Human African trypanosomiasis

A neglected disease

Benjamin Jelle Visser

This *Global Medicine's* Neglected Disease is human African trypanosomiasis (HAT), also known as sleeping sickness. HAT is a vector-borne parasitic disease that exists exclusively in Africa.

Typology

There are two forms of HAT, one of which is endemic mainly in East Africa and is caused by *Trypanosoma brucei rhodesiense*. This form represents less than 10% of the reported cases of sleeping sickness. The other form is endemic mainly in West and Central Africa and is caused by *Trypanosoma brucei gambiense*. This form represents more than 90% of the reported cases in Africa. These protozoan parasites are both transmitted by the tsetse fly (*Glossina* genus), which name refers to the sound it makes. The two trypanosome species have indistinguishable morphologic appearances. However, the infections differ in clinical presentation, prognosis and treatment.

Epidemiology

Sleeping sickness occurs in 36 sub-Saharan countries within the habitat of the tsetse fly. About 60 million people are at risk of acquiring the disease. Countries particularly affected include Sudan, the Democratic Republic of the Congo (ex-Zaire), Angola, Uganda and Tanzania (see figure on page 12). The resurgence of sleeping sickness in the past few years has been facilitated by civil war, emigration, economic crisis, reduced health financing and a lack of human resources in these areas.

According to WHO estimates, at least 300 000 to 500 000 people are presently infected and 100 000 deaths can be attributed to HAT each year. Sleeping sickness is also reported more frequently among tourists, especially among those traveling to wild park areas near Lake Victoria, to the Tarangire, Serengeti and Lake Manyara National Parks, all of which are located in East Africa.

Transmission

Transmission usually takes place through a bite of the tsetse fly. Tsetse flies are prevalent in warm, shaded places of vegetation along-

DRC
Democratic Republic of the Congo

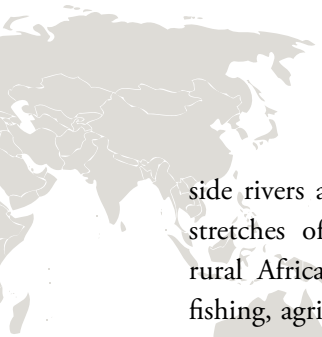
60 644 000
inhabitants

$ 270
income per year

♂ 46yrs ♀ 49yrs
life expectancy

4.3%
of GDP for health

1.0
doctors/10 000 people



side rivers and lakes, in forests and in vast stretches of wooded savannah. Therefore, rural African populations that depend on fishing, agriculture, cattle breeding or hunting and that live in regions where transmission occurs are at the highest risk of becoming infected. People are often bitten during activities such as bathing and washing.

In West African HAT humans are the main reservoir for *T.b. gambiense*, whereas in East African wild animals are the reservoir for *T.b. rhodesiense*. Hence, East African HAT is a zoonotic disease, a difference which has important consequences for strategies to control the disease.

Besides transmission via the bite of the tsetse fly, mother-to-child transmission can also occur. The parasite can cross the placenta and infect the fetus, leading to death or congenital deformities. Also, accidental infections have been reported due to accidents with contaminated needles.

Comparison of West African and East African trypanosomiasis

	West African HAT	East African HAT
Organism	*T.b. gambiense*	*T.b. rhodesiense*
Vectors	Tsetse flies	Tsetse flies
Primary reservoir	Humans	Antelope and cattle
Human illness	Chronic	Acute
Duration of illness	Months to years	<9 months
CNS involvement	Late CNS disease	Early CNS disease
Lymphadenopathy	Prominent	Minimal
Epidemiology	Rural populations	Workers in wild areas, rural populations, tourists in wild parks

Clinical features

Any bite from a tsetse fly, whether the fly is infected or not, produces a local reaction. Since the bite can be painful, patients may have noticed the exposure. When the bite is infected, a small local wound typically appears approximately after 5-15 days. A well-circumscribed, rubbery, painful papule, with a central blister or ulcer develops, surrounded by red infiltrated skin. This typical skin lesion is called a *trypanosomal chancre*. The diameter can range from 2-5 centimetres and is described at a frequency of 40-50% of the patients. After healing, which usually takes about a month, a depigmented scar can remain.

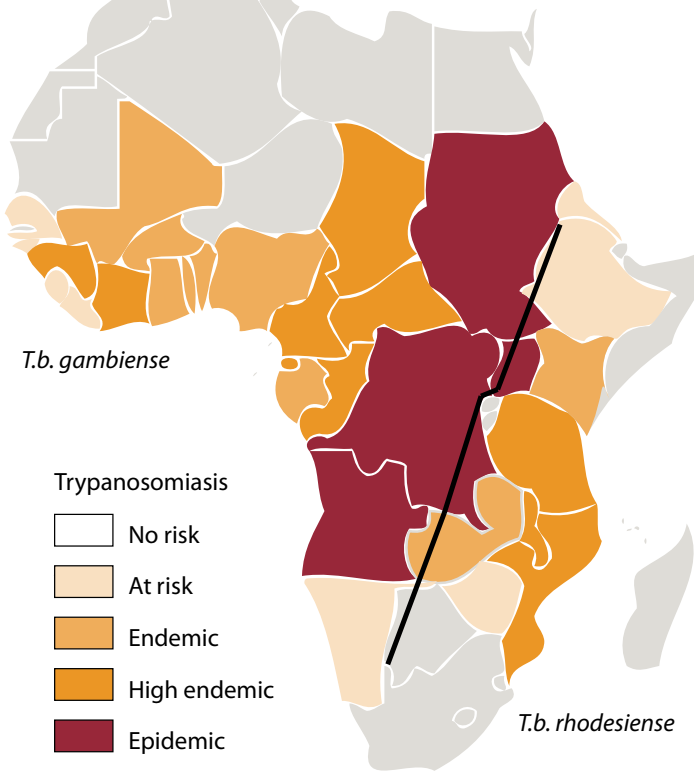
Both *T.b. gambiense* and *T.b. rhodesiense* infections are characterized by an early stage, the preliminary haematolymphatic stage, during which trypanosomes are found circulating in the blood and in lymph nodes, and a second (late) stage, with symptoms of meningoencephalitis. The differentiation between these stages is made by finding the parasite in the cerebrospinal fluid. This distinction is important because of its consequences for treatment.

The first stage, the haematolymphatic stage, lasts 6-12 months or longer. It is characterized by irregular headaches, arthralgias, malaise and intermittent peaks of pyrexia (fever), corresponding with successive waves of parasitaemia and antibody production. Trypanosomes travel from the skin to the regional lymphatics, where they cause lymph

***Global Medicine* presents**
Neglected Diseases

About one billion people in the world are affected by one or more neglected tropical diseases (NTDs). Neglected, because these diseases persist exclusively in the poorest and the most marginalized communities, and have been largely eliminated and thus forgotten in wealthier places.
www.who.int/neglected_diseases

This is the third article in a series on neglected diseases. Read the previous articles on www.globalmedicine.nl.



Distribution of trypanosomiasis in Africa

T.b. gambiense is endemic mainly in West and Central Africa, *T.b. rhodiense* mainly in East Africa. The black line represents the division between both.

node swelling (lymphadenopathy).

In *T.b. gambiense*, lymphadenopathy is typically seen in the posterior cervical nodes. The nodes are soft, mobile and not painful, and are classically referred to as *Winterbottom's sign*. The British doctor Thomas Masterman Winterbottom, who was working in Sierra Leone, first described the disease in 1803. He was struck by the abundant occurrence of swollen cervical lymph nodes in sick persons. Slave-traders at the time also knew about this sign and avoided buying people with cervical lymphadenopathy.

Besides lymphadenopathy there is organomegaly, in particular enlargement of the spleen. Other non-specific symptoms may be present, including pruritus, anaemia, leukocytosis, weight loss, facial swelling and thrombocytopenia. Occasionally pancarditis develops, leading to arrhythmias and cardiac failure. There can also be endocrine involvement, leading to impotence in men and amenorrhea in women.

In the late stage of *T.b. gambiense* infection, which lasts three to six months, progressive diffuse meningoencephalitis and parenchymal edema of the brain develop, ultimately resulting in coma and death. Symptoms include headache, difficulty concentrating, personality changes, psychosis and sensory disorders. Basal ganglia involvement in the brain results in ataxia and tremors, which are similar to those seen in Parkinson's disease. Damage to the hypothalamus leads to alteration of the circadian sleep-wake cycle. Consequently, patients develop daytime somnolence and nighttime insomnia. Hence the name *sleeping sickness*. The patient can still be woken up, but will quickly fall asleep again. Ultimately, the patient's deterioration progresses to a stuporous state (coma).

In the *T.b. rhodesiense* infection, the same sequence of events is seen as in *T.b. gambiense* infection, but the presentation and progression are very fast, developing CNS signs within weeks.

Both infections are fatal if untreated or if the trypanosomes are resistant to therapy.

Diagnosis

The diagnosis HAT is made based on symptoms and laboratory test findings. A definite diagnosis is made by detection of the parasite. The parasite can be found in fluid from the inoculation chancre, blood (thin & thick smear), lymph node fluid (needle aspiration) or cerebrospinal fluid (lumbar puncture). Examination of the cerebrospinal fluid (CSF) is mandatory whenever the diagnosis of HAT is suspected, both to help to confirm the diagnosis and to stage the infection. Late stage HAT usually presents as CSF pleocytosis. A white blood cell count of ≥5 per mm or an abnormal protein concentration is considered evidence of central nervous system (CNS) involvement. An uncommon but for HAT characteristic finding in the CSF are Mott cells. These are thought to be large eosinophilic plasma cells containing IgM that have failed to secrete their antibodies. There are also diagnostic methods available for low-resource regions. A cheap and practical method is a direct agglutination reaction of trypanosomes on a plastic card, with macroscopic read-off (CATT = Card Agglutination Test for Trypanosomiasis), which is based

upon agglutination of freeze-dried trypanosomes in the presence of a variant-specific antibody. This is also a good screening method in population studies and an easy tool in control and prevention programmes of the disease.

Treatment

Treatment differs for *T.b. gambiense* and *T.b. rhodesiense* infection, although there is some overlap. Treatment recommendations also vary according to the stage of the disease. During the first stage, treatment with suramin sodium or pentamidine is usually successful. In the second stage these drugs are considered ineffective, presumably because the blood-brain barrier prevents the drugs from reaching trypanocidal levels in the CSF. Melarsoprol is commonly used for treatment during this stage, but has severe side effects. It causes vomiting, abdominal pain, hepatotoxicity, peripheral neuropathy, paraplegia, cardiac arrhythmias and albuminuria. It is estimated that between 3-5% of those treated in the late stage of HAT die from side effects of the treatment itself. Eflornithine has been successfully used to treat patients in the second stage of *T.b. gambiense* disease, but does not seem to be effective against *T.b. rhodesiense*.

All drugs mentioned here are expensive. Therefore, many poor people are denied necessary treatment and die as a consequence.

Prevention

Chemoprophylaxis is not recommended, and no vaccine is available for HAT. Due to the recent resurgence of sleeping sickness, an effective control and surveillance programme is a necessity. The two main tools available to prevent transmission are vector control and early case finding. Vector control makes use of impregnated traps and screens. Also, the release of sterile tsetse males has been attempted and has proven quite successful in several areas. Case detection and early treatment aim to reduce the human reservoir. Both measurements are incorporated in the WHO Control and Surveillance Programme, which ultimately aims to eliminate sleeping sickness in Africa.

Through these control and surveillance programmes, considerable progress has been made in some regions. Major epidemics however continue to occur. At present time, HAT is nowhere near elimination, let alone eradication, despite a number of WHO programmes. Human African trypanosomiasis remains a significant cause of burden of disease on the African continent.

American trypanosomiasis

Chagas disease, or American trypanosomiasis, is a potentially lethal parasitic zoonosis which is prevalent in Latin America. It is caused by the flagellate protozoan parasite *Trypanosoma cruzi*. *T. cruzi* is transmitted among its mammalian hosts by hematophagous triatomine insects, often called reduviid bugs. Chagas disease has three different stages: an acute, an indeterminate and a chronic phase. Acute Chagas disease is usually a mild febrile illness, accompanied by local lymphadenopathy. After the acute infection, most infected people remain for life in the indeterminate phase of chronic Chagas disease, which is characterized by phases of parasitaemia and absence of symptoms. A minority of chronically infected persons will develop cardiac, nervous system or gastro-intestinal lesions, which can result in serious morbidity and death.

About the author

Benjamin Jelle Visser is a fourth year medical student from the University of Amsterdam.

Further reading

Kennedy PG. The continuing problem of human African trypanosomiasis (sleeping sickness). Annual Neurology 2008 Aug; 64(2): 116-26