NYASALAND TRYPANOSOME FEVER.

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SYNONYMS.

Native names—*Kaodzera*, to nod. This term is of recent European introduction, unknown to the native, and probably taken from the Luganda word *mongota*, to nod. The native name for Trypanosome disease, though confused by them with other diseases and certain forms of poisoning, has always been *Ndulu* in the Dowa "Sleeping Sickness Area."

DEFINITION.

An endemic trypanosome fever occurring in Nyasaland, and characterised by pyrexia, usually of a regularly intermittent type, early acceleration of the cardiac and respiratory rates, tremors, local œdemas, progressive emaciation and weakness; later, some implication of the nervous system, terminating in death by acute or subacute stages.

HISTORY.

One cannot do better than refer to Dr. SANDERSON'S account in this connection, which was published in the TRANSACTIONS of the JOURNAL OF TROPICAL MEDICINE AND HYGIENE, Vol. V., No. 8, pp. 295, 296. July, 1912. Two points, however, need to be mentioned, namely (1) That Dr. J. E. S. OLD, of the Nyasaland Medical Staff, was the first to discover trypanosomes in cattle; and (2) that Dr. W. A. MURRAY, of the Mvera Mission, Dowa, diagnosed the first case of the Nyasaland disease in man.

DISTRIBUTION.

Cases have been found in other parts of the Protectorate, but it has been conjectured that these chiefly originated in the "proclaimed area," the flat country lying between the Lintipi and the Lingadzi Rivers of the Dowa sub-district. The returns from the middle of May till the end

of October give a total of 32 cases, namely, 18 from the villages along the course and below the junction of the Lintipi and Lilongwe rivers, as compared with 14 cases for the rest of the area.

AGE INCIDENCE.

The age incidence appears to be between youth and old age. No child has so far been found infected, but elderly or old people return a good proportion of cases:—males, 65·62 per cent.; females, 34·37 per cent.

SYMPTOMS AND SIGNS.

After a varying but short incubation period, the patients in most cases complain of headache (*litsipa*) or pain in the legs (*kasipa*), frequently both. Pains in the chest and, in a few cases, abdominal pain and diarrhoea mark the onset of the disease. These symptoms are either constant and occur concurrently, or one or other is a prominent feature. Later changes in the mental condition are shewn by marked dullness and apathy, slovenly habits, the absolute disregard of personal cleanliness, and marked maniacal symptoms have been noted during the early stages. Local oedemas are constant, the face, feet and hands, sometimes also the arms and legs, being involved. The feet often are much swollen; the face, though puffy, is seldom swollen to any marked extent. There was great oedema, however, of the cheeks, lips and eyelids, accompanied with lachrymation noted in one case. The oedemas are frequently evanescent, attacking different situations at intervals. The tendency to sleep at odd hours is not common, yet a typical somnolent stage of some three weeks has been recorded in three instances. The cases are usually found in the intermediate stage of the disease, the common clinical picture being:—Patient's expression dull and dreamy; slight puffiness of the face; speech somewhat thick—in some people, thin-voiced and high-pitched. The lips are dry, with particles of food adhering to them and between the teeth; this is very typical. The breath is foul. There are fine tremors of the tongue and hands. Intelligence is somewhat impaired. Skin dry, rough and scabby. Glandular enlargement in the posterior triangles × or – (variable though usually palpable, and sometimes puncturable, are frequently not so). Epitrochlears almost invariably palpable and enlarged, sometimes puncturable. (The position of the epitrochlear

glands is not constant; in some they are situated just above the internal condyle, in others, inches above. Of twenty-one cases where this enlargement has been looked for it has been absent in only one). Gait shuffling. Pulse rate, 110 to 140 per minute. Respirations shallow, rate, 25 to 40 per minute. Temperature taken during the course of examination varies with the condition of the patient and with the time of day, whether above normal or subnormal. When the disease is well established there is an evening rise of usually some degrees, and a morning fall to subnormal, rarely normal, *i.e.*, a regular daily, markedly swinging, intermittent fever. For some days before death, as seen in Chart No. 1, the temperature falls to subnormal and stays there till the end. In an early case the temperature is remittent or irregularly intermittent. There are no concomitant symptoms with the rise of temperature and the patient appears not to be inconvenienced.

Circulatory System.—The frequency of the pulse has been found to range between 100 to 142 per minute. There appears to be no definite correlation between the temperature and the pulse and respiration rates. Depending on the height of pyrexia the pulse and respiration rates are of course somewhat accelerated, but the ratio is unreliable. With great fluctuations between morning and evening temperatures the pulse and respiration rates differ slightly from day to day. The pulse and respiration rates, however, shew an almost constant ratio of 4 : 1. The force and frequency of the pulse is regular, the wave is easily compressible, the volume is small. When the temperature becomes subnormal before death the pulse and respiration rates also diminish in frequency, and this diminution is progressive until the fatal issue.

On examination of the heart one sees in most cases præcordial pulsation over the mitral area. Pulsation is always present, and sometimes strikingly so, above the clavicles and upwards along the course of the carotids at the root of the neck. This is more particularly marked in strong robust individuals in whom a moderate hypertrophy of the heart precedes degenerative changes and dilatation. In such cases, on palpation, a strong cardiac impulse is felt, of a slightly heaving character. In the majority of cases, however, hypertrophy—if it does occur—does so only to a small extent, and dilatation on the other hand is never extreme. A soft, blowing murmur over the apex has been heard in two cases, but no irregularity of the pulse or other indications of endocardial mischief

have been observed. Whatever changes take place are myocardial, and these of probably such a nature that the heart's muscle is not rapidly damaged. Sudden death from syncope does not occur; nor has acute dilatation or any history of cardiac uneasiness, palpitation, dyspnœa, etc., been recorded, except in one instance, when it occurred during the onset of the disease, and was therefore of different origin. The early tachycardia indicates that it is due to nervous influence rather than to myocardial causes. At the period when myocardial changes are established, indicated by floppy heart sounds, badly sustained pulse-pressure, and some increase in the transverse diameter of deep cardiac dulness, the pulse-rate diminishes slightly in frequency, and from this time onwards there is a gradual diminution till the end. The time of ventricular systole is lengthened and the first and second sounds are almost equally spaced, so that on auscultation a pendulum rhythm is heard. It is in those individuals with strong hearts and good arteries that the greatest resistance is offered to the disease, the course of which is prolonged. Young people under 20 appear to succumb quickly; a girl, aged about 18 years, died in two months; a boy, aged 14 years, in about the same time.

Respiratory System.—The respirations are regular in frequency but are quiet and shallow. The rate lies between 24 and 40 per minute. Sometimes, but not commonly, Cheyne-Stokes breathing closes the scene; at other times pulse and respiration gradually diminish till they quietly cease. Cough, bronchitis and œdema of the lungs are associated with most cases at some period.

Alimentary System.—Complaints relating to this system are unusual. The appetite is good and patients eat well until nearing their end. The lips are dry, the tongue dirty, and the breath foul. Sometimes there is abdominal pain, rarely vomiting, more frequently diarrhœa. In two cases great enlargement of the spleen was observed. The organ was firm, somewhat hard and presented a well-defined rounded edge, extending to about three inches below the costal border. The liver was found enlarged in one case only.

Integumentary System.—A harsh, dry skin, with a scaly, brawny desquamation which is best observed on the trunk and the lower part of the neck, above the clavicles. A papulopustular eruption on the

wrists, arms, inner surfaces of the thighs and on the pubes has been noted. Large patches of localised œdema of the skin has only been observed in one case. Loss of hair is often seen, even in young people.

Lymphatic System.—The enlargement of glands in the posterior triangles of the neck is not a prominent feature; they are sometimes impalpable, and often merely shotty. The epitrochlears have been found enlarged, with only one exception. The size varies between that of a small bean to that of a large almond; they are frequently puncturable, *vide* table.

Nervous System.—The expression of the face is dull and dreamy, and the speech is thick and mumbling. Cerebration is inhibited early, though the intelligence and memory are affected later. Headache and neuralgic pains in the legs are the rule.

Sensory Functions.—Hyperæsthesia, deep (kerandets) and superficial, is constantly present but varies in intensity with the condition of the patient. There is no anæsthesia. Patients are very sensitive to cold.

Motor Functions.—There is general muscular weakness; the patient is lethargic, and fatigue occurs. The muscles are flaccid and wasted. Tremors of the hands and tongue are very constant; sometimes of the legs and neck. The gait is shuffling. Later there is occasionally loss of power in the legs and sometimes rigidity of muscles. Epileptiform movements of not a very definite character were once noted.

Reflex Functions.—The superficial reflexes are undisturbed, the deep reflexes are at times exaggerated early; later elicited with difficulty or not at all. No ankle clonus; no Babinski. The bladder and rectum are unaffected, but shortly before death the sphincters are sometimes relaxed.

Special Senses.—Eyes. Pupils are equal and regular; they react to light and accommodation. Some diminution of acuity of vision has been complained of, irrespective of interstitial keratitis present in 5 out of 29 cases. Nystagmus was very remarkable in one case, and was well displayed on orienting upwards and onwards to either side.

Mental Condition.—There is a decided change in character. In early cases the patients appear highly-strung and nervous. Later they lose interest in their surroundings and the effort of thinking is irksome. Then there follows an inability to concentrate the mind in order to

answer questions, and at this stage they are sometimes emotional. Still later they appear confused and can neither express themselves intelligently nor comprehend what is being said. Delirium and maniacal symptoms are not usually early manifestations. Three cases were distinctly somnolent for some three weeks before death.

Sexual Functions.—Impotence develops during this fever, apparently early.

Hæmopoietic System.—The red blood corpuscles have been found to be about 3,200,000 to 3,500,000 per c.m. The hæmoglobin per cent. taken in over 25 cases at various periods of the disease was between 35 per cent. to 40 per cent. It has been seen as low as between 25 per cent. to 30 per cent., but only in one case was it as high as 60 per cent. The colour index calculated in two cases was about .5. The white blood corpuscles were between 7,000 to 12,000 per c.m. Differential leucocyte counts indicate an early relative increase of lymphocytes, sometimes an actual increase, over the polymorphonuclear neutrophils, which are diminished. About midway during the course of the disease actual increase of the lymphocytes is uncommon, and during the last stages there is invariably a return or approximation of the polymorphonuclear neutrophils to its normal per cent. Eosinophils are generally absent, or in small numbers: .40 per cent. basophils, .20 per cent. abnormal mononuclears are present, and the large mononuclears (hyaline cells) are increased, *i.e.*, 10 per cent. to 14 per cent. Myelocytes are seldom seen. While making differential counts normoblasts are sometimes found, when this is so they return between .20 per cent. to .40 per cent. Megaloblasts are extremely rare. Counts of 500 cells were made as a rule; in three cases over 1,000 cells were counted. Slides from 12 different cases were used. The blood platelets appear to be much increased. Trypanosomes shewing dividing forms are of frequent occurrence late in the disease.

Urinary System.—Urine pale, low sp. g., no sugar, no albumin. But many examinations have not been made.

Complications.—Bedsores have not been met with. Bronchial catarrh is almost invariable. Œdema of the glottis and of the lungs is not uncommon; in fact the latter appears to form part of the disease. Otitis media has been seen in one case; keratitis in several.

Incubation Period and Course of the Disease.—Histories point to a period of from 5 to 10 days; after which symptoms, usually severe, immediately supervene. In two cases after this initial period a remission of the severe symptoms, from about a week to fifteen days, took place. Patients, nevertheless, get progressively worse. There are roughly three stages, divisible in the majority of cases as follows:—

1. Incubation period and subsequent headache, pains in the chest and limbs, or abdominal pain and diarrhoea. There is no loss of intelligence, or indication of any organic interference with mental functions. Delirium is, however, sometimes associated with the intensity of the initial pyrexia which is remittent (*vide* chart No. 2). There is an increase of pulse and respiration rates, well above the normal, and the patient appears nervous. Trypanosomes few in number.

2. With these symptoms a change in character takes place. Cerebration is impaired; asthenia marked and increasing; oedema of feet and other oedemas; muscular wasting; tremors. The temperature, swinging and intermittent. Pulse and respiration rates continue high. The patient can still walk or sit about. Trypanosomes increased.

3. Patient is now unable to sit up, and crawls. Marked mental change; seems oblivious of surroundings; mumbles or is unable to talk; drowsy or comatose. Temperature either still intermittent for a few days, or absolutely subnormal for the 24 hours. Pulse and respiration rates subnormal, and diminishing in frequency. Trypanosomes numerous. Death.

The duration of these stages is approximately three weeks to a month for the first, up to four or even five months for the second, a few days to four weeks for the third. An average duration for the whole course is about four-and-a-half months. Six months has been found to be exceptional. In the young the course is very rapid. The trypanosomes must be observed to justify the diagnosis of trypanosomiasis. Sick people are seen among natives, who have a striking superficial resemblance to this disease—*e.g.*, oedema and a puffy countenance is frequently seen in ankylostomiasis, or illness with oedema due to other causes. On the other hand, a case of some months' standing has been seen where several of the outstanding symptoms were insignificant or absent. One example may be quoted:—A woman ill from early in

February, 1912, till the 30th July, when she died. She was first seen and diagnosed on the 11th June, when her condition was as follows:—Pulse 100, respirations 18, temperature 98·8° F. Still carries her child, and works in the garden. Glands in the posterior triangles few and small. Epitrochlears palpable. Some diminution of acuity of vision. No œdema of face or feet. Nothing else to note. She was again seen on the 19th and 28th June, when she appeared much about the same. Slides from this woman were sent in during February, April and May, and late in May I had an opportunity of examining some. Mine were negative, presumably also the previous one. A fresh preparation examined on the 11th June (the first time this had been done) shewed two trypanosomes in over a hundred fields (obj. $\frac{1}{6}$). This experience is not a solitary one, and much more importance is therefore to be attached to the examination of fresh coverslip preparations than to films. When trypanosomes have once been observed they have invariably been found at every subsequent examination. The blood of suspects has never subsequently shewn trypanosomes, though examined repeatedly at various intervals for a month or longer; this in well over 100 different individuals. I therefore conclude that the trypanosomes, from their first appearance in the blood, shortly after infection, are always present, and markedly so during the last month. Six per field, or even eight or more, are quite usual till death. Autoagglutination is not at all marked on all occasions, even with trypanosomes numerous in the blood. It is also seen in people not suffering from trypanosomiasis, and lately has been observed here in tick fever.

In the average cases the points to observe in diagnosis are:—The expression and puffiness of the face; mental condition; tremors; emaciation; enlargement of epitrochlear glands. The glands in the posterior triangles variable, $\times$ or $-$. Increased frequency of pulse and respiration rates. Temperature depends on the time of day when examination takes place, but if markedly subnormal in the morning indicates a fairly advanced stage, *i.e.*, of two or three months' duration; as also any decided change in the mental condition. Speech thick, sometimes the voice is high-pitched, at other times hoarse. Skin harsh, dry and scabby. Œdemas usually of feet. Gait shuffling, short-stepped; the feet just clear the ground as if the patient were pushing something along with them. Interstitial keratitis occurs in some 17 per cent. of

cases. The above combined with a history of headache, pain in the chest or legs, sometimes abdominal pain and diarrhoea or vomiting, as features marking the onset are almost pathognomonic. The headache as once described was a left-sided hemicrania with pains shooting backwards to the occiput, and forwards to the left eye-ball.

To differentiate this from the acute form of the Uganda disease one may say that there is nearly always a very definite and usually severe onset in our cases, which is far from insidious. The diagnostic value of the glands in the posterior cervical triangles is practically nil, as regards palpation. A large per cent. of cases shew interstitial keratitis, and further in 27 cases examined (fresh cover slip preparations) the trypanosomes have always been found in the peripheral blood whenever sought for. They are invariably few in the early stages, one or two in the whole preparation; later they are numerous, several to a field. It has never once been necessary to examine a second fresh preparation of a known case in order to find the organisms. This cannot be said for the Uganda fever.

PROGNOSIS.

The disease is invariably fatal in a few months. The first well-defined diminution in the frequency of the pulse-rate indicates that the case is on its downward course, and that vital resistance has been overcome. The state of the pulse is the main feature in prognosis.

TREATMENT.

Few attempts have been made in this direction. Tartar emetic 10 c.gm. given intravenously did not entirely banish the trypanosomes from the peripheral circulation. Arsamin grs. X on the following day however, did so, and with another 10 c.gm. tartar emetic, on the second day following, the trypanosomes did not reappear, after their first disappearance, till the tenth day. A method of subcutaneous introduction of tartar emetic, in normal saline solution, mixed with egg albumin has been tried without the production of pain, swelling or inflammation; some eucaine was added; but as the patient, who was in an advanced condition, died a few days later, one is unable to state whether there may not have been any after ill-effects.

PROPHYLAXIS.

The methods of investigation recently adopted have been as follows :—

1. The abolition of the pass-census system, mainly because (a) It is not possible to maintain for months such a rigid system among a peaceful population. (b) Too many possibilities of error arise unless large numbers of police are relegated for this purpose and their duties stringently carried out ; this is not found desirable.

2. The "Patrols" now act as "Itinerant Informers of Sick," of which there are five ; the Medical Officer making it his duty to visit and examine each sick person as soon after being reported as possible.

3. Slides made by the "Informers" are chiefly confined to those who are seriously ill, in the event of the Medical Officer not been able to arrive before death takes place.

4. Importance has been attached entirely to the examination of fresh coverslip preparation.

5. A figure of eight circuit round the district has been made practically every month, in order that the "Informers," S.S. Police, Chiefs, Headmen and relatives of the sick may have frequent access to the Medical Officer. In this manner the sick over an area of 10 to 15 or more miles can be examined in a day with better results than by inspecting of healthy people in two or three villages.

DIFFERENTIAL LEUCOCYTE COUNTS OF TWELVE CASES.

Chimpazi of Chimubvi, male.—Ill since February, 1912. Slide made 16th May, 1912. Died 24th May, 1912. Polymorphs, 63·05 per cent. Lymphocytes, 26·39 per cent. Hyaline cells, 10·55 per cent. (1,800 cells counted).

Mawapano of Chiunda, female.—Ill since February, 1912. Slide made 11th June, 1912. Died 30th July, 1912. Polymorphs, 49·14 per cent. Lymphocytes, 44·56 per cent. Hyaline cells, 10·56 per cent. Mast cells, 1·14 per cent.

Delekena of Mulungu, female.—Ill since April, 1912. Slide made 15th June, 1912. Died 17th June, 1912. Polymorphs, 76 per cent. Lymphocytes, 12·72 per cent. Hyaline cells, 11·26 per cent.

Chitukula of Mkohiawambo, male.—Ill since early May, 1912. Slide made 20th July, 1912. Died 13th August, 1912. Polymorphs, 50·59 per cent. Lymphocytes, 40·35 per cent. Hyaline cells, 9·05 per cent. (508 cells counted). See *Chart 1*.

Ndachiona of Mtonga, female.—Ill since May, 1912. Slide made 28th June, 1912. Died 4th August, 1912. Polymorphs, 37·80 per cent. Lymphocytes, 51 per cent. Hyaline cells, 8·60 per cent. Abdominal cells, 2·60 per cent. (500 cells counted).

Chemvenuzia of Mtonga, female.—Ill (?), 1912. Slide made 20th June, 1912. Died a few days after. Polymorphs, 48·40 per cent. Lymphocytes, 41·40 per cent. Mast cells, 0·20 per cent. Hyaline cells, 8·80 per cent. Abdominal cells, 1·20 per cent. Four normoblasts observed. (500 cells counted).

Chinkankeni of Chimonyo, male.—Ill since end of May, 1912. Slide made 7th July, 1912. Died 26th July, 1912. Polymorphs, 45·50 per cent. Lymphocytes, 39·25 per cent. Hyaline cells, 13·25 per cent. Abdominal cells, 1 per cent. Eosinophils, 1 per cent. (400 cells counted).

Chipochola of Njati, male.—Ill since 3rd week June, 1912. Slide made 23rd July, 1912. Died 22nd September, 1912. Polymorphs, 39·80 per cent. Lymphocytes, 45·20 per cent. Hyaline cells, 10·80. Eosinophils, 1·40 per cent. Mast cells, 0·80 per cent. Myelocyte, 0·20 per cent. (500 cells counted). See *Chart 2*.

Inje of Kawanga, male.—Ill since early May, 1912. Slide made 1st August, 1912. Died 3rd September, 1912. Polymorphs, 39·80 per cent. Lymphocytes, 47·80 per cent. Hyaline cells, 11·60 per cent. Eosinophils, 0·80 per cent. (500 cells counted).

Thumweke of Mtonga, female.—Ill since second week February, 1912. Slide made 31st July, 1912. Died 17th August, 1912. Polymorphs, 61·40 per cent. Lymphocytes, 22·40 per cent. Hyaline cells, 6·00 per cent. Mast cells, 0·20 per cent. (500 cells counted).

Bendu of Kamfummu, male.—Ill since middle June, 1912. Slide made 3rd August, 1912. Died 23rd September, 1912. Polymorphs, 46·75 per cent. Lymphocytes, 45·36 per cent. Hyaline cells, 7·04 per cent. Eosinophils, 0·56 per cent. Abdominal lymphocytes, 0·57 per cent. Mast cells, 0·20 per cent. (1,050 cells counted).

Diwa of Kambwiri, male.—Ill since last week May, 1912. Slide made 13th August, 1912. Died 16th August, 1912. Polymorphs. 50·40 per cent. Lymphocytes, 42·80 per cent. Hyaline cells, 5·50 per cent. Abdominal cells, 0·90 per cent. Eosinophils, 0·40 per cent. 2 Normoblasts observed. (1,000 cells counted).

Comparative Table of enlargement of glands in the posterior cervical triangles, and epitrochlear glands, in 21 cases where both have been looked for.

—	Shotty.	× —	×	× P
Posterior Triangles, 33·33 per cent	9·52 per cent.	38·57 per cent.	4·71 per cent.	14·28 per cent.
Epitrochlear Glands, 4·71 per cent.	—	19·04 per cent.	47·61 per cent.	28·57 per cent.

Percentages of frequency of palpable glands in posterior cervical triangles and epitrochlear glands, in the sick.

Posterior Triangles, 66·66 per cent.

Epitrochlear Glands, 95·23 per cent.

Percentages of 100 healthy people examined for enlargement of epitrochlear glands; sexes about equally divided.

—	Shotty.	× —	×	× P
53 per cent.	14 per cent.	11 per cent.	13 per cent.	9 per cent.

Comparison between epitrochlear enlargement.

In healthy 47 per cent.

In trypanosomiasis 95·23 per cent.

N.B.—× — about $\frac{1}{4}$ inch diameter.

× „ $\frac{1}{2}$ „ „

× P more than this, and easily puncturable.

The 100 healthy people were composed of men and women in villages, and carriers and machilamen who are constantly travelling with me, in the “ area.”