

Resurgence of sleeping sickness in Southern Sudan

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Abstract

Human African trypanosomiasis (HAT), or sleeping sickness, has been a public health problem in Sudan for much of the 20th century. Endemic foci of *Trypanosoma brucei gambiense* are found in southern Sudan in a belt bordering Central African Republic, Democratic Republic of Congo and Uganda. Gambiense sleeping sickness runs a chronic clinical course and is invariably fatal if left untreated. The disease has a significant impact on the economic fabric of affected communities. An increase in the number of passively detected cases of sleeping sickness in Tambura County, southern Sudan during 1996-1997 alerted the International Medical Corps to the possibility of an epidemic. With assistance from the Centers for Disease Control and Prevention (CDC), a statistically valid population-based prevalence survey was conducted that documented epidemic levels of trypanosomiasis. The overall seroprevalence was 19.4% with one village recording a seroprevalence of 45%. This paper describes how the epidemic was identified, and provides a review of sleeping sickness including its epidemiology, diagnosis and treatment.

Keywords: African Trypanosomiasis, sleeping sickness, southern Sudan, tsetse fly

Introduction

In remote communities disrupted by political unrest and civil war, environmental health is left to languish when other priorities, such as survival, are paramount. Consequently, the health of the population deteriorates and epidemic diseases emerge that prior to these conflicts were well controlled. A prime example of this effect is the epidemic of Human African Trypanosomiasis (HAT), better known as sleeping sickness, assailing the population of Tambura County in Western Equatoria, Southern Sudan.

Sleeping sickness is a parasitic disease unique to sub-Saharan Africa found between 15 degrees north and 20 degrees south latitude (Benenson 1995). Two protozoa subspecies, *Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense*, both transmitted through the bite of the tsetse fly (*Glossina* spp) cause the disease in humans. Infection with *T. b. gambiense* occurs in West and Central Africa and causes a chronic disease that takes several years to reach the advanced stage. Whereas sleeping sickness caused by *T. b. rhodesiense* is confined to Eastern Africa and is extremely virulent, causing death within weeks to months. Both types of sleeping sickness are invariably fatal if left untreated.

In 1996, International Medical Corps (IMC), a humanitarian medical non-government organization (NGO), implementing an emergency medical care program in Tambura County, realized that the number of patients presenting to Tambura hospital with sleeping sickness was greater than the expected average prevalence of 0.1-2 percent found in endemic regions. Local health workers confirmed that many people in diverse villages in the county were suffering with symptoms resembling those of sleeping sickness. An unpublished prevalence study conducted in 1997 confirmed the overall actual seroprevalence to be 19.4%, with some villages found to have prevalence levels as high as 45%.

Trypanosomiasis imposes a considerable public health and socio-economic burden by decreasing the labor force and hampering production and work capacity in susceptible populations. Through the very nature of the endemic foci existing in isolated rural areas operational capacity to respond to epidemic situations is poor and sleeping sickness remains a major obstacle to the development of entire regions.

Review

Human African Trypanosomiasis is a daily threat to more than 60 million people of the 400 million people who live in the 36 countries of sub-Saharan Africa where the disease is endemic (Barrett 1999). Only 5-10% of these people are under surveillance hence the 45,000 cases reported to the World Health Organization (WHO) in 1999 do not reflect the reality of the situation, but simply show the absence of case detection. In reality between 300,000 and 500,000 people are estimated to have the disease (WHO 2001b).

Gambiense sleeping sickness generally occurs in historically endemic foci in lowland rainforests of Western and Central Africa (WHO 2000). Sleeping sickness is endemic in southern Sudan where the

foci of disease extend from Kajo Keji County in Eastern Equatoria to Tambura County in Western Equatoria. Outside southern Sudan, the disease historically extends to northern Uganda (Arua and Moyo districts), Democratic Republic of Congo (DRC) and Central African Republic (CAR). An important feature of African trypanosomiasis is its focal nature. It tends to occur in circumscribed zones. Observed prevalence rates of trypanosomiasis vary greatly from one geographical area to another, and even between one village and another within the same area. Thus, it is important to understand the ecology and resulting transmission patterns in each locality (WHO 2000).

Sleeping sickness is transmitted primarily through the bite of the tsetse fly. In southern Sudan, it is *Glossina fulcipipes fulcipipes* (Moore 2001), a riverine tsetse fly that is the vector for *T. brucei gambiense*. These flies feed preferentially on human blood, but may take meals from animals. Trypanosomes from the infected host are taken up by the tsetse fly during this blood meal. The parasite undergoes an extrinsic incubation period while multiplying in the fly for 12 to 30 days. Once the tsetse fly is infected, it remains infective for the balance of its life span, which is an average of 3-6 months (Bell 1995). The tsetse fly requires a warm, moist, shaded habitat and is found in vegetation near small rivers, streams or pools of water that are frequented by people. Close contact between the tsetse fly and humans as they perform their daily activities – water collection, clothes washing, bathing – complete the transmission cycle for sleeping sickness. This cycle is magnified due to the chronic nature of trypanosomiasis where the long latency period of the disease results in people being infective for years without their knowledge.

At the beginning of the 20th century, sleeping sickness was the most important public health problem in Africa (Ekwanzala 1996). Huge epidemics occurred in 1896-1906 and large areas of the continent were devastated during the 1920. The current epidemic began in 1970 (WHO 2001a). The discovery of the parasite and its tsetse fly vector in the early 1900's followed by initial treatment methods, directed measures to eradicate both the habitat of the tsetse fly and the reservoir of disease. Undergrowth from villages, water sources, paths, and bridges was cleared, wild animals were culled, and colonial powers carried out strategic mass depopulations of epidemic areas to segregate people temporarily from the unhealthy environments (Hoppe 1997). People living in endemic areas were coerced into being screened for the disease and infected individuals were treated (Barrett 1999). Mass campaigns that combined active case detection of mostly symptom free cases and chemo prophylaxis with pentamidine practically eliminated sleeping sickness by 1960 (WHO 2001a).

Detection of people infected with sleeping sickness and subsequent patient care requires well-trained staff, resources, drugs and well-equipped health centers. Once African countries gained their independence from their colonial rulers, national health budgets frequently lacked adequate finance, wars disrupted or destroyed health infrastructure and people were displaced. Sleeping sickness surveillance and control diminished and by the 1970s sleeping sickness had once again become an epidemic disease, debilitating and eventually killing populations, perpetuating the cycle of economic poverty in these regions.

Analysis

To understand the current sleeping sickness epidemic in Tambura County and its devastating effect on the population, the political, geographical and socio-economic context existing within must be comprehended as well as the actual disease. In Sudan, there has been a long history of conflict between the largely Islamic North and the Christian/Animistic South. When Sudan gained independence in 1956, southern Sudan's demand for secession was rejected and civil war against the incumbent Government of Sudan (GOS) broke out. The war ended in 1972 when the southern provinces were granted autonomy, but peace was short lived. In 1983, the region's autonomy was removed and hostilities were resumed. The rebel movement, the Sudanese People's Liberation Army (SPLA), quickly gained control of most of the southern region. Due to its isolation, Tambura County was under government control until 1989.

Tambura County is situated at the southwestern tip of Western Equatoria (Figure 1). It is considered the breadbasket of southern Sudan, exporting surplus food to other SPLA-held territories, primarily through the NGO and United Nations (UN) network. Conditions in the region are mixed: basic health care programs, although dependant on external support from NGOs and missionaries, reach large numbers of the population and the road infrastructure has been improved through the efforts of NGOs and local workgroups. The SPLA has taken control of a growing number of areas in neighboring regions formally controlled by the GOS, however the fighting has resulted in an influx of returnees, refugees and displaced persons, straining the meager resources for health care.

Prior to the ousting of the GOS and the takeover of Tambura County by the SPLA, active treatment and control programs were incorporated into the health infrastructure to address endemic and epidemic diseases in the region such as leprosy, tuberculosis, malaria, sleeping sickness, and river blindness. Dedicated sleeping sickness hospitals were located at Source Yubu and Li Rangu funded by the Belgian government. These facilities provided diagnosis and treatment services, management for patient follow-up and sleeping sickness control measures for the residents of Tambura County and the adjacent Yambio County. The Li Rangu facility (in Yambio County) was the base for the Trypanosomiasis Control Program for the region. With these initiatives, sleeping sickness was controlled at a prevalence of 0.5 percent. Both facilities ceased to be operational in 1989 when the Belgian government was forced to withdraw its support following the SPLA take over. The Sudan Relief and Rehabilitation Association (SRRA), the civil society arm of the SPLA, lacked the resources to maintain the health care system.

Tambura County shares borders with Democratic Republic of Congo (DRC), and Central African Republic (CAR). Themselves politically unstable and with debilitated or non-existent health services, sleeping sickness in these countries is rife (Figure 1). For example, the village of Bazigbiri in CAR, 70 kilometers from Source Yubu, completely disappeared after all the residents died from sleeping sickness or fled from the disease (Moore 2001). Frontiers between these countries are porous and allow mass movement of populations escaping civil unrest in what sometimes seems a cyclic progression. When these infected people flee from one place to another the spread of sleeping sickness is perpetuated to contiguous non-endemic areas.

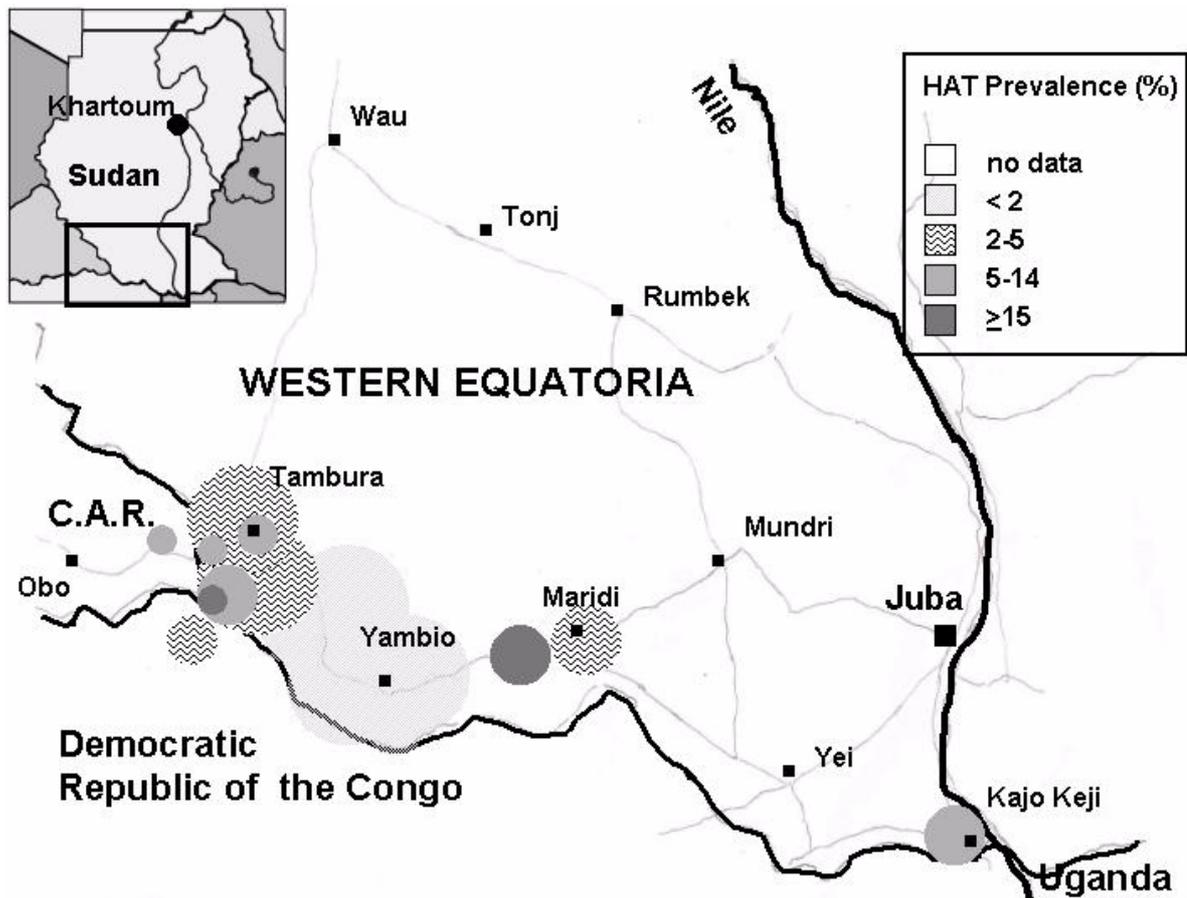


Figure 1. Map of Southern Sudan indicating foci of Sleeping Sickness and Prevalence Levels. Reproduced with kind permission of Dr Anne Moore (2001).

Identification of Sleeping Sickness Outbreak

In 1995, IMC began a passive treatment program for sleeping sickness based at Tambura Hospital in Tambura County as an adjuvant to their emergency primary care program begun in 1994. During 1995, 16 cases of sleeping sickness were diagnosed and treated. As community awareness grew, the number of people seeking medication and treatment rapidly increased. In 1996, 86 cases of sleeping sickness

were treated. In late 1996, IMC received reports from health workers in outlying payams (districts) of Tambura County that as many as 800-1000 persons could be suffering from the disease.

The Medical Director of IMC, consulted with trypanosomiasis experts from the WHO in Geneva and the Centers for Disease Control and Prevention (CDC) in Atlanta to determine how best to elucidate whether the resurgence in sleeping sickness cases was an unrecognized epidemic and how to approach the problem. It was decided to conduct a statistically valid population-based prevalence survey to quantify the number of people affected by sleeping sickness, identify geographic areas most at risk and facilitate the development of the most effective treatment strategy.

Epidemiologists and parasitologists from the CDC in collaboration with IMC and CARE staff conducted the prevalence survey. The Card Agglutination Test for Trypanosomiasis (CATT), a serodiagnostic test to detect anti trypanosomal antibodies in blood, was used to screen the sample population. The CATT is limited by the sensitivity and specificity of the antigen, as trypanosomes share antigens with several other protozoa and bacteria (Bell 1995). Nevertheless, it is a valuable tool for screening populations, many of whom are asymptomatic. Once identified using the CATT, patients can undergo further laboratory testing to confirm the diagnosis. Confirmation rates of parasite positive cases range from 15-80% of seropositive people tested (IMC data).

Permission to conduct the survey was gained from the District Commissioner and the SRRA representative for Tambura. Headmen in each village were informed and the population mobilized. The initial survey began in May 1997, in the town of Ezo, thought to be the epicenter of the resurgence from analysis of the hospital data. The survey was interrupted during the first week by a security incident requiring the evacuation of all expatriate staff and could not be recommenced until late June 1997. The study was concluded on July 18, 1997 after 34 clusters (1,360 persons) were screened from 16 selected villages. The cluster survey represented a population base of approximately 20,000 persons (source, SRRA 1997) in the epidemic area. The overall seroprevalence was 19.4 percent, indicating that 3,880 people in Ezo payam were potentially infected with sleeping sickness. In the actual town of Ezo II, the epicenter of the epidemic, seroprevalence of sleeping sickness was 45%. Seropositive patients from the prevalence survey were examined for parasites and 56% (148) were confirmed parasite positive. Of these, two-thirds had Stage I disease and one-third had already advanced to Stage II (IMC data).

Extrapolating these results to the remaining payams excluded from the prevalence survey, 8,000 out of a population of 60,000 people may be infected with sleeping sickness. When compared with data from earlier sleeping sickness surveys the results are staggering. In 1988, the last year formal surveillance was conducted, health workers employed by the former Belgian Sleeping Sickness Control Program cited a prevalence of approximately 0.3-0.5 percent. In addition, only 50 percent of villages screened were positive for the disease. In contrast, 100 percent of villages screened during the current prevalence survey were positive while the seroprevalence of 19.4% represents a forty-fold increase in disease in only nine years.

The SPLA do not have the resources or expertise to combat such an epidemic and without intervention from external sources, the epidemic will continue to accelerate. As the prevalence of HAT rises, the human reservoir increases and subsequently the transmission of the disease increases. To implement an effective treatment and control program is expensive. Mobilization and education of communities in epidemic foci, active case detection, treatment and follow up require not only laboratory equipment, trained personnel, costly drugs but man power and time. To control the current epidemic in Tambura County would involve an acute management program extending over two years followed by continued surveillance and vector control.

The Disease

Gambiense sleeping sickness is a protracted disease that has two distinct phases corresponding to the site of the parasite infection.

Stage I

The initial infection, known as Stage I, occurs in the blood and lymph and may last for two or more years. Symptoms are non-specific and include intermittent chronic fever, headache, lethargy, fatigue, anemia, skin rashes, general pruritus and characteristic posterior cervical lymphadenopathy.

Stage II

Stage II occurs when the parasite crosses the blood brain barrier and invades the central nervous system (CNS), causing symptoms akin to an organic dementia. The infected individual suffers from an altered mental state, which results in erratic and socially unacceptable behavior. There is gradual loss of speech, and progressive sensory and tone disorders with loss of coordination and mobility. The circadian sleep/wake pattern is disrupted; the individual will fall asleep during the day and be awake at night. Somnolence progresses until the person is sleeping for most of the time. As sleeping sickness increasingly disables the patient, they become totally reliant on the family for all care. If the disease continues without treatment, the victim will lapse into a coma and die. Once CNS involvement occurs sleeping sickness is usually fatal within twelve months.

Diagnosis

Laboratory diagnosis of sleeping sickness is time consuming and difficult. Confirmation rates depend on the laboratory personnel skill and the parasite detection technique used. Trypanosomes can be difficult to find in the blood, especially in late presentations (Bell 1995). All sleeping sickness patients must undergo a lumbar puncture to obtain cerebrospinal fluid (CSF) for microscopic examination to determine what disease stage they have. Effective treatment of sleeping sickness requires accurate diagnosis and 'staging' of patients. This process is standardized by using the World Health Organization case definitions for trypanosomiasis. (Deresinki 2001)

- Confirmed: Trypanosomes observed in blood, lymph gland fluid, or cerebrospinal fluid (CSF).
- Stage I: Trypanosomes in blood or lymph gland fluid, but not CSF and with less than or equal to 5 white blood cells (WBC).
- Stage II: One or more of the following: Trypanosomes in CSF and/or CSF WBC greater than 5.
- Suspected relapse: after appropriate treatment of confirmed disease, develops either/or an increase in CSF WBC of greater than or equal to 2-fold with a total CSF WBC greater than 5.
- Confirmed relapse: After appropriate treatment of confirmed infection has trypanosomes observed in CSF, blood or lymph gland fluid within a 2-year post-treatment follow-up.

Treatment

Trypanosomes are able to evade the immune system of the host because of their enormous potential for antigenic variation. Over 1000 variants have been identified (WHO 2000). Sleeping sickness is very difficult to treat, particularly after it has crossed the blood-brain barrier. The medicines themselves are often in short supply, difficult to administer, and can be fatal. Once treated, sleeping sickness patients require a two-year follow-up period before they can be considered cured of the disease.

Stage I treatment of Gambiense sleeping sickness consists of a consecutive 10-day course of pentamidine via intramuscular injection at an average cost of US\$20 per patient. (IMC data). This is normally given on an outpatient basis. Pentamidine does not cross the blood brain barrier and therefore is ineffective against Stage II disease. Treatment of Stage II disease requires hospitalization of the patient. Melarsoprol, an arsenical, is administered intravenously over a period of 22 days at a cost of US\$100 per patient. Melarsoprol is extremely toxic and is often accompanied by severe side effects including reactive encephalopathy, which is fatal in 3-10% of cases. (Barrett 1999; Bell 1995). Even after successful treatment, the neurological damage is often irreversible.

Treatment of Stage II disease has significant cost implications for a resource poor health system and a fragile economy. Melarsoprol is expensive and its administration is labor and resource intensive, the patient must be cared for and provided with food, in the African environment a carer will remain with the patient throughout their hospitalization. This has ramifications for the household economy; a healthy member will be absent for up to a month unable to contribute. In a subsistence agricultural economy, the loss of what amounts to two laborers can be catastrophic for the family.

Summary

The re emergence of African trypanosomiasis is a major public health threat. The epidemic situation in Tambura County in 1997 can be explained by the absence of disease control activities over the preceding nine years. Without intervention, 12,000 people were considered at risk of dying within the following two years. The premature loss of life mainly affects adults aged 15 to 45 years who are the

major income earners and care givers within the family. The impact of uncontrolled sleeping sickness can be expected to seriously hamper economic recovery in a region whose stability remains fragile.

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