 379.

who bases his deductions on 104 Lumbar punctures made in Sleeping Sickness Cases on the Congo, are as follows:—

1. In many cases the trypanosomes never find their way into the Cerebro-Spinal fluid, and in the cases in which they do, they are more frequently to be found towards the termination of the disease.

2. The commencement of the fever or other symptoms is in no way correlated to the entrance of the parasites into the Cerebro Spinal fluid.

3. A large number of trypanosomes in the Cerebro Spinal fluid is rare, but when it does occur, there is usually an access of temperature.

4. The parasites may come and go in the Cerebro Spinal fluid as in the blood.

5. Enormous numbers of trypanosomes may appear in the blood without appearing in the Cerebro Spinal fluid, and to some extent vice-versa.

6. When trypanosomes are present in the Cerebro Spinal fluid, its white cell elements are apt to be increased.

7. In cases where the parasites gain access to the Cerebro-spinal fluid, mania and other head symptoms are more likely to be prominent.

The Secondary Infections and Complications. Out of 22 necropsies performed at Leopoldville 13 showed Complications or obvious secondary infections as follows:—

Purulent meningitis	4.
Purulent pleurisy and pneumonia	1.
Pneumonia + localised tubercle of lung	1
Localised gangrene of lung	1
Enlarged caseating and breaking down glands in thorax and abdomen. No tuberculous lesions in organs. (Tubercle bacillus in glands seen in one case).	2.
Dysenteric ulceration of large bowel. (perforation in one case)	2.
Universal adherent pericardium (~~Recent~~ Recent infiltration of pus in femoral inguinal + intestinal iliac glands – gonorrhoea).	1 / 1

Other complications occurring which might be mentioned are, bedsores; boils of a pemphigoid nature. ulcerations of the hands and feet due to chiggers; laryngitis, bronchitis; and pseudo-dysenteric symptoms,

due to Bilharzia infection.

The Duration of the Disease

In Uganda. The acuter forms last about six weeks or so. In the more chronic ones the symptoms develop more slowly and they remain more constant for considerable periods of time without any advance. But ultimately the patients pass into the later stages and eventually die, Average duration 4 to 8 months. (Low & Castellani)(1)

Congo Cases. The duration is 2 to 4 months from the date of recognition of the disease. (Dutton Todd & Christy)(2)

Portuguese West African Cases. The Portuguese Commission(3) states that Cases of speedy death were heard of but could not be verified. As a rule those attacked did not die within twenty days and the average duration

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(1) Reports of the Sleep. Sick. Com., Royal Soc., No II p. 19 & 32.

(2) 2nd Prog. report of the exped. of the Liv. School & and Brit. Med. Jour. 20/8/04 p 371

(3) The Lancet. 27/9/02 p. 886.

was two to three months, though some cases outlived a year.

German West Africa. K Hunty[1] gives the average duration as from four months to three years.

The Question of Recovery.

There is no authentic information as to any Sleeping Sickness case, ever having recovered from the disease, when once the symptoms had become established and the malady recognisable.

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(1) The Lancet 11/6/04 p 1692.

Chapter XIV

Further Considerations as to Etiology and Pathology.

Preliminary Note Most of the points regarding the Etiology and Pathology of the disease have already been dealt with; but a few still remain, and the consideration of these was deferred, for the reason that it was not possible nor convenient to discuss them with profit until the Pathological Anatomy and the Clinical features of Sleeping Sickness were disposed of; and these will now help us in elucidating as far as is possible at the present time, the problems that remain.

The Questions requiring answers are.

1. Is the trypanosome the definitive cause of the disease?

2. What part does it play in the Symptomatology, the morbid anatomy,

and in the causation of death?

3. In the same manner, what relation has the diplostreptococcus to the causation of the disease?

4. What connection has Trypanosoma fever with Sleeping Sickness?

5. Does the entrance of the Trypanosome into the Cerebro spinal fluid initiate the symptoms of Sleeping Sickness?

6. Does every case of Trypanosoma fever inevitably pass into Sleeping Sickness proper?

These queries are to a considerable extent dependant one on the other, and therefore it is convenient to discuss them together.

The Ascertained facts.

What are the facts so far ascertained?

1. The blood and the Cerebro-Spinal fluid of practically every case of Sleeping Sickness examined, contain Trypanosomes.

2. The blood of Trypanosoma fever patients also contains trypanosomes.

3. The curious fact established in countries where the point has been investigated, that the trypanosomes are present in the blood of a percentage

of the population in the epidemic and endemic areas of Sleeping sickness whilst the people living outside these areas are entirely free.

In Gambia where cases of Sleeping Sickness are rarely seen (Dr R M Forde of Bathurst stated that perhaps one case a year came under his care), only 6 out of 1000 odd natives were found to be infected by the examination of fresh coverslip preparations. In an almost exactly equal number of a similar class of natives, examined in the same way in the Congo, 46 were infected. In Uganda where the disease occurred in epidemic form, the percentage of infection among the general population was much higher; and as already remarked, in those places which were entirely free from the disease, no natives were found infected by the parasite.

4. There is a curious similarity between the symptoms and pathological anatomy of some of the trypanosome diseases of the lower animals, and those of Trypanosoma fever, even of some cases of Sleeping Sickness proper, (those of a mild type).

5. The Trypanosome of the blood

(Tryp Gambiense) and that of the Cerebro spinal fluid (Tryp Ugandense) seem identical morphologically, as well as in animal reactions.

6. There is no reason for stating that the diplostreptococcus exhibits to Sleeping Sickness any of the relations above described.

7. The diplostreptococcus is found only in the later stages of the disease. The trypanosome can be demonstrated in the blood in the earlier stages, and in the Cerebro-spinal fluid in the later stages.

8. Trypanosomes have been found in the lymphatic glands of both Trypanosoma Fever and Sleeping Sickness cases.

9. It has been well established that some patients exhibiting the symptoms of Trypanosoma Fever with the parasites in the circulatory system, have later exhibited undoubted signs of Sleeping sickness, have died from the malady and have shown pathological changes in their system, identical with the conditions found in the latter disease.

The Conclusions.

The facts having been given, what are the conclusions that can fairly be drawn from them?

1st That in all probability the Trypanosome Gambiense will be found to be the true cause of Sleeping Sickness. It is agreed that the matter is not definitely proved, but the facts all tend to that conclusion, and the circumstantial evidence is strong.

Enumerated shortly these are, the almost invariable presence in the blood and Cerebro-Spinal fluid of trypanosomes in nearly every case of Sleeping sickness; the fact that a proportion of the population in the endemic and epidemic areas are infected with the parasite whilst the population outside those centres are entirely free; the similarity between some of the trypanosome infections of the lower animals and this disease of man; the greater resemblance to Sleeping sickness of the malady produced in inoculated monkeys as compared with the acute septicaemia produced by the Coccus; these are all important.

The subsidiary points are the local areas of distribution; the

distribution and habits of Glossina palpalis; the comparitive immunity of Europeans and of the better class natives in the infected areas; the fact that the disease is incommunicable outside these areas; the long incubation period and course of the disease; all these facts seem to favor the hypothesis of trypanosome causation.

The great hindrance so far, to the establishment of this hypothesis, has been the inability to cultivate the parasite with success. Until a pure culture is obtained and experimented with, there will of course always be some doubt.

Another method which might be tried for the attainment of the same object, would be to follow out the metamorphosis of the parasite (if such a process does exist) in the body of the Tsetse fly, to breed the insects used in the experiments, in fact to repeat the inoculation and transmission experiments of the Second Commission of the Royal Society, this time of course with full scientific precautions, and in a manner that will admit of no subsequent Criticism.

2nd We have no proof that

the diplostreptococcus takes any part whatever in the primary causation of the disease itself, but it may play an important role in the production of the secondary infections and may possibly be the cause of the fatal termination.

3rd. The so called Trypanosoma fever does actually appear to be the first stage of sleeping sickness proper, the chief reason for this conclusion, being founded upon the facts derived from Manson's case, and from those other examples of Trypanosoma fever which have been followed up in Uganda.

4th. It is not proved that every case of Trypanosoma fever must necessarily go on to the stage of Sleeping sickness. One case (that of Dr Broden of Leopoldville,) has already been cited in example of this statement.

In addition, it is known that animals infected with Trypanosomiasis by experimental inoculation, may after some period of time, show no traces of the parasites in their system.

5th. There is no evidence that the entrance of the parasites from the blood into the cerebro spinal fluid, is the determining cause of the symptoms

of Sleeping Sickness. Christy and others declare that in many cases the trypanosomes never find their way into the Cerebro spinal fluid. This statement however, is not considered important; for, it only means that in certain cases the observers have not succeeded in finding the parasites, not that the organisms were not there. It is admitted that the trypanosomes are very few and that they may appear and disappear from the fluid.

The Causation of the Symptoms, of the Pathological Changes and of death.

This in particular is a very difficult subject and the opinions of Mott(1) are given:—

The view obtaining at present is, that the trypanosome is the essential cause and the diplococcus a secondary infection of great importance in the disease. Mott's observations allow him to support this hypothesis. The diplococcus has been found in a

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(1) "The Cerebro Spinal fluid in relation to disease of the Nervous System." Brit. Med. Jour., 10/12/04 p 1554 et seq. and discussion on Trypanosomiasis, The Lancet, 23/1/04 p 231.

great many of the cases in the vessels of the brain. The heart blood is affected also, in this respect differing from the epidemic cerebrospinal meningitis where the diplococcus of Weichselbaum is present in the cerebrospinal fluid, but not in the blood. Again, diplococcal infection should give rise to polymorphonuclear leucocytosis, as in epidemic cerebrospinal meningitis; and the existence of these organisms in the blood and cerebrospinal fluid, also in the tissues is rather the result of a late or terminal infection which hastens death, but has no relationship to the characteristic perivascular lesion of the nervous system.

Moreover, Mott has found the diplococcus in the brain of monkeys inoculated with the blood of sleeping sickness cases and yet no signs of the perivascular cell infiltration.

The profound changes of the nerve cells, Mott thinks, are doubtless due to the anaemia produced by the capillary obstruction.

He has reason for believing that the trypanosome does not kill by the action of a toxin the same as microorganisms do, for Dr Plimmer's experiments show that the serum of Nagana blood taken

from an animal that has died of the disease and filtered through a Chamberland filter, does not upon injection into an animal, produce any toxic effects, nor does it give any immunity to the inoculation of the parasite.

If therefore the parasites act mechanically the organisms should be capable of demonstration in sections of vessels, and it is only in extremely few instances that Mott has succeeded in finding them in those positions.

He thinks that the characteristic symptoms of the disease are undoubtedly due and proportional to the extent and degree of the meningo-encephalomyelitis, and it is his opinion, that the lethargy is due to the cerebral anaemia caused by compression of the small vessels by the accumulation of leucocytes in the perivascular spaces and the mechanical effects thus produced on the circulation, and to the obstruction to the biochemical changes incidental to the activity of the neurons.

"The tremors, fits, paresis, attacks of mania and hyperpyrexia are probably the results of irritation phenomena associated with stasis in the vessels, degeneration changes in the neurons,

and neuroglial proliferation"

"The early affection of the cerebellum, the mesencephalon and the medulla oblongata by the lymphocyte infiltration is very probably connected with the noxious agent in the large collection of the fluid in the subarachnoid space at the base of the brain. In cases which linger to the end of the third stage, marked bulbar symptoms may arise due to anaemia of the medulla and degenerative changes of the neurons."

As to the enlargement of the lymphatic glands, Mott asks whether it is secondary to the irritation caused by the trypanosomes (see Greig and Gray's Communication in the Proc. Royal Soc., Vol LXXXIII June 1904), or some modified and at present unrecognised forms of these parasites; or to a diplococcal infection the toxin of which causes irritation and increase of lymphocytes discharged into the circulating blood?

The latter alternative however, does not explain why the lymphocytes should migrate from the blood into the perivascular spaces of the brain.

Chapter XV

On Diagnosis.

In the Chapters on the Clinical features of Sleeping Sickness, the subject of diagnosis was briefly entered into.

General Diagnosis. It has already been stated, that in the early stages the disease is difficult of diagnosis, in fact in some cases the difficulty may amount to an impossibility.

Sleeping Sickness has a very long incubation period from a few months to several years, during which trypanosomata may be found in the blood stream only occasionally. During this period there may be no other signs or symptoms, and even the periodical fever may be entirely absent. It is a fact that in this stage it is only by the microscopic examination of the blood, (Cerebro spinal

or other fluids?) that the diagnosis can be arrived at, and it follows (the parasites being only occasionally present), that a negative diagnosis cannot be made although a positive one is possible in some cases.

Later, in the febrile stage, although still difficult, the chances of a successful diagnosis are increased. Now we have in addition to the fever, the increased rate of the pulse (not corresponding to the temperature) due to the peculiar cardiac irritability, — and the combination of these might lead the observer, in cases where patients have previously resided in the endemic or epidemic areas, to the regular examination of the blood, with the result that the parasites are detected if present.
In this stage we have the enlarged glands to help in the decision, also the headache and lassitude and if present the peculiar twitching of the tongue; the last sign being very important in the early diagnosis.

If ordinary blood film examinations are found useless, then recourse must be had to the examination of a larger quantity of centrifugalised blood, or the

examination of the Cerebro spinal fluid; but these operations require a considerable degree of skill in manipulation, and it is easily understood that these methods of examination cannot of necessity be carried out in every instance.

Again it follows, that though a positive result is valuable a negative one is quite useless, for the case may still be one of Sleeping Sickness.

Later on, when the general symptoms appear, there is little difficulty, and it is here unnecessary to recapitulate the various data required to establish a diagnosis, and which have already been enumerated in the Chapter on the Clinical features of this disease.

Differential Diagnosis. The only diseases for which Sleeping Sickness is liable to be mistaken are Beriberi, Intracranial Syphilis and tumours, Chronic Nephritis; and Tabes and General paralysis of the Insane.

Beri Beri. This affection is a peripheral neuritis whilst Sleeping Sickness is a disease affecting the Central Nervous System. In the former the Knee reflex is abolished,

and hyperaesthesia of the muscles is a prominent feature. In Sleeping sickness the knee jerk is exaggerated in the beginning to be abolished only in the later stages, and hyperaesthesia of the muscles is not present.

In the wet form of Beriberi, there is marked oedema; whilst in Sleeping sickness the tremor, the pyrexia and the lethargy are distinguishing features.

Intracranial Syphilis and tumours with tendency to somnolence. Such cases, which are very rare, occurring in the endemic area, may be distinguished by other evidences of syphilis in the former, and by the definite stigmata of intracranial tumours in the latter instance.

Chronic Nephritis with Uraemic Symptoms. An examination of the urine for albumen and of the eye for albumenuric retinitis may reveal the true state of affairs.

Tabes and General paralysis of the Insane. In those rare cases of Sleeping sickness which show a sluggish reaction of the pupils to light, presence of Romberg's symptom and absence of the knee jerk, the diagnosis may be

difficult. The presence of tremor and pyrexia will help to a definite Conclusion against Tabes. General paralysis of the Insane which is very uncommon in Central Africa may be distinguished from cases of Sleeping Sickness with symptoms of insanity, by the temperature and by the microscope.

It is understood that the blood at least is examined in all available Cases.

Chapter XVI

On Immunity of Races and of Individuals.

We have seen that neither native nor European is immune to this disease.

As regards individuals, it is to be conjectured that in the case of Sleeping Sickness as in every other disease, there exists a certain individual resistance to the action of the pathogenic organism. We have no means at present of ascertaining the quality of this resistance and we know nothing whatever about it.

The comparitive immunity of Europeans and of the better class natives can be readily explained on the grounds of more complete clothing (hence a better protection from insect bites), the sites of their habitations, and considerations of a like nature.

The Prognosis.

The prognosis is somewhat different in Sleeping Sickness to what it is in Trypanosoma fever.

In the former the prognosis is hopeless and so far as information goes, the mortality is 100%.

In Trypanosoma fever on the other hand, the outlook though bad is not despairing. One case is known at any rate where the infection has apparently been overcome.

Investigations have not been made for the purpose of determining whether patients who show the trypanosome in their system at one period, systematically fail to show it at another.

Possibly the trypanosome, given favorable conditions, might disappear altogether from the blood as has been shown to be the case in some of the lower animals experimented on. But negative observations of this nature will require very careful confirmation before they can be accepted.

Chapter XVII

On Prophylaxis; and the Prevention of the Spread of the Disease.

Personal Prophylaxis. Assuming that the disease is inoculated by a blood sucking insect, the care necessary would be

1st To wear proper Clothing in the daytime so as to expose little surface to the action of the fly; also to use at night suitable curtains to keep off the insect from the body of the sleeper.

2nd. To avoid living, or sleeping or working in the jungle and in the forest.

3rd. To avoid the Tsetse fly Zones.

General Prophylaxis and Prevention of the spread of the disease. Various remedial measures have been suggested but none have been put to a practical trial.

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1. A systematic clearing of the usual places of living and working, of the villages, watering places, landing places &c of the natives and the removal of the sick into open spaces, would to much to diminish the risk run by the majority. The more they aggregate into large villages and clearings and the less they live like animals in uncleared jungle, the less likely they will be to be bitten by the tsétse fly; and though of course some occupations such as fishing and wood cutting will always be dangerous, the smaller the number exposed to infection, the less probability will there be of the occurrence of widespread epidemics." (1)

2. Other measures aim at preventing as far as possible the movement of natives from sleeping sickness areas into any part of the country where any species of tsetse fly is found;— also restrictions against the movements of healthy natives into infected areas. These measures we believe to be impracticable in Central Africa, where it must be remembered the routes are not railways or broad highways, but innumerable paths through the jungle, and it

(1) Sleeping sickness: a Resumé; The Lancet 30/5/04 p 292

is easily understood how difficult it will certainly be, even to attempt to put a stop to these.

3. The compulsory vaccination of the presumably narrow area of the mainland and of all the islands (the hotbeds of the disease) in countries such as East Central Africa, has been proposed; this measure to be carried out of course only where the fly zones have been accurately mapped out. It is said that if the persons evicted were sent sufficiently far inland to be out of reach of the Tsetse fly and prevented from returning for seven years at least; by that time all those affected with sleeping sickness would probably have died out.(1)

This measure also seems impracticable; for it would mean the accurate delimitation of large areas; also, although eviction might be practicable in the comparatively limited area of East Central Africa, it would be quite impossible in the thousands of miles of the Congo and Gambia riverine basins.

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(1) Christy. Sleeping Sickness. Brit Med Jour. 26/11/04 p. ~~1504~~ 1456.

4. Other methods are the removal of habitations, resthouses and stations to more healthy sites; the screening or clearing of all forest and bush from all watering and washing places, and the segregation of all sleeping sleeping cases.

5. The extermination of the Tse tse fly.

The last method, if it can be carried out, would seem to be the best of all.

Chapter XVIII

On Treatment.

It must be confessed that there is no means at present discovered which has any beneficial effect whatever on the ultimate progress of the disease, and on its invariably fatal termination.

Many drugs have been tried. Of these

Arsenic and its salts seemed at one time to promise well. In Nagana it was found that temporary benefit followed large doses of the drug, but the disease sooner or later proved fatal to the animals infected. Bruce stated about treatment of cattle by means of this drug, that it was either death from the effects of the Arsenic or death from the effects of the disease. In man the same statement would seem to hold good.

Besides Fowler's solution, the various salts that have been

tried are Atarhenzal, Sodium Cacodylate, arseniate of iron and sodium arseniate.

Iron and Quinine. Temporary benefit may accrue from the use of these especially in cases complicated by malaria, but the effect, as has been stated, is only transitory.

Free opening of the Bowels by means of Magnesium Sulphate to overcome the persistent Constipation gives Considerable Relief.

The Thermo cautery and Blistering of the head and Spine with Solutions of Iodine, always caused in Uganda a temporary alleviation of the Symptoms.

Tryparosth first used by Laveran (1), or better still a combination of Tryparosth with Arsenic seems to give better results than Arsenic alone; but details and the results of further trial are wanting.

Malachite Green was found by Wendelstadt to have a destructive effect on the trypanosome of the blood of infected animals.

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(1) Compt. Rent. Acad. de Sc. Paris. Vol 139 p. 177 & Jour. Royal. Army Med. Corps. Vol iii p. 93, 1904.

Methylene blue has also been used.

Injections of Horse Serum were tried in Manson's case with disastrous results. It was found that the temperature and the pulse rate rapidly advanced; great depression set in, and the haemolytic action of the serum was so pronounced that the blood count dropped by one third within a week. At one time, alarming symptoms suddenly developed; namely, choreic movements of the hands arms and trunk, together with high fever and rapid pulse. Severe convulsive movements of the muscles of the trunk were then apparent and the patient became dull and apathetic; at the same time the erythematous condition of the skin became more pronounced and more dusky. The patient recovered from the effects of the injections when they were discontinued.

Testicular Extract was found by Laveran to be good for infected rats.

Chrysoidin is the latest substance suggested for trial.

All these methods of treatment are still in the stage of trial by laboratory experiments, and it is not yet known how they will work out in actual practice.

With care, proper attention, and good feeding life may be prolonged for a considerable period but the end comes sooner or later.

Chapter XIX

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Fig. 1. Trypanosomes from Cerebrospinal fluid. Sleeping Sickness. x 2000.

Fig. 2. Trypanosomes from Blood. Sleeping Sickness.

Appendix.

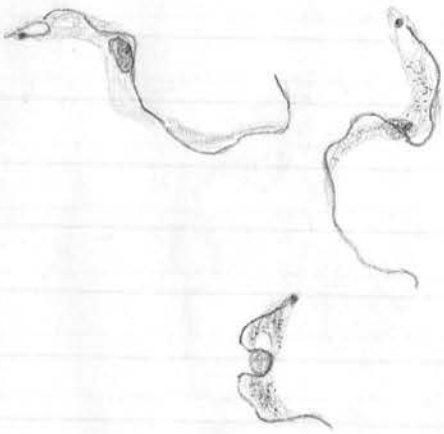


Fig. 1. Trypanosomes from Cerebrospinal fluid.
Sleeping Sickness. x2000.

Fig. 2 Trypanosomes from Blood.
Sleeping Sickness.

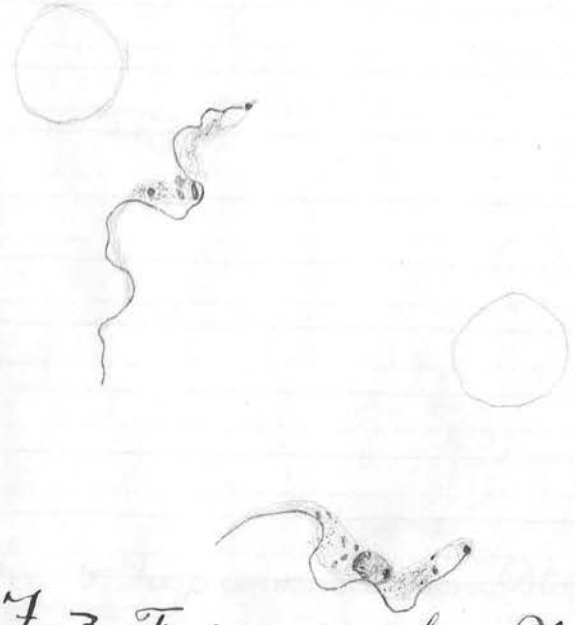


Fig 3. Trypanosomes from Blood
Sleeping Sickness.

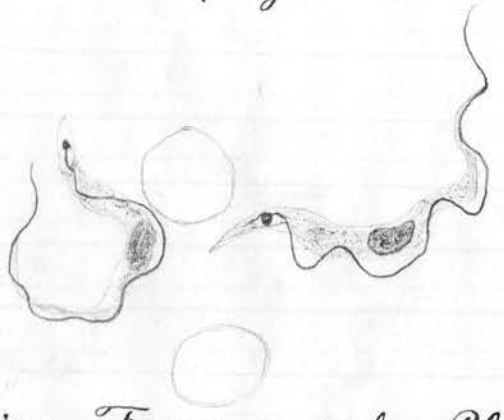


Fig. 4. Trypanosomes from Blood.
Trypanosoma fever

Fig. 5. Trypanosomes from Blood
Trypanosoma fever

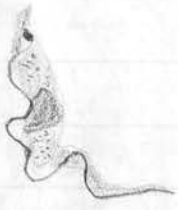
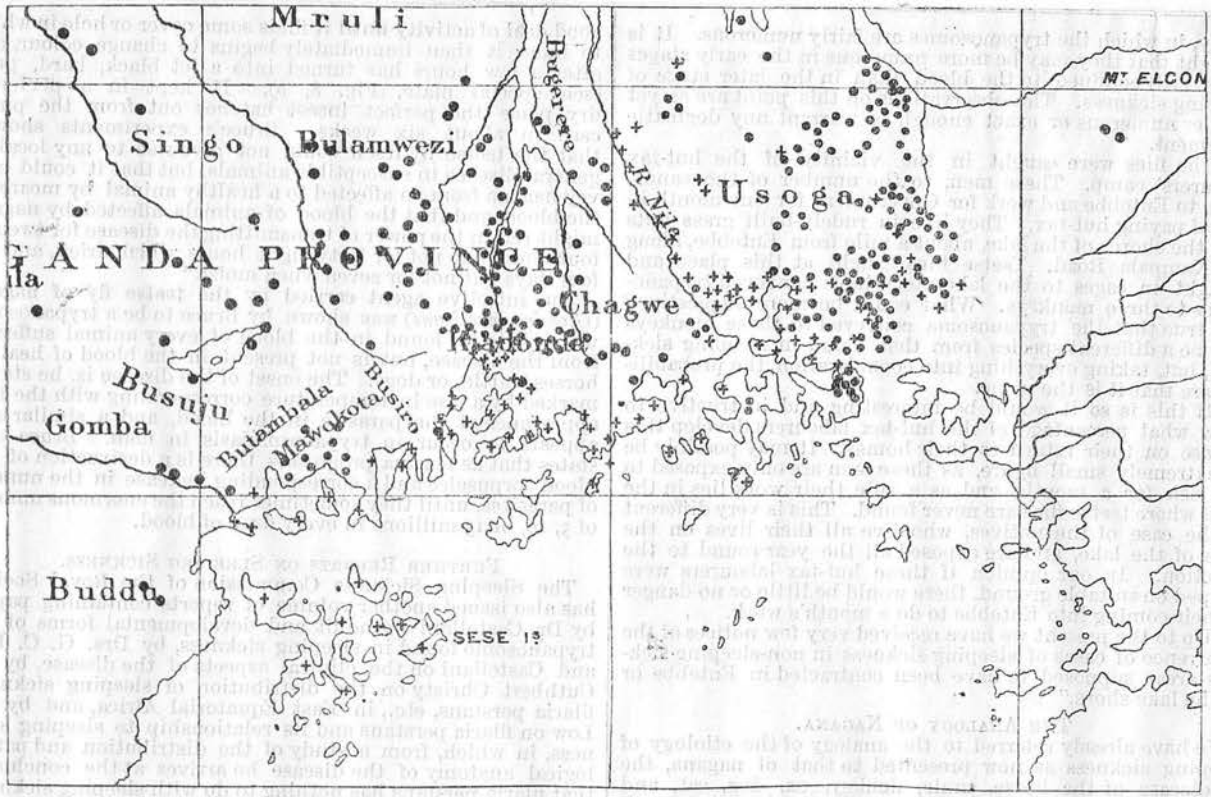
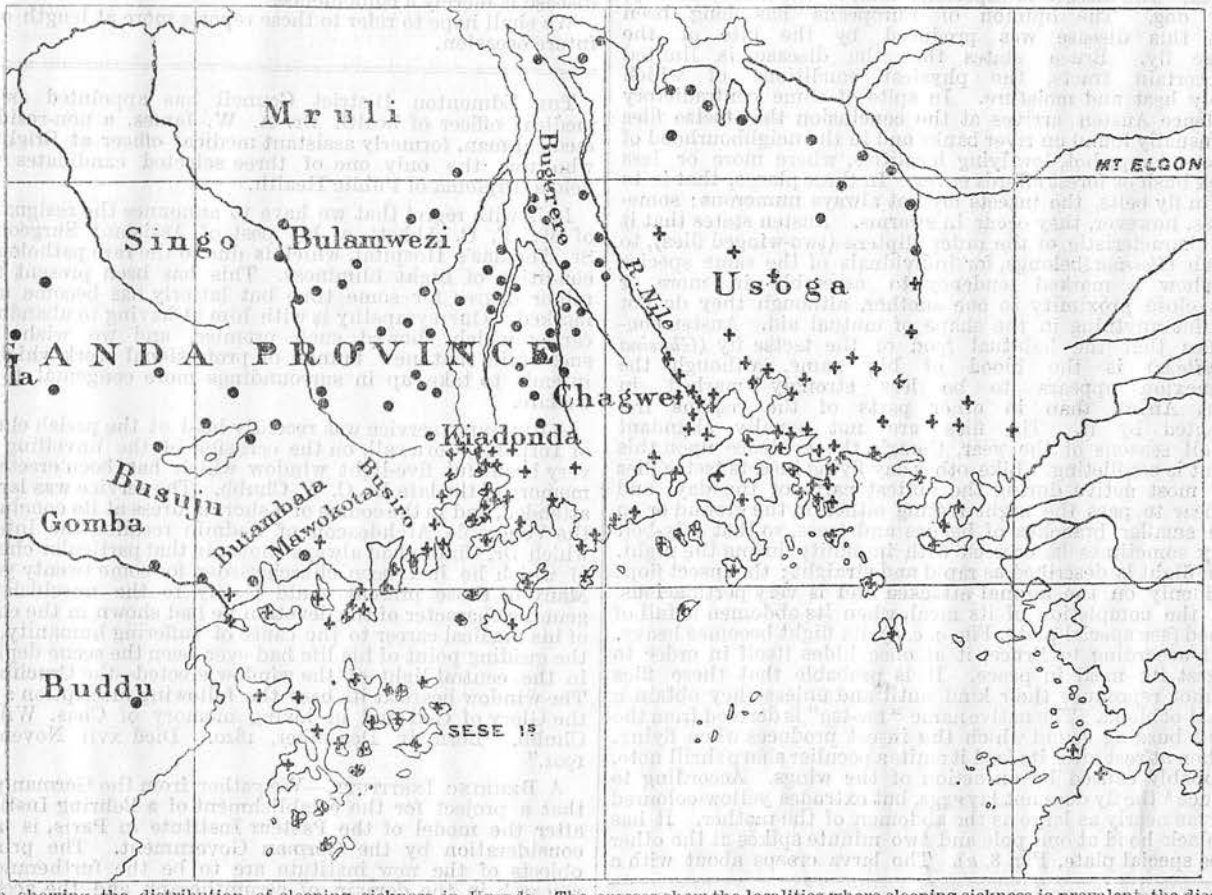


Fig. 6. Trypanosomes from Blood
of Monkey.

Fig. 7.



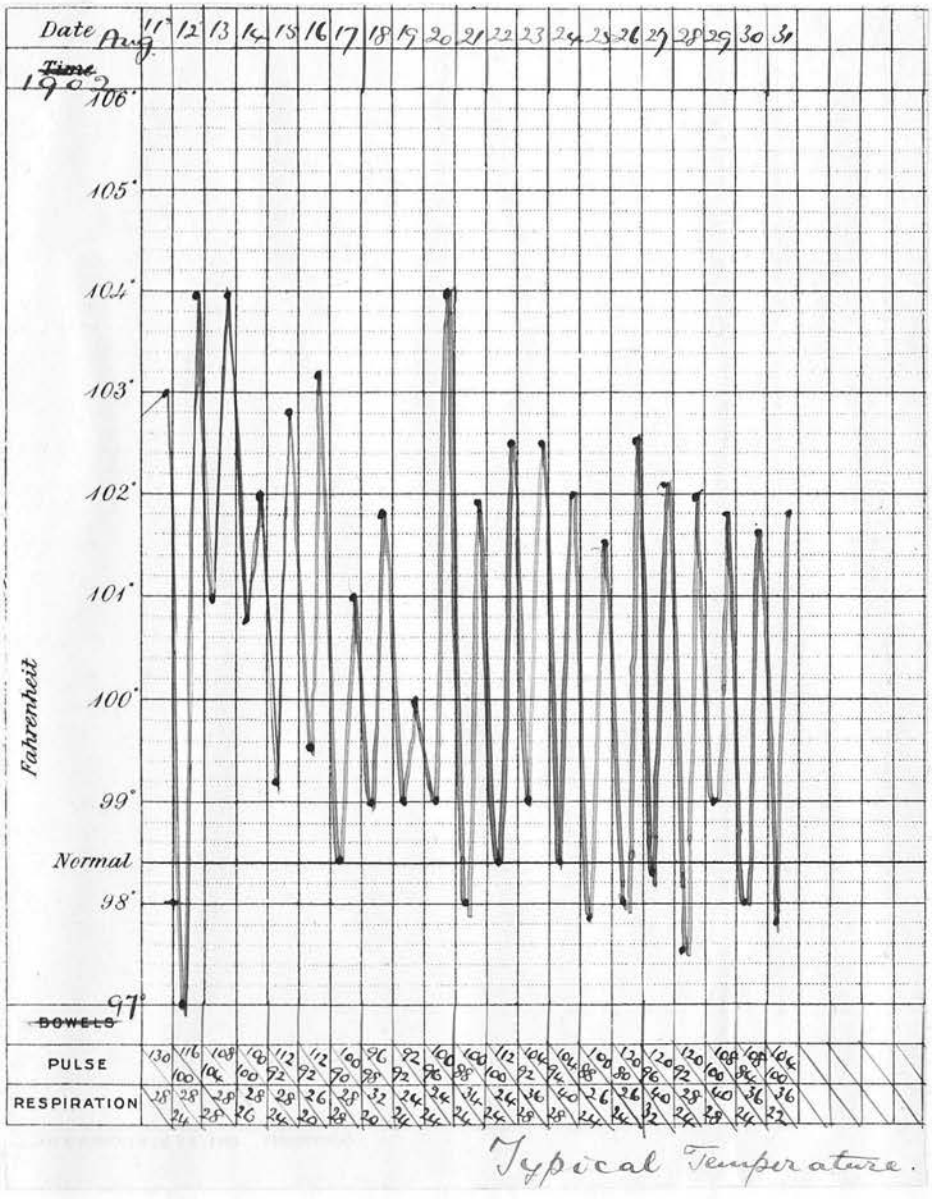
Map showing the distribution of *Glossina palpalis* in Uganda. The crosses show places where the fly was obtained, the discs where other biting flies were obtained but not the tsetse.



Map showing the distribution of sleeping sickness in Uganda. The crosses show the localities where sleeping sickness is prevalent, the discs where it is absent.

The comparative distribution of Sleeping Sickness & Glos. Palpalis in Uganda.

Fig. 8.



Typical Temperature.

Sleeping Sickness. Typical Temperature chart.