**African trypanosomiasis (sleeping sickness)**

**DEFINITION OF THE DISEASE**

Human African Trypanosomiasis, also known as sleeping sickness, is a vector-borne parasitic disease. The parasites concerned are protozoa belonging to the *Trypanosoma* Genus. They are transmitted to humans by tsetse fly (*Glossina* Genus) bites which have acquired their infection from human beings or from animals harbouring the human pathogenic parasites. Tsetse flies are found in Sub-Saharan Africa. Only certain species transmit the disease. Different species have different habitats. They are mainly found in vegetation by rivers and lakes, in gallery-forests and in vast stretches of wooded savannah.

- Sleeping sickness occurs only in sub-Saharan Africa in regions where there are tsetse flies that can transmit the disease. For reasons that are so far unexplained, there are many regions where tsetse flies are found, but sleeping sickness is not.
- The rural populations living in regions where transmission occurs and which depend on agriculture, fishing, animal husbandry or hunting are the most exposed to the bite of the tsetse fly and therefore to the disease.
- Sleeping sickness generally occurs in remote rural areas where health systems are weak or non-existent. The disease spreads in poor settings. Displacement of populations, war and poverty are important factors leading to increased transmission.
- The disease develops in areas whose size can range from a village to an entire region. Within a given area, the intensity of the disease can vary from one village to the next.

Human African Trypanosomiasis takes two forms, depending on the parasite involved:

- *Trypanosoma brucei gambiense* (*T.b.g.*) is found in west and central Africa. This form represents more than 90% of reported cases of sleeping sickness and causes a chronic infection. A person can be infected for months or even years without major signs or symptoms of the disease. When symptoms do emerge, the patient is often already in an advanced disease stage when the central nervous system is affected.
- *Trypanosoma brucei rhodesiense* (*T.b.r.*) is found in eastern and southern Africa. This form represents less than 10% of reported cases and causes an acute infection. First signs and symptoms are observed after a few months or weeks. The disease develops rapidly and invades the central nervous system.

Another form of trypanosomiasis occurs in 15 Central and South American countries. It is known as American Trypanosomiasis or Chagas disease. The causal organism is a different species from those causing the African form of the disease.

**ANIMAL TRYPANOSOMIASIS**

Other parasite species and sub-species of the *Trypanosoma* Genus are pathogenic to animals and cause animal Trypanosomiasis in many wild and domestic animal species (in cattle the disease is called *Nagana*, a Zulu word meaning “to be depressed”). Animals can host the human pathogen parasites, especially *T.b. rhodesiense*; thus domestic and wild animals are an important parasite reservoir. Animals can also be infected with *T.b. gambiense*, however the precise epidemiological role of this reservoir is not yet well known. This disease kills animals. The disease in domestic animals and particularly cattle is a major obstacle to the economic development of the rural areas affected.

**MAJOR HUMAN EPIDEMICS**

There have been several epidemics in Africa over the last century: one between 1896 and 1906, mostly in Uganda and the Congo Basin, one in 1920 in a number of African countries and the most recent one beginning in 1970. The 1920 epidemic was controlled thanks to mobile teams who organized the screening of millions of people at risk. By the mid 1960s, the disease had almost
disappeared. After that success, surveillance was relaxed, and the disease reappeared in several areas over the last thirty years. Recent WHO efforts and those of national control programmes and nongovernmental organizations (NGOs) have stopped and begun to reverse the upward trend of new cases.

**GEOGRAPHICAL DISTRIBUTION OF THE DISEASE**

Sleeping sickness threatens millions of people in 36 countries of sub-Saharan Africa. However, only a small fraction of them are under surveillance with regular examination, have access to a health centre that can provide diagnostic facilities, or are protected by vector control interventions.

- In 1986, a panel of experts convened by WHO estimated that some 70 million people lived in areas where disease transmission could take place.
- In 1998, almost 40 000 cases were reported, but this number did not reflect the true situation. It was estimated that between 300 000 and 500 000 more cases remained undiagnosed and therefore untreated.
- During recent epidemic periods, in several villages in the Democratic Republic of Congo, Angola and Southern Sudan, prevalence has reached 50%. Sleeping sickness was considered the first or second greatest cause of mortality, even ahead of HIV/AIDS, in those communities.
- By 2005, surveillance had been reinforced and the number of new cases reported throughout the continent had substantially reduced; between 1998 and 2004 the figures for both forms of the disease together fell from 37 991 to 17 616. The estimated number of cases is currently between 50 000 and 70 000

**Progress in disease control**

- In 2000, WHO established a public-private partnership with Aventis Pharma (now sanofi-aventis) which has enabled the creation of a WHO surveillance team, providing support to endemic countries in their control activities and the supply of drugs free of charge for the treatment of patients.
- In 2006, success in curbing the number of sleeping sickness cases has encouraged a number of private partners to sustain the WHO’s initial effort towards the elimination of the disease as a public health problem.

**CURRENT SITUATION IN ENDEMIC COUNTRIES**

The prevalence of the disease differs from one country to another as well as in different parts of a single country. In 2005, major outbreaks have been observed in Angola, the Democratic Republic of Congo and Sudan. In Central African Republic, Chad, Congo, Côte d’Ivoire, Guinea, Malawi, Uganda and United Republic of Tanzania sleeping sickness remains an important public health problem. Countries such as Burkina Faso, Cameroon, Equatorial Guinea, Gabon, Kenya, Mozambique, Nigeria, Rwanda, Zambia and Zimbabwe are reporting fewer than 50 new cases per year. In countries such as Benin, Botswana, Burundi, Ethiopia, Gambia, Ghana, Guinea Bissau, Liberia, Mali, Namibia, Niger, Senegal, Sierra Leone Swaziland and Togo transmission seems to have stopped and no new cases have been reported for several decades. Nonetheless, it is difficult to assess the current situation in a number of endemic countries because of a lack of surveillance and diagnostic expertise.

**INFECTION AND SYMPTOMS**

The disease is transmitted through the bite of an infected tsetse fly. At first the trypanosomes multiply in subcutaneous tissues, blood and lymph. In time, the parasites cross the blood-brain barrier to infect the central nervous system. The process can take years with *T.b. gambiense*.

- Mother-to-child infection: the trypanosome can cross the placenta and infect the fetus.
- Mechanical transmission is possible. However, it is difficult to assess the epidemiological impact of transmission through other blood-sucking insects.
Accidental infections have occurred in laboratories due to pricks from contaminated needles.

The first stage of the disease, known as a haemolymphatic phase, entails bouts of fever, headaches, joint pains and itching. The second stage, known as the neurological phase, begins when the parasite crosses the blood-brain barrier and invades the central nervous system. In general this is when the signs and symptoms of the disease appear: confusion, sensory disturbances and poor coordination. Disturbance of the sleep cycle, which gives the disease its name, is an important feature of the second stage of the disease. Without treatment, sleeping sickness is fatal.

**DISEASE MANAGEMENT**

Disease management is performed in three steps:

- Screening for potential infection. This involves the use of serological tests and/or checking for clinical signs - generally swollen cervical glands.
- Diagnosis shows whether the parasite is present.
- Staging to determine the state of progression of the disease entails examination of cerebrospinal fluid obtained by lumbar puncture and is used to determine the course of treatment.

Diagnosis must be made as early as possible and before the neurological stage in order to avoid complicated, difficult and risky treatment procedures. The long, asymptomatic first stage of *T.b. gambiense* sleeping sickness is one of the factors that requires the use of exhaustive active screening of the population at risk in order to identify patients at an early stage and reduce transmission. Exhaustive screening of exposed populations requires a major investment in human and material resources. In Africa such resources are often scarce, particularly in remote areas where the disease is mostly found. As a result, many infected individuals may die before they can ever be diagnosed and treated.

**TREATMENT**

The type of treatment depends on the stage of the disease. The drugs used in the first stage of the disease are less toxic, easier to administer and more effective. The earlier the identification of the disease, the better the prospect of a cure. Treatment success in the second stage depends on a drug that can cross the blood-brain barrier to reach the parasite. Such drugs are quite toxic and complicated to administer. Four drugs are registered for the treatment of sleeping sickness and provided free of charge to endemic countries through a WHO private partnership with sanofi-aventis (pentamidine, melarsoprol and eflornithine) and Bayer AG (suramin).

First stage treatments

- **Pentamidine**: discovered in 1941, used for the treatment of the first stage of *T.b. gambiense* sleeping sickness. Despite a few undesirable effects, it is well tolerated by patients.
- **Suramin**: discovered in 1921, used for the treatment of the first stage of *T.b. rhodesiense*. It provokes certain undesirable effects, in the urinary tract and allergic reactions.

Second stage treatments

- **Melarsoprol**: discovered in 1949, it is used in both forms of infection. It derives from arsenic and has many undesired side effects. The most dramatic being a reactive encephalopathy (encephalopathic syndrome) which can be fatal (3% to 10%). An increase of resistance to the drug has been observed in several foci particularly in central Africa.
- **Eflornithine**: this molecule, less toxic than melarsoprol, was registered in 1990. It is only effective against *T.b. gambiense*. It is an alternative to melarsoprol treatment. The regimen is strict and difficult to apply.

**THE ROLE OF THE WORLD HEALTH ORGANIZATION**
The resurgence of sleeping sickness since the 1970s led WHO to reinforce its Human African Trypanosomiasis programme. The objective is to coordinate activities in endemic countries and mobilize a wide range of partners.

The WHO Programme provides support and technical assistance to national control programmes. A network has been established including donor countries, private foundations, NGOs, regional institutions, research centres and universities to participate in surveillance and control, and to undertake research projects for the development of new drugs and diagnostic tools.

The objectives of the WHO Programme are to:

- Strengthen and coordinate control measures and ensure field activities are sustained;
- Strengthen existing surveillance systems;
- Support monitoring of treatment and drug resistance through the network;
- Develop information database and implement training activities.
- Promote inter-agency collaboration with the Food and Agriculture Organisation (FAO) and the International Atomic Energy Agency (IAEA). This agency is dealing with vector control through flies males made sterile by radiation. In addition there is a joint Programme Against African Trypanosomiasis (PAAT) including WHO (human health), FAO (animal health) and IAEA (vector control).