East African Trypanosomiasis in Nkhotakota District

M Delbaere, JB Matengele

A marked increase in trypanosomiasis has been seen at Nkhotakota District Hospital since September 1989. This report presents background information, the extent of the recent outbreak and a suggested revised treatment protocol. Suggestions are made for preventative measures against the spread of trypanosomiasis.

Introduction

East African Trypanosomiasis (sleeping sickness) is seen in East and Central Africa and is caused by the parasite *Trypanosoma brucei rhodesiense*. West African Trypanosomiasis is caused by *Trypanosoma brucei gambiense* and is not seen in Malawi. WHO statistics for the period 1976 - 1983, estimated that out of a total population of 6.4 million in Malawi there were 1.2 million people at risk of infection with *T. b. rhodesiense* [1]. Total reported cases of trypanosomiasis for Malawi are shown in the Table.

Table Reported cases of trypanosomiasis in Malawi from two data sources (1973 - 1984)

YEARS												
73	74	75	76	77	78	79	80	81	82	83	84	SOURCE
			13	32	27	7	38	18	-	-		1
14	8	-	13	32	32	28	23	21	17	-	55	2

Epidemiology of trypanosomiasis in Nkhotakota

MORBIDITY AND MORTALITY: In Nkhotakota there were 2 cases reported in 1973, 1 case in 1979 and 1 case in 1980 [2]. However from 1989 there was a marked increase in cases seen: 21 cases for 1989, 209 cases for 1990 and 64 cases for the first two months of 1991 (Nkhotakota District Hospital statistics). This data is shown in further detail in Figure 1. Since the beginning of 1991 more than 1 patient suffering from trypanosomiasis has been admitted *every day*.

Patients with trypanosomiasis were classified as being either **early** or **late** stage. The "early" stage is were the disease has not affected the central nervous system (CNS), whereas the "late" stage is when CNS spread has occurred. A lumber puncture is done to "confirm" the presence or absence of trypanosomes in the CNS.

During the period of the study there were 61 patients "confirmed early stage", 55 patients "suspected early stage", 24 patients "confirmed late stage" and 29 patients "suspected late stage". Overall there were 116 (69%) in the early stage (suspected or confirmed) and 53 (31%) in the late stage (suspected or confirmed). A further 40 patients were classified as stage unknown. In 1990 there were 152 (73%) male and 57 (27%) female admissions with trypanosomiasis. The age and sex distribution is shown in Figure 2.

The mortality rate of trypanosomiasis is 100% in the untreated patient. In the advanced late stage of the disease the prognosis is poor though treatment is not hopeless. In 1990 trypanosomiasis accounted for 11% of all hospital deaths. Needless to say many deaths will occur in the villages in tsetse infested areas.

The extent of the disease in the community is not known. There is no organised active case detection established in the villages within the tsetse infested area. Probably the hospital based figures

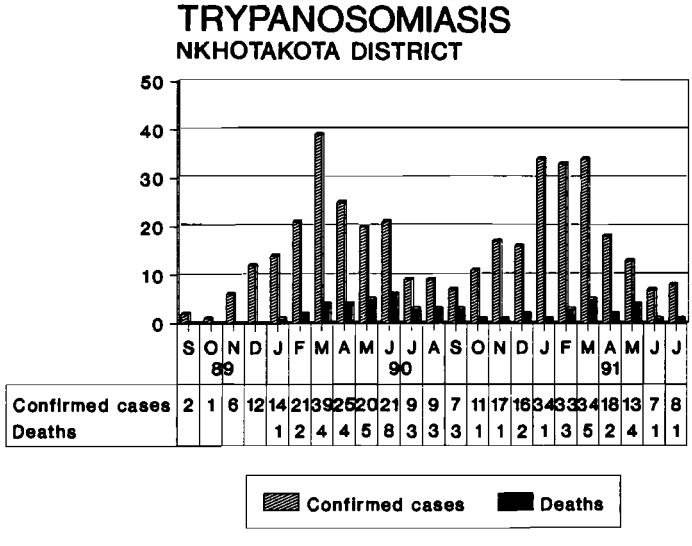

Figure 1

Nkhotakota District Hospital
M Delbaere, JB Matengele

Correspondence to:
JB Matengele
Nkhotakota District Hospital
P.O. Box 50
Nkhotakota

represent the tip of the iceberg. The disease is associated with a great deal of suffering and misery to both the patient and family, especially in late stage.

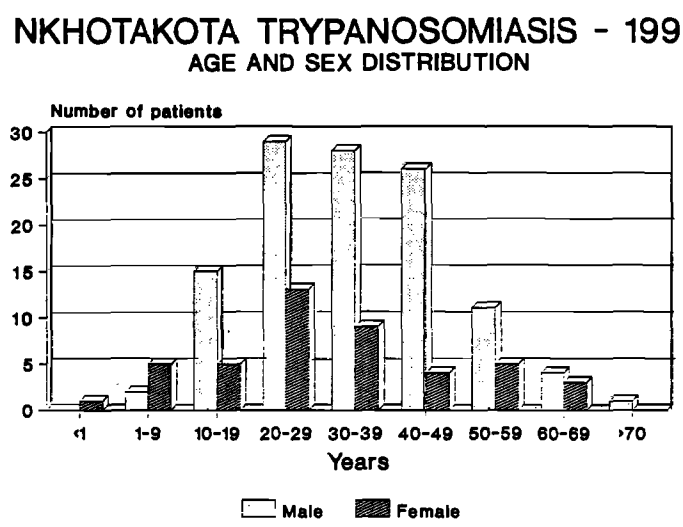

Figure 2 RHO(C) 30/1/91 Source:DHO Nkhotakota

GEOGRAPHIC DISTRIBUTION: The spread of trypanosomiasis depends on the host-vector-parasite relationship. In an **endemic** situation "game-fly-man" cycle predominates whilst in an **epidemic** situation (as seen in Nkhotakota) "man-fly-man" and "domestic animal-fly-man" cycles predominate. Domestic animals that can serve as reservoir hosts include cattle, sheep, goats and dogs.

The game hosts that have been identified as reservoirs are the bushbuck (which is perhaps the most important) waterbuck, hippopotamus, warthog, hyena and hartebest. All these animals are found in Nkhotakota game reserve. The tsetse fly species *Glossina morsitans* and *Glossina pallidipes*, whose reproduction conditions require warm, shady and humid soils, feed preferentially on this wide range of game. Thus high-risk groups include hunters, poachers, firewood collectors, women collecting water and farmers from the estates close to the Nkhotakota Game Reserve boundary. Occasional unsuspected spread may also occur e.g. a stranded bus (due to a breakdown) was seen adjacent to the Game Reserve with at least 40 - 50 people waiting until the problem was solved.

Most of the patients with trypanosomiasis admitted to Nkhotakota District Hospital or seen as outpatients come from certain areas: T.A. Malengachanzi (79) and STA Mphonde (70), T.A. Mwadzama (14) and STA Mwansambo (8). Villages which are seriously affected are Mwalwatongole, Sesani, Ungwe, Makhenjere, Kabululu, Nkhongo and others, situated along Nkhotakota Game Reserve. There have been 2 patients from Ntchisi District and 2 from Kasungu District.

Clinical and laboratory diagnosis

CLINICAL PRESENTATION: It is not possible to make a diagnosis of trypanosomiasis on clinical manifestations alone and only parasitological examination will confirm the diagnosis. There are certain symptoms which suggest the diagnosis especially when they occur in combination. There is a

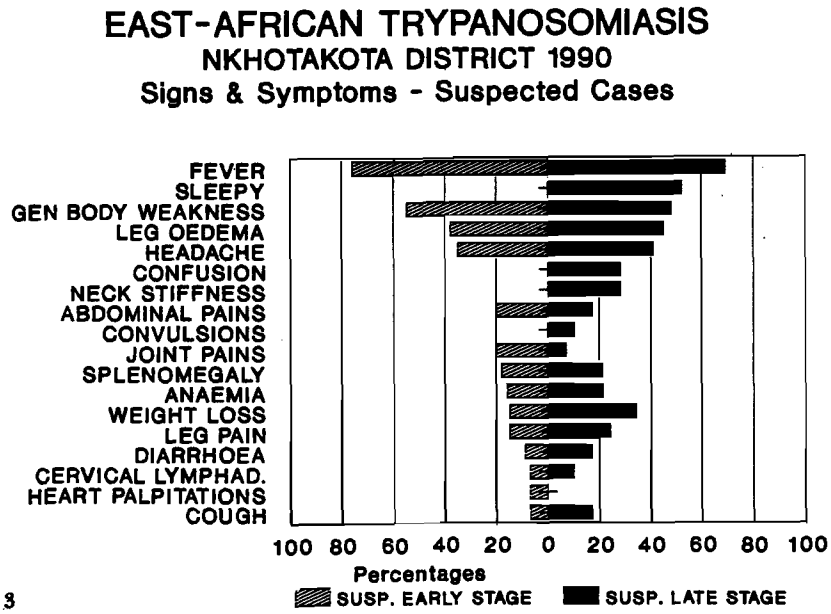

Figure 3
DHO, Nkhotakota

difference between West African trypanosomiasis (*T. b. gambiense*) and East African trypanosomiasis (*T. b. rhodesiense*). Symptoms of the latter are more severe and acute.

Trypanosomiasis caused by *T. b. rhodesiense* has an incubation period of 1 - 3 weeks. The most common signs and symptoms are fever, headache, general body weakness, leg oedema, splenomegaly, cervical lymphadenopathy and in the advanced stage of the disease there is confusion, convulsions, neck stiffness and drowsiness (i.e. a range from "decreased level of consciousness" to coma). These clinical features according to the stage of the disease are shown in Figure 3.

Trypanosomiasis can thus present a diagnostic problem in view of the wide possible differential diagnosis, especially when the blood-film is negative. Many infections have been misdiagnosed as malaria (certainly in children), typhoid fever and hepatitis. Lymphadenopathy with fever in a wasted patient must be differentiated from HIV infection or tuberculosis. Trypanosomiasis may be confused with congestive cardiac failure, nephrotic syndrome or even malnutrition. In the advanced stage of the disease it must be differentiated from cerebral malaria and meningitis. The diagnosis may be masked when combined with other pathology e.g. patients have been seen with HIV infection and trypanosomiasis, and a child with bacterial meningitis and trypanosomiasis.

LABORATORY DIAGNOSIS: The diagnostic methods used in Nkhotakota District Hospital laboratory, are a blood-film (Field stain) for parasite detection, a direct cerebrospinal fluid (CSF) examination for parasite detection and white blood cell count and differential. Concentration techniques by centrifugation were not done due to lack of equipment and materials. Elevations in protein level in the CSF are detected with urine protein sticks since there are no materials to perform a flocculation reaction or the method of Sicard and Cantaloube.

The single laboratory assistant, besides performing all other diagnostic tests for the hospital, has little time to go through all the fields per slide to pick up the parasites in so many slides every day. The disease cannot be confidently excluded on the basis of a single negative blood film only.

Treatment of East African Trypanosomiasis

The choice and schedule of treatment depend on the stage of the disease. As already mentioned, the CSF results, though not completely satisfactory, will be a guide to what treatment should be given.

Suramin (an ureum derivative) is used for early stage trypanosomiasis. A combined course of Suramin and Melarsoprol (an arsenic derivative) will treat late stage patients.

The supply of both Suramin and Melarsoprol is erratic. Between November 1989 and June 1990 a large proportion of our patients were discharged without treatment or with partial treatment, only to die later in the villages.

The two drugs, besides having a curative effect, are potentially toxic to the patient. Reactive encephalopathy from Melarsoprol probably accounts for 5% of all deaths in patients who have the late stage of the disease [1].

Broad guidelines for treatment have been published by the WHO expert Committee on Trypanosomiasis, but they do not give preference for any treatment scheme. We have followed an abbreviated course of treatment which has been used at Kamuzu Central Hospital (Table 1). The results of using this treatment at Nkhotakota District Hospital during 1990 are summarised.

Suramin treatment alone: 56 patients had an interrupted course due to drug shortage (50) or because patients absconded (6). 64 patients received a full course of Suramin and most of them improved. 11 patients died (7 arrived in very bad condition and during treatment developed fever and died - presumably late stage). 4 patients developed high fever and died (2 of these patients had coma). 1 patient died 2 months after an interrupted course of Suramin.

Reactions to Suramin were noted in a few patients: fever (6) and diarrhoea (6). One lady, who became hysterical on the 4th day of Suramin treatment and had diarrhoea and convulsions, recovered fully.

Suramin and Melarsoprol Treatment: There were 10 patients with negative CSF results but with clinical late stage disease. They all improved clinically, but 1 patient had residual brain damage, 1 patient had diarrhoea during the course and 1 patient had a reactive encephalitis (the family wanted to take the patient home in this bad condition).

There were 17 patients confirmed late stage disease (trypanosomes identified in the CSF). 1 patient had previously had a negative CSF examination. They all improved, except 1 child who developed reactive encephalitis and hepatitis (possibly drug induced). The child was taken home with severe brain damage and died later in the village.

There were an additional 3 patients who arrived in a very bad condition. The first patient received the first series of Melarsoprol injections and developed severe diarrhoea and died. The second

patient, who was also HIV reactive, died after the Melarsoprol course. The third patient died after 2 doses of Melarsoprol, probably due to reactive encephalitis.

Comments on this treatment: Following this 6 months experience in treating trypanosomiasis, and after consulting all available literature on the subject, a modified treatment protocol is proposed. (Table 2).

Some doctors, with many years experience treating *T. b. gambiense* infection in Zaire, claim that the trypanosomes are already present in the CNS even without changes in CSF [1,4,5]. These trypanosomes may be responsible for relapses seen after the classic treatment schemes. They therefore administer 1 series (3 days) of Melarsoprol (at full dosage) after Suramin treatment in "early stage" trypanosomiasis. Adopting this treatment policy would also seem reasonable in our setting since *T. b. rhodesiense* invades the CNS relatively early. Further arguments in support of this approach is the difficulty in following up patients (theoretically should be at 3, 6, 12 and 24 months after treatment), and the fact that our laboratory detection methods for CSF changes are not that reliable. We believe that several patients with early central nervous system involvement were missed. These patients may then die in the village.

We believe that 4 doses of Suramin before giving Melarsoprol in late stage disease is too many. In Kenya and Zambia 3 doses are given, and in Tanzania and Uganda only 2 doses are given. The interval before starting Melarsoprol should only be 1 day instead of 1 week. These modifications will save drugs, shorten the hospital stay and do not appear to affect outcome.

In Malawi Melarsoprol has been administered in a dextrose solution, whereas in surveys of other countries it is given IV STAT. We have therefore started giving Melarsoprol IV STAT. Early experience after 4 weeks has shown good results and no adverse reactions.

Cost of Hospital Treatment: We expect the epidemic to increase during 1991 (so far January 34 patients, and February 34 patients). We expect to see 30 patients per month during 1991 (20 in early stage, and 10 in late stage of the disease). Using the modified treatment scheme shown in Table 2, we would need 140 vials of Suramin, 180 ampoules Melarsoprol, 140 IV giving sets, 140 litres of 5% Dextrose, 2050 tablets Prednisolone (5 mg) and 60 urine sticks (protein). Calculations based on Malawi Central Medical Stores prices show a monthly cost for 30 patients of K 17,426 and a yearly cost of K 209,113. Even excluding the very expensive Suramin and Melarsoprol the monthly expenses for 30 patients will still be K 2,006 and a yearly cost of K 24,074. The latter represents 15% of the 1990 Drug Budget for Nkhotakota District Hospital. Other effects not easily costed are: increased nursing workload; higher bed-occupancy; extra food for patients; and a heavy laboratory workload (blood-film, CSF examinations, and urine examinations).

A donation of drugs from the EEC will last till March 1991. The Belgian Government has provided Melarsoprol, and it is hoped that other donors will help in the future with treatment as well as screening and prevention.

Prevention of Trypanosomiasis

With the rapid population growth, land which was previously allocated as "Reserves" (close to the boundary of the Game Reserve) has now been released for settlement and agricultural use. However public concern is now to avoid or even abandon these tsetse fly infested areas.

In the control of disease there has been progress in collecting baseline data on the tsetse fly population and their behaviour, which is necessary to draw up a strategy for vector control. However medical surveillance of the human population is virtually non- existent. So far the emphasis of the National Tsetse and Trypanosomiasis Control programme has been towards control of the disease in domestic and game animals and vector control. This programme should be extended towards the control of the disease in the human population. Regular medical surveillance of the population at risk and mass treatment for those infected (coupled with vector control) is the only hope for controlling the disease in Nkhotakota. Given the present precarious situation we wonder whether we should be using limited resources to treat patients who will return to the same environment only to be re-infected. Unless there is a combined response from the medical surveillance and vector control sectors, we will never be successful in our hospital treatment.

A comprehensive situation analysis is required. Information is needed on the prevalence and spread of trypanosomiasis; demographic data on the population at risk; information on the vegetation of the area with emphasis on demand for land and food; future development in the district e.g. the proposed expansion of the Dwangwa Sugar plantation and the construction of the road from Kasungu to Nkhotakota; prediction on population growth; information on potential vector and animal reservoirs.

Prevention can be achieved by a combination of various strategies. First the identification of car-

riers/cases (both actively and passively) and treatment of all patients infected is needed to break the transmission cycle (man-fly-man). This will require a sufficient stock of drugs. Resources for follow-up will be needed as unfortunately some villagers abscond or do not cooperate with treatment. Community awareness can be increased through health education. Primary health care based programmes should involve villagers and follow up of treated patients. Advising villagers to abandon their villages is not a solution since acquisition of alternative land is not feasible and survival depends on having sufficient land for food production. Vector control is possible with the use of odour baited insecticide impregnated targets. In Zimbabwe trials have shown that placing targets at a density of 4 per square km achieved more than 95% reduction of tsetse flies [1].

Conclusion

Nkhotakota District is witnessing a resurgence of tsetse flies responsible for the transmission of trypanosomiasis. The expanding population and increased demand for agriculture land has made this devastating disease a major communicable disease in this district.

A combined approach of active medical surveillance to detect trypanosomiasis cases, treatment and education of those infected and vector control with "targets" is the only hope of reducing the spread of this major communicable disease in Nkhotakota. Given sound planning, organisation, and financial resources this should be possible.

Selected References

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Table 1 *Treatment Chart Trypanosomiasis* (Abbreviated Course Based On Schedule Used At Kamuzu Central Hospital)

If any reaction to the drug is observed (exfoliative dermatitis, rash or reactive encephalitis) STOP TREATMENT and immediately inform the Clinical Officer.

DAY OF TREATMENT	EXAM	EARLY STAGE DRUG	LATE STAGE DRUG	PREDNISOLONE
0	Urine	SUR 0.5 G	SUR 0.5 G	40 mg
1	Urine	SUR 1.0 G	SUR 1.0 G	40 mg
2	LP	SUR 1.0 G	SUR 1.0 G	40 mg
3		SUR 1.0 G	SUR 1.0 G	40 mg
4				40 mg
5				40 mg
6	Urine			40 mg
7		SUR 1.0 G		40 mg
8				40 mg
9				40 mg
10			MEL B 5 ml	40 mg
11			MEL B 5 ml	40 mg
12			MEL B 5 ml	40 mg
13	Urine			30 mg
14		SUR 1.0 G		30 mg
15 - 19				30 mg
20			MEL B 5 ml	25 mg
21			MEL B 5 ml	25 mg
22			MEL B 5 ml	25 mg
23 - 29				25 mg
30			MEL B 5 ml	
31			MEL B 5 ml	
32			MEL B 5 ml	
33 - 39				
40			MEL B 5 ml	
41			MEL B 5 ml	
42			MEL B 5 ml	

SURAMIN: must always be freshly prepared with sterile water for injection to a 10% solution. Dose for children is 20 mg/kg. Adult (50 kg) = 1 G (1 vial maximum). Add to 200 ml 5 % Dextrose and give over 2 hours.

MELARSOPROL: Dose is STRICTLY 3.6 mg/kg. Adult dose 180 mg (one 5 ml ampoule). Dissolve in 200 ml 5% Dextrose and run over more than 2 hours. Avoid tissuing of the drug because it is highly irritant.

PREDNISOLONE: Dose for children is 1 mg/kg once daily.

Table 2 New Treatment Scheme for Trypanosomiasis

If any reaction to the drug is observed (exfoliative dermatitis, rash or reactive encephalitis) STOP TREATMENT and immediately inform the Clinical Officer.

DAY OF TREATMENT	EXAM	EARLY STAGE DRUG	LATE STAGE DRUG	PREDNISOLONE
0	Blood-film + Urine			
1		SUR 0.5 G	SUR 0.5 G	40 mg
2		SUR 1.0 G	SUR 1.0 G	40 mg
3	LP	SUR 1.0 G		40 mg
4		SUR 1.0 G	MEL B 5 ml	40 mg
5			MEL B 5 ml	40 mg
6			MEL B 5 ml	40 mg
7	Urine			40 mg
8		SUR 1.0 G		40 mg
9 - 13				40 mg
14	Urine		MEL B 5 ml	30 mg
15		SUR 1.0 G	MEL B 5 ml	30 mg
16		MEL B 5 ml	MEL B 5 ml	30 mg
17		MEL B 5 ml		30 mg
18		MEL B 5 ml		30 mg
19 - 23				30 mg
24			MEL B 5 ml	25 mg
25			MEL B 5 ml	25 mg
26			MEL B 5 ml	25 mg
27 - 33				25 mg
34			MEL B 5 ml	25 mg
35			MEL B 5 ml	25 mg
36			MEL B 5 ml	25 mg

SURAMIN: must always be freshly prepared with sterile water for injection to a 10% solution. Dose for children is 20 mg/kg. Adult (50 kg) = 1 G (1 vial maximum). Add to 200 ml 5 % Dextrose and give over 2 hours.

MELARSOPROL: Dose is STRICTLY 3.6 mg/kg. Adult dose 180 mg (one 5 ml ampoule). Give as IV PUSH but take great care to avoid tissuing of the drug because it is highly irritant.

PREDNISOLONE: Dose for children is 1 mg/kg once daily.

FOLLOW-UP: Review the patient for repeat blood film and lumbar puncture at 3, 6, 12, and 24 months post-treatment.