

Elimination of sleeping sickness hindered by difficult diagnosis

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Sleeping sickness or human African trypanosomiasis (HAT) is a fatal disease caused by *Trypanosoma brucei gambiense* and *T. b. rhodesiense* and transmitted by tsetse flies occurring in sub-Saharan Africa. Almost 80% of cases are detected in the Democratic Republic of the Congo. Control of infection by *T. b. gambiense*, which causes chronic disease, relies primarily on case detection followed by treatment. The prevalence of this form of HAT has been greatly reduced through intensive campaigns based on active screening by mobile teams that travel to high-incidence settings and test the population. This “vertical” approach is no longer sustainable or cost-effective in light of decreased incidence, and a proposed alternative has been to integrate HAT control activities into the “horizontal” health system.¹ However, organizational, logistical and technical difficulties, especially related to diagnosis, may jeopardize elimination, which is now an established goal.²

The signs and symptoms of sleeping sickness are diverse and non-specific and resemble those of many other diseases, including malaria, human immunodeficiency virus (HIV) infection, tuberculosis, toxoplasmosis, viral encephalitis, brucellosis, lymphoma and typhoid fever. Because of this, diagnosis must rely on laboratory tests, yet none of the available techniques for the laboratory diagnosis of HAT has the features of the ideal diagnostic test: affordable, user-friendly, fast and accurate; requiring no special equipment; and available where needed.³ The card agglutination test for trypanosomiasis, which detects antibodies to *T. b. gambiense*, is particularly suited to active mass screening campaigns, but it is not an individual test and has poor thermal stability. Since specificity is limited, parasitological confirmation is required. Although wet preparations of lymph node aspirates and Giemsa-stained thick blood films for parasite detection can be easily examined microscopically at the primary care level, these tests lack the necessary sensitivity.³ Concentration techniques have higher sensitivity but are costly and rely on electricity and

specialized equipment often unavailable in primary-care facilities, where most patients are tested by thick blood film examination alone. As a result, HAT may remain undiagnosed.

Rapid diagnostic tests (RDTs) are increasingly being used to diagnose HIV infection and malaria. Although their sensitivity and specificity for HIV infection usually exceed 98%, in patients with HAT, specificity can be as low as 39%⁴ and false positives cannot be entirely excluded by serial testing algorithms. Similarly, RDTs for malaria can have a specificity as low as 11% in patients with HAT.⁵ This poses an additional risk, since RDTs for malaria are assumed to be accurate enough to substitute for microscopy. In addition, the replacement of microscopy by RDTs for the diagnosis of malaria eliminates the opportunity to incidentally detect trypanosomes in blood. The risk of misdiagnosing sleeping sickness as HIV infection or malaria is thus considerable and even higher in co-infected HAT patients.

The health system's competence for laboratory testing represents an additional problem, as suggested by reports for thick blood film microscopy. During external quality assessments of malaria microscopy in diagnostic laboratories of the Democratic Republic of the Congo, only 49% of laboratories recognized trypanosomes⁶ and fewer than 20% produced good Giemsa stains.⁷ This illustrates the difficulty of procuring quality in vitro diagnostics and reagents.⁸ In health centres, routine thick blood film examination for malaria had a false positivity rate of 66%.⁹ Similar or poorer diagnostic quality can be expected in the case of HAT.

Integration of sleeping sickness control into the health system is hindered by various factors, including the limitations of current diagnostic tests. Health systems must be strengthened to reduce diagnostic delays. A supply of basic quality consumables should be assured⁸ and refresher trainings in microscopy and laboratory management need to be organized, along with regular external quality assessments to maintain competency and help

monitor test and end-user performance.⁷ Furthermore, when RDTs are used to diagnose other diseases in areas where HAT is endemic, the decrease in specificity observed in HAT patients and the risk of misdiagnosis should be kept in mind. Diagnostic algorithms should be adapted accordingly. Finally, individual RDTs for the detection of antibodies specific for *T. b. gambiense* are being developed. Such tests will facilitate HAT screening in primary health centres, although parasite confirmation will be required, especially since current drugs for the treatment of HAT have side-effects and are difficult to administer. ■

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