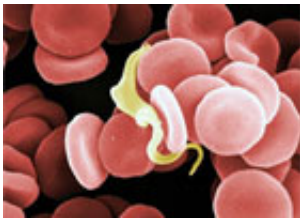


African sleeping sickness: a tale of two parasites

December 8 2011



A scanning electron micrograph showing a bloodstream form of a trypanosome (yellow) among host red blood cells. Credit: Gull Lab, Sir William Dunn School of Pathology/Wellcome Images.

(Medical Xpress) -- The savannahs and rainforests of Africa bring to mind romantic notions of wildlife, adventure and exploration. But beneath this natural beauty lies a deadly, long-neglected disease: trypanosomiasis, otherwise known as African sleeping sickness.

Trypanosomiasis is caused by the parasite *Trypanosoma brucei*. Transmitted by the tsetse fly, one bite is enough to let it loose in the bloodstream. Although trypanosomiasis is present in many parts of sub-Saharan Africa, two forms of the disease have largely remained isolated on either side of the [Great Rift Valley](#). Somewhere, however, these two forms must meet, putting more of the local population at risk. That place is Uganda.

The form that the disease takes - acute or chronic - depends on the

subspecies of parasite present inside the fly. Ninety per cent of trypanosomiasis cases are chronic, suffering the disease for many years before eventual death. Chronic infection is caused by *Trypanosoma brucei gambiense* (T.b. gambiense), which is found only in humans.

Acute infection, by contrast, can cause death within weeks, and the causative parasite, *Trypanosoma brucei rhodesiense* (T.b. rhodesiense), can be found in domesticated animals as well as humans, increasing the spread of disease throughout the country.

Over the past five years, the number of trypanosomiasis cases has actually fallen - from 500-600 in 2005 to 300 in 2010. But the disease is spreading to entirely new districts, with occurrences in 38 out of the 112 districts in Uganda. And according to Vincent Alibu, a veterinary parasitologist at Makerere University, the disease's spread into new districts is largely down to the increased movement of cattle harbouring T.b. rhodesiense.

"Cattle rustling in the mid '80s and early '90s saw cattle being taken from northern Uganda. The government developed a programme to restock these cattle, and most of these livestock came from the Busoga region in south-eastern Uganda, which was endemic for T.b. rhodesiense," says Alibu. "As people traded and bought cattle, all that cattle went back up to the north with a good number of them infected. There is still trade now, which is why rhodesiense is moving a lot faster than gambiense."

Resistance

The forests of the west of the Rift Valley house T.b. gambiense and the savannahs of the east yield T.b. rhodesiense, but the effects of these two subspecies meeting in one region are largely unknown. This is something Wellcome Trust-funded researchers at the University of Glasgow in the UK and Makerere University, Uganda, are investigating. They have

identified a variety of consequences: drug resistance is the first.



Card agglutination test for rapid diagnosis of infection with *T.b. gambiense*.
Credit: Meera Senthilingam.

Trypanosomiasis infects in two stages. In the first, the patient presents flu-like symptoms as the parasite flourishes in the [bloodstream](#). This leads to neurological disturbance as the parasite penetrates the blood-brain barrier.

Because the first stages resemble malaria, many patients receive the wrong treatment, meaning infection often reaches the neurological stage. Sadly, there are only two effective drugs to combat the second stage: melarsoprol and DFMO (α -difluoromethylornithine).

Uganda's Ministry of Health currently has enough melarsoprol in stock to last until the end of 2012. The problem is the development of resistance.

"Outbreaks of *T.b. gambiense* in northern Uganda have shown the parasite to be quite resistant to melarsoprol, with up to 30 per cent treatment failures," says Annette Macleod, a Wellcome Trust Senior

Research Fellow at the University of Glasgow. "DFMO is used instead, but this is not effective against T.b. rhodesiense."

Macleod's worry is that if the two subspecies find themselves inside the same tsetse fly and mate, they could create a doubly resistant subspecies with no drugs available to fight it: a death sentence for anyone infected. Thankfully, there is some - small - distance between them, for now. In regions where trypanosomiasis is endemic, the two [subspecies](#) have been found within 50 km of each other, with incidence of actual disease recorded 100 km apart.

Diagnosis

The more immediate concern for healthcare workers is diagnosis and the logistics of screening for two forms of a disease requiring different tests. Rapid diagnostic cards allow health workers to diagnose T.b. gambiense onsite, simultaneously screening numerous blood samples for the presence of antibodies against the parasite, which are clearly visible under a microscope. T.b. rhodesiense, however, requires more complex testing done in the lab.

In the past, specific tests could be allocated to each district based on the types of cases occurring there. But the merging of endemic regions means resources will be needed for both types of disease across all areas. In a resource-poor setting, such availability on the ground and on a country-wide scale just isn't possible. A further worry is that this, combined with patients self-diagnosing themselves with malaria, could lead to misdiagnosis becoming commonplace and the wrong treatment leading to fatal results.

Dr Charles Wamboga, Programme Manager for Sleeping Sickness at the Ugandan Ministry of Health, says the solution requires a multidisciplinary approach. It needs scientists and the Ministry of

Agriculture and Fisheries, as well as the Ministry of Health, to target and treat the human population, tsetse flies and cattle all at once.

This has included the training of village health teams, based within communities, to increase early diagnosis on the ground. "We are engaging village health teams to identify people who live in their communities, have had malaria-like symptoms for three weeks or more and who, despite taking antimalarials, have not improved," says Wamboga.

Throughout endemic regions, cattle are now sprayed with insecticides at regular intervals, reducing the numbers of tsetse flies feeding on them and lowering their chances of becoming a reservoir for disease. The spraying of cattle traded at markets is also compulsory.

In addition, humans are protected from tsetse flies by the use of large nets hanging by roadsides and riverbanks. Bright blue colours are used to attract the flies, which are killed with chemicals once they are trapped inside.

The idea behind these interventions is to introduce a barrier between the two diseases, stopping the tsetse fly in its tracks and preventing the two [parasites](#) from mingling. This is further aided by accurate and up-to-date mapping of disease outbreaks to monitor and treat disease.

Wamboga says concurrent deployment of flytraps, spraying of animals with insecticides and screening of the human population has given encouraging results. The interventions have seen the number of fatal [trypanosomiasis](#) cases going down, but he emphasises the need to keep up the pressure: the attack must be consistent and the barrier strong. If the two forms of parasite do meet one day, the consequences don't bear thinking about.

Provided by Wellcome Trust

Citation: African sleeping sickness: a tale of two parasites (2011, December 8) retrieved 9 May 2024 from <https://medicalxpress.com/news/2011-12-african-sickness-tale-parasites.html>

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