Human African trypanosomiasis (HAT), or sleeping sickness, is a parasitic disease transmitted by the bite of an infected tsetse fly. The form of disease caused by *Trypanosoma brucei gambiense*, which accounts for more than 95% of all HAT cases, can be fatal if left untreated. However, diagnosis is a challenge, particularly because in the early stages symptoms are not specific to the disease.

In 2012 the London Declaration endorsed the roadmap for HAT elimination by 2020, as defined by the World Health Organization (WHO). The government of Uganda has responded by working with partners to implement a national initiative to accelerate elimination of the disease.

Uganda has made major advances in reducing the prevalence of *T.b. gambiense* HAT, from a peak in the early 1990s to only 20 cases by 2012. This decline made eliminating the disease a distinct possibility. Yet, as cases become fewer, there are enormous increases in the costs and the effort required to identify those remaining.

**ISSEP: Intensified Sleeping Sickness Elimination Programme**

ISSEP is an initiative of the Government of Uganda, FIND and WHO to accelerate HAT elimination through better access to diagnosis. It began in 2013 in the seven north-western districts where *T.b. gambiense* HAT is found (16,460 km², 2.22 million people). The programme is based on:

**Innovation** - Three diagnostic tests for HAT are implemented at different levels of the health system:
- A rapid diagnostic test (RDT) used in primary health facilities to enable initial screening close to home.
- Two follow-up tests: one to increase the index of suspicion (LAMP test) and one to confirm HAT (LED fluorescence microscopy) performed in health centres at the district level.

**Adaptability** - The programme is responsive to the changing epidemiology and diagnostic needs:
- In 2013, RDTs were introduced in 212 health facilities. By the end of 2014 participating facilities were reduced to 125, based on the changing distribution of identified cases. However, surveillance capacity was maintained in all endemic districts.
- In 2015, the number of facilities using RDTs was increased to 149 to include private clinics and health facilities serving refugee camps near the border with South Sudan.
Despite the presence of health-care facilities in most villages, only four facilities (marked on the map below) had the capacity to diagnose *T.b. gambiense* HAT prior to ISSEP’s launch in 2013. The distance between these facilities and the homes of people affected by the disease was an average of 25.1 km. As cases of sleeping sickness declined, knowledge of the disease and willingness to travel for diagnosis also declined. In order to intensify surveillance and identify the few remaining cases, diagnostics had to be made more accessible to potential cases. However, the screening test in routine use could only be deployed in a few health facilities because electricity was needed to perform the test and to refrigerate the reagents. New tests requiring only minimal equipment, expertise and electricity were needed for rural health facilities to provide the capacity for HAT diagnosis closer to where patients live.

Uganda is the only country where both forms of HAT (caused by *T.b. gambiense* and *T.b. rhodesiense*) are reported. This map of Uganda shows the seven districts with *T.b. gambiense* HAT and the four facilities that performed confirmatory diagnosis of HAT prior to 2013.

Three diagnostic tests for sleeping sickness have been developed in collaborations between FIND and academic, manufacturing and endemic country partners:

**SD BIOLINE HAT rapid diagnostic test (RDT)**
(By Alere/Standard Diagnostics)
- Simple to use and store (can be stored at 40°C for 2 years)
- Inexpensive (50 US cents)
- Very sensitive
- Imperfect specificity: some people not having HAT test positive, so they must be confirmed by other tests

The RDT can be performed by staff at the smallest health-care facilities as well as by mobile teams.

**Primo Star iLED fluorescence microscope (LED FM)**
(By Carl Zeiss MicroImaging)
- Low power requirements and long-lasting light sources
- Versatile — can also be used for malaria and TB
- Does not require a dark room
- Low sensitivity — LED FM misses many cases

With the option for bright field microscopy, the LED FM can be used to perform all parasitological confirmation tests for HAT. It can be powered from solar panels.

**Loop-mediated isothermal amplification (LAMP) of DNA**
(By Eiken Chemical Co.)
- Highly sensitive
- Identifies HAT suspects missed by microscopy
- Also works on blood samples dried on filter paper
- Requires reliable power and a reasonably well equipped lab

LAMP can be performed by technicians with no training in molecular biology and can be deployed at district- or microscopy-level laboratories.
THE STRATEGY

Since the Government of Uganda initiated ISSEP, the capacity for HAT screening was significantly expanded by:

- Introducing HAT RDTs in rural and urban health facilities in endemic districts, the majority of which are primary health centres.
- Upgrading 9 facilities to perform HAT RDTs and confirmation by microscopy, including LED FM.
- Upgrading 3 laboratories to perform RDTs, microscopy (including LED FM) and LAMP tests.

This network of centres has allowed the implementation of a tiered strategy for intensive surveillance to identify HAT cases:

1. Patients suspected of having HAT are screened in health facilities using HAT RDTs.
2. Patients found positive by RDT are referred to a microscopy (LED FM) centre for confirmation, which requires demonstration of parasites.
3. If a suspected case is found positive by microscopy, the patient is confirmed as a HAT case and referred for treatment. If found negative by microscopy, a blood sample is dried on filter paper and transported by programme motorcyclists for further analysis at a LAMP centre.
4. Patients found positive by LAMP are considered highly likely to have HAT and undergo further tests by microscopy for confirmation.

The strategy also includes re-training of technicians and health-care workers in all the facilities, an external quality assurance system in the various laboratories to ensure that diagnostic tests are performed correctly, and awareness-raising of health-care workers and communities.

Below: An illustration of the diagnostic pyramid for HAT being implemented in Uganda.

3 LAMP facilities

9 LED FM facilities

137 RDT facilities

CURRENT STATUS

As of December 2015, 15,677 patients had been tested for HAT using RDTs. Out of 412 who were positive with the RDT, 13 were confirmed as HAT cases. Only 4 of these cases were identified during 2015 from 5,514 patients screened and 141 RDT-positive suspects. The 9 other cases were found during 2014. As the endemic region continues to shrink, villages where cases come from are closely monitored. During 2015, the Government of Uganda carried out active screening with support from Liverpool School of Tropical Medicine (LSTM) to measure the impact of their tsetse control activities on HAT incidence. No HAT cases were confirmed among 100 suspects identified after screening 11,000 people. WHO also supports targeted active screening in villages where the most recent cases originated.

Social research is used to devise ways of successfully referring RDT positive patients to microscopy centres for confirmation. This is critical to ensuring programme success. Screening efforts are supplemented by control of tsetse fly vectors with the support of LSTM.

The ISSEP model is considered a success and is being replicated in other HAT endemic countries.
OVERCOMING EMERGING CHALLENGES

To eliminate *gambiense* HAT, all cases should be identified and treated as soon as possible. The challenges encountered are being addressed by:

- Monitoring the use of HAT tests and results remotely to ensure ISSEP can respond promptly to the needs of patients and health facilities. To enable this, a new system of data transfer using mobile phones will be put in place in 2016.
- Implementing strategies to ensure that RDT-positive HAT suspects are successfully referred for confirmation.
- Assuring the quality of the tests conducted through regular monitoring of activities.

FUNDING FOR *GAMBIENSE* HAT ELIMINATION IN UGANDA

ISSEP is supported by FIND with funding from the Bill & Melinda Gates Foundation (BMGF), the Republic and Canton of Geneva, the German Federal Ministry of Education and Research through KfW, the Swiss Development Cooperation and UK aid. WHO and Liverpool School of Tropical Medicine (LSTM) support targeted active screening in affected villages. These efforts are complemented by tsetse control activities conducted by district entomologists with funding from BMGF and technical support from LSTM. Social research is carried out in partnership with the London School of Hygiene and Tropical Medicine and Passion Africa Ltd.

FURTHER INFORMATION

Information regarding diagnosis of HAT is available at:

http://www.finddx.org/ntd/