Human African Trypanosomiasis (HAT)

WHAT IS HUMAN AFRICAN TRYPANOSOMIASIS?
Human African trypanosomiasis (HAT or sleeping sickness) is a parasitic, neglected tropical disease transmitted to humans by the tsetse fly. Approximately 60 million people in 36 countries in sub-Saharan Africa are at risk. The seven most affected countries represent 97% of all reported cases, and the Democratic Republic of Congo alone accounts for 2/3 of reported cases. HAT occurs in the poorest rural areas of Africa, where difficulty of diagnosis, political instability, and lack of health surveillance make surveillance and care difficult. HAT was a historical scourge in Africa, but major efforts last century meant that by the 1960s it was thought to be a plague of the past. However, from the 1970s onwards there have been several serious epidemics. Major efforts have been made to actively detect and treat HAT within specific control programs during the last decade, resulting in decreasing numbers of reported cases over the last years. However, given the ‘hot spots’ that occur mainly in areas of conflict or instability, HAT still poses a major risk for outbreaks causing a serious public health threat.

TRANSMISSION AND DIAGNOSIS
HAT comes in two forms: Trypanosoma brucei (T. b.) gambiense (West African) and T. b. rhodesiense (East African). The most widespread form is the T. b. gambiense, which has a long period before becoming symptomatic. The sickness occurs in two stages. Symptoms begin with fever, headaches, and joint pains. Stage 2, the neurologic phase, occurs when the parasite crosses the blood-brain barrier and infects the central nervous system. The patient can suffer from confusion and reduced coordination; then the sleep cycle is disturbed, which leads to bouts of fatigue punctuated with manic periods. The sickness progresses to daytime slumber, night-time insomnia, and mental deterioration, and finally leads to coma. Without treatment, the disease is 100% fatal. Even if treated, the damage caused in the neurological phase can be irreversible.

Currently the diagnosis and staging of the disease requires a complicated series of painful tests (e.g. lumbar puncture) and the treatment is long, toxic or difficult. Both necessitate trained medical supervision and are furthermore difficult to administer in remote areas where the disease occurs. There is an immediate need to improve current diagnostic and treatment options, particularly for patients in the advanced stages of this disease.

TREATMENT
Current diagnostics are difficult and require a lumbar puncture to confirm the stage of the disease. Available treatments are few, dated and stage-specific. Stage 1 treatments, pentamadine (dating from 1941) and suramin (dating from 1921), are fairly well-tolerated but require injections. They do not, however, pass the blood brain barrier and are thus ineffective for the treatment of advanced (stage 2) HAT. The most commonly used treatments for stage 2 include:

- **Eflornithine** (dating from 1990): Relatively well tolerated, efficacious, but resource-intensive and difficult to administer. It requires trained health staff and constant hospitalisation and care with 56 intravenous (IV) infusions over a period of 14 days. The potential for resistance, when used in monotherapy, is an increasing concern.
- **Melarsoprol** (dating from 1949): An arsenic derivative, highly toxic, rising rates of treatment failure, but in 2008 still half of stage 2 HAT patients received it. The treatment is painful, long with 10 days of intravenous injections. It is increasingly ineffective with up to 50% treatment failure in some areas, and kills 5% of those who receive it.
- **NECT** (nifurtimox-eflornithine combination therapy): In May 2009, WHO added NECT to the Essential Medicines List (EML) for the treatment of stage 2 HAT. NECT was developed by Médecins Sans Frontières (MSF), Epicentre, DNDi and its partners like the Swiss Tropical Institute (STI), with the support of the HAT Platform (platform of partners who develop research capacity in countries where HAT is endemic) including national HAT control programs of most affected countries. NECT is a simplified combination treatment of IV eflornithine with oral nifurtimox. This improved treatment is a step in the right direction, reducing current eflornithine treatment from 56 infusions over 2 weeks, to 14 infusions over 7 days, with oral tablets 3 times a day for 10 days.
MSF AND SLEEPING SICKNESS

MSF provides medical and humanitarian assistance in 60 countries to people whose survival is threatened due to armed conflict, epidemics, malnutrition, exclusion from health care or natural disasters. For over two decades, since 1986, MSF has been a leading organization working in the diagnosis and treatment of HAT, particularly in war-torn areas, screening more than 2.6 million people and treating more than 48,000 cases of HAT in 6 countries (Uganda, Southern Sudan, Central African Republic, Republic of Congo, Democratic Republic of Congo and Angola). Current projects include Central African Republic, Democratic Republic of Congo, Uganda, and Chad, and an assessment is underway in South Sudan.

CHALLENGES

MSF is concerned by the current discourse that elimination of HAT is feasible; given the current constraints with difficult diagnostics, treatment and the remote and often insecure contexts where HAT has high prevalence. In these contexts elimination is not possible without new tools. Moreover, the current donor policy drive for project integration into existing health structures poses a serious risk to contain HAT in certain contexts. These policies could potentially give rise to a neglect of the most at-risk areas and be counterproductive.

MSF IS CALLING FOR:

- **New and simplified diagnostic tools**: The first step towards a patient being treated is the diagnosis. Current diagnostic algorithms need to be simplified.

- **Targeted research on final staging**: Most of the current research about diagnostic tools focuses on improving existing tools for the detection of the parasite in blood, but lumbar puncture is still needed for final staging of the disease. A new biomarker that allows diagnosis and staging of HAT in patients using whole blood or serum, removing the need for a lumbar puncture, is urgently needed.

- **Improved, practical treatments**: While the development of NECT is a huge advancement, it is still far from an ideal treatment. More research and investment are urgently needed to improve treatment (without injections) to ensure they are affordable, effective in both stages of the disease, and easy to use in remote, primary health posts close to the patients.

- **Robust surveillance and response mechanisms**: Ongoing efforts are needed for robust surveillance and response mechanisms necessary to diagnose and treat HAT in areas where it poses a serious public health threat. This can be achieved by increasing financial support to national control programs, creating systems that are more reactive and use active screening and notification systems.

- **Investment in R&D**: As with all neglected diseases, investment in R&D for better diagnostics and treatments is insufficient; this needs to change in order to respond properly to HAT.