Catalysing success through partnerships:

NEW DIAGNOSTIC SOLUTIONS
FOR HUMAN AFRICAN
TRYPANOSOMIASIS

HAT – commonly known as sleeping sickness – is transmitted by the bite of the tsetse fly. The disease presents in two distinct forms: a chronic West African (gambiense) form, which accounts for over 95% of all cases and generally lasts for months to several years without showing major signs or symptoms, and an acute eastern African (rhodesiense) form, that lasts from a few weeks to several months. Both can be fatal if left undiagnosed and untreated.

The challenge with sleeping sickness lies in its complexity: there are no clinical signs indicative of the disease, which makes it difficult to diagnose. Diagnosis and staging (a procedure to determine whether parasites have invaded the brain) guide the choice of treatment. The drug used for the first stage cannot be used for second stage disease. Conversely, the one used for the second stage is effective against both forms of the disease but is associated with adverse reactions and therefore is not recommended for treatment of first stage HAT.

About Human African Trypanosomiasis (HAT)
Currently, more than 70 million people live in geographic areas that present risk of exposure to HAT; almost two-thirds of them live in the Democratic Republic of the Congo, which accounted for 84.5% of total cases in 2014. Despite the fact that the World Health Organization’s (WHO) mapping of the disease’s trajectory shows a significant reduction in new cases over the past two decades (30,000 in 1995 versus fewer than 4,000 in 2014), determining the true burden of the disease is problematic.

The road to elimination

In January 2012, a consortium of partners from governments, humanitarian organizations, and pharmaceutical companies came together to sign the London Declaration on Neglected Tropical Diseases, which underlined the need for an integrated and comprehensive approach towards the control, elimination, or eradication of 10 neglected tropical diseases (NTDs), including sleeping sickness. Approximately two-thirds of all NTD-endemic countries have now developed national NTD plans to help guide their control and elimination efforts.

Diagnosis is central to any elimination strategy. Disease elimination and eradication require effective diagnostics to target interventions, identify outbreaks and monitor progress towards these goals. We believe that, through continued efforts with our partners, we shall make a significant contribution to the goal of WHO of eliminating sleeping sickness by 2020.

FIND and partners are developing and implementing tests for early and accurate diagnosis and staging of HAT patients in order to ensure safe treatment. Other tests for early detection of treatment failure will ensure proper re-treatment, reduced transmission and accelerated control of the disease, all important steps on the pathway to elimination.

Accelerating access to better diagnostics for HAT: Milestones

- **FIND and Alere/Standard Diagnostics (SD) have developed a rapid diagnostic test (RDT) to screen for gambiense HAT that is cheap and easy to use. Our priority was to develop a method for accurate screening of HAT among populations at risk. Working with many partners, among them the Institute of Tropical Medicine in Belgium and SD in the Republic of Korea, a prototype RDT was developed and evaluated on more than 14,000 participants in Angola, the Democratic Republic of the Congo and the Central African Republic. The test is inexpensive, accurate, easy to use and provides results in 15 minutes. It can be used in resource-poor health facilities, requires no electricity and only minimal training of health care workers. The test was launched in 2012, breaking new ground in the fight against HAT. Communities with limited access to health services can easily be screened for sleeping sickness at the village health centre – something that was unthinkable just a few years ago.**

- **Currently in development, a second generation RDT is expected to be available in 2016. Partnering with the University of Dundee and SD, FIND is working to drive down the price of testing: the second generation RDT uses recombinant antigens, which are cheaper to produce and easier to standardize than the native antigens used for the first generation test.**

- **Since all settings where HAT is found are also endemic for malaria, an RDT for combined testing of HAT and malaria is in development to ensure surveillance and detection of cases and prevent re-emergence. The test will also be important for surveillance to sustain elimination.**
• Working in collaboration with Carl Zeiss GmbH, FIND has introduced a dual-purpose LED-based fluorescence microscope. It provides improved accuracy and speed in microscopy. Whereas normal bright-field microscopes use bulbs with a short lifespan, the LED microscope light source can last for over 10,000 hours, uses very little power and can be run on a battery or solar energy.

• Originally developed for tuberculosis testing, loop-mediated isothermal amplification (LAMP) of DNA is a highly sensitive molecular tool for detecting HAT. FIND and Eiken Chemical Co. Ltd. have developed a LAMP kit for HAT that has been evaluated at multiple sites in the Democratic Republic of the Congo and Uganda, and is now included in a number of implementation projects in seven countries. This test is attractive because it can also be performed on blood samples dried on filter paper and takes just 40 minutes to give results.

• Determining if parasites have invaded the brain is the single most important piece of information needed by clinicians who treat HAT patients. Traditionally, a lumbar puncture – a technique that is invasive, painful, and requires skilled clinicians – is performed and the cerebrospinal fluid is examined for presence of the parasite and changes in the number of white cells. FIND has been working with partners to develop new tests for staging and confirmation of cure with improved accuracy to guide treatment, and for follow-up to assess treatment success. A number of biomarkers have been identified, including neopterin and CXCL13, that accurately detect patients who have reached the neurological phase of the disease and those who have failed treatment.

Priorities 2015-2020

During the period 2015 to 2020, FIND will continue to support WHO’s goal of eliminating sleeping sickness, with a focus on the implementation of new emerging tools. Together with safer, easier to administer drugs, this work will allow the move to new approaches that will accelerate and sustain elimination.

FIND’s strategy for HAT is focusing on two objectives:
1. Increasing detection of HAT through improved screening
2. Facilitating faster, less-burdensome confirmation of HAT through improved tools

Human African Trypanosomiasis
FIND 2015 – 2020 Priorities and Interventions

Development / Policy priorities for new tools:

1. A second generation rapid test
2. A combined rapid test with malaria
3. A low-cost tool for confirmation

Enabling interventions:

• Provide specimens for product development
• Conduct implementation research to support roll-out of new rapid tests and other diagnostics
• Support countries in designing implementation strategies to scale-up new / existing tools
• Demonstrate feasibility and impact of next-generation rapid tests in a “test and treat” approach, once suitable drugs are available
The way forward

Today, the novel tools that FIND and partners have developed are contributing to the diagnosis of sleeping sickness all across Africa – Guinea, Ghana, Togo, Benin, Côte d’Ivoire, Cameroon, the Democratic Republic of the Congo, Uganda, Chad, Nigeria, South Sudan, Congo and soon Angola. Many of these countries are using the HAT RDT, LED fluorescence microscopy and LAMP to screen for and confirm the presence of sleeping sickness.

The impact of FIND’s accomplishments to date, combined with on-going research and development, ensure that revolutionary approaches to diagnostics will lead the way in disease elimination. Linking with industry, academia, international health agencies, donors and governments, we are helping to forge a critical path towards the goal of eliminating sleeping sickness by 2020.

Fast Facts: Human African Trypanosomiasis (HAT)

- **70 million**
  Estimated number of people at risk of HAT infection

- **3,796**
  Reported cases in 2014

- **20,000**
  Current estimated cases

- **36**
  Number of endemic countries in sub-Saharan Africa

References and further reading:


Increased acute immune response during the meningo-encephalitic stage of *Trypanosoma brucei rhodesiense* sleeping sickness compared to *Trypanosoma brucei gambiense*. Tiberti N. et al. (2015). *Translational Proteomics* 6: 1–9


