PROJECT UPDATE: KONGO CENTRAL

Driving elimination of human African trypanosomiasis in a challenging transboundary region

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Human African trypanosomiasis (HAT), or sleeping sickness, is a parasitic disease transmitted by the bite of a tsetse fly. The disease has two forms: a chronic form caused by *Trypanosoma brucei gambiense* and an acute form caused by *Trypanosoma brucei rhodesiense*. Gambiense HAT accounts for more than 95% of all cases and can last for months to several years without symptoms, whereas symptoms of rhodesiense HAT emerge within weeks and the disease develops rapidly. Both forms can be fatal if left untreated.

Early diagnosis is a challenge because the chronic form of HAT often shows no signs or symptoms until it is more advanced. The World Health Organization (WHO) roadmap on 10 neglected tropical diseases, which was endorsed by the London Declaration of 2012, targets HAT for elimination by 2020.

The Democratic Republic of the Congo (DRC) records the highest number of HAT cases globally and accounted for 84.5% of cases reported in 2014 (n=3206). Among the provinces in DRC that are endemic for HAT, Kongo Central (formerly Bas Congo) is one of the smallest, and its HAT focus is isolated from the other foci in the country. Over the past 10 years, only a relatively small number of HAT cases have been reported annually, making it a good candidate for elimination of the disease through intensified control. The outer limits of this HAT focus extend into the neighbouring countries of Angola and the Republic of Congo, making cross-border collaboration critical to achieving the goal of elimination.

Enhanced passive screening for HAT in Kongo Central

Armed with new diagnostic tools co-developed by FIND and partners, HAT screening in Kongo Central has been radically enhanced. HAT RDTs and trainings have been provided to 597 health facilities, which are now conducting the first stage of screening. To confirm disease in HAT suspects, 23 of these 597 facilities have been upgraded and equipped to perform parasitology, including LED fluorescence microscopy (FM), and a select five of them have been in addition equipped with LAMP. These facilities have been strategically chosen across the Kongo Central HAT focus to ensure that distances travelled by referred patients or samples for confirmation are minimised. As a consequence, the distance that a referred patient has to travel has been brought down to 11.2 km, while the mean distance for transporting samples for LAMP is 33 km (see figure on p. 3).

Application of blood from a suspected HAT patient to a filter paper at a parasitology centre in the DRC. After the sample has dried, it is put into a plastic pouch and sent to a LAMP centre for further testing.

Photo: J. Ndung’u / FIND
PROBLEM

Twenty-three out of 31 health zones in Kongo Central province, an area of approximately 33,800 km², are endemic for HAT, with more than 4.5 million people at risk of infection. In recent years, disease surveillance in this vast province has consisted of active screening using CATT by a single mobile team and passive screening at just 36 health facilities. The terrain of the province has numerous rivers and is difficult to navigate, meaning that the mobile team cannot access most endemic villages and health facilities that offer screening are often far from the population at risk. Achieving elimination of HAT in Kongo Central requires a cost-effective strategy to deliver screening services as close as possible to the villages where people live, and harmonization of activities with neighbouring Angola and the Republic of Congo.

SOLUTION

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

SD BIOLINE HAT rapid diagnostic test (RDT)

(manufactured 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: 3 in 100 people who do not have HAT test positive for the disease, so positives must be confirmed by other tests

The SD HAT RDT requires minimal expertise and training, and can be performed by staff at the smallest health-care facilities as well as by mobile teams. The RDT kit (pictured above) contains all materials necessary to perform the test.

Primo Star iLED fluorescence microscope (LED FM)

(manufactured by Carl Zeiss MicroImaging)

✓ Low power requirements
✓ Long-lasting light sources
✓ Slides are quick and easy to stain using acridine orange
✓ Versatile – can also be used for malaria and TB
✓ Does not require a dark room
✗ Low sensitivity – microscopy misses many cases

With options for conventional bright field and fluorescence microscopy, the LED FM can be used to perform an extended range of parasitological confirmation tests for HAT. Low electricity requirements mean that it can be powered from solar panels such as these installed at Bangumi health centre, in Bangundu (see photo on the right).
Loop-mediated isothermal amplification (LAMP) of DNA
(manufactured by Eiken Chemical Co.)
✓ Highly sensitive
✓ Identifies sleeping sickness cases 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 specialized training in molecular biology. LAMP can be deployed at district- or microscopy-level laboratories that have a reliable electricity supply.

Screening process

1. Patients with symptoms suggestive of HAT are first tested with a malaria RDT because the symptoms can be similar.
2. If a patient is negative for malaria (or positive for malaria but still symptomatic after malaria treatment), then a HAT RDT is performed.
3. If the HAT RDT is positive, the patient is referred to the nearest facility for parasitological confirmation, including with LED FM.
4. If found positive by microscopy, the patient is staged and treated for HAT. When a patient is negative by microscopy, further testing is required at one of the five facilities equipped to perform LAMP. If the patient is at a facility that does not have LAMP, a blood sample is dried on filter paper and transported to the nearest LAMP facility by a motorcycle belonging to the project.
5. Patients found positive by LAMP are considered as strong HAT suspects and undergo further tests by microscopy because demonstration of parasites by microscopy is required for case confirmation according to WHO guidelines.

CURRENT STATUS

Upgrading of health facilities was initiated in 2014, while implementation of the strategy started in July 2015. By the end of October 2015, all 597 facilities were participating. From July through November 2015, 3,609 RDTs were performed and out of 119 (3.3%) positives, 10 (0.4%) were confirmed as cases. Seven of the 10 cases were initially screened at facilities that were not previously testing for HAT, and one of the cases was from Angola. Importantly, seven of the diagnosed cases were in the early or first stage of disease, which is safer and easier to treat than the late stage when the brain is affected. By comparison, in all of 2014, only 30 cases were detected in Kongo Central by passive screening using the older card agglutination test for trypanosomiasis. By the time of this update, samples dried on filter paper from 38 RDT-positive HAT suspects had been tested using LAMP and all were negative.

For HAT screening, 597 facilities have been equipped with HAT RDTs, 23 of these to perform parasitology, including with LED FM, and 5 for parasitology and LAMP. They are spread across the Kongo Central HAT focus to minimise the distance referred patients or samples have to travel for confirmation. The map shows health facilities where RDT-positive HAT suspects and cases were reported from July through November 2015.

(Left) An illustration of the diagnostic pyramid for HAT being implemented in Kongo Central.
CHALLENGES

Ensuring that RDT-positive suspects travel for confirmatory testing is a challenge that still has to be addressed through social research and community education. Due to the magnitude of the programme in a difficult environment, successful implementation requires significant coordination efforts, and accurate and timely reporting of data. This will be made easier by introduction of an eHealth system of reporting using mobile phones, targeted for 2016. Furthermore, achieving and sustaining elimination of the disease requires similar and harmonized activities in cross-border areas in the Republic of Congo and Angola, which have now been initiated.

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FURTHER INFORMATION

More information regarding the diagnosis of HAT is available at:
http://www.finddx.org/programs/hat-ond/hat/