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Control of human African trypanosomiasis

Report by the Secretariat

BACKGROUND

1. In resolution WHA56.7, on the Pan African tsetse and trypanosomiasis eradication campaign, the Health Assembly called attention to the severe health problems caused by human African trypanosomiasis and the significant impairment of socioeconomic development that has followed the resurgence of the disease in both human beings and livestock. It also recognized that eradication of the tsetse fly vector was the only effective, long-term solution in fighting the disease. The Director-General was requested to report on progress made in implementing the resolution to the Executive Board at its 113th session and to the Fifty-seventh World Health Assembly.

2. This report outlines features of the disease that are important for control and describes activities in the areas of screening, diagnosis, treatment and the search for better drugs. It also discusses the impact on control of WHO's collaboration with endemic countries and participation in international networks and partnerships.

CLINICAL FEATURES

3. Human African trypanosomiasis, which occurs uniquely in sub-Saharan Africa, constitutes a major public health problem because of its epidemic potential and its 100% fatality rate in untreated cases. The disease is caused by two different species of protozoal parasites, namely *Trypanosoma brucei gambiense* in western and central Africa, and *T. b. rhodesiense* in eastern and southern Africa. Infection, which begins with the bite of an infected tsetse fly, evolves through two stages. In the first, trypanosomes multiply in the bloodstream and lymphatic system. During this stage, which may last for years in the case of infection due to *T. b. gambiense*, there are few specific symptoms; as a result, many cases go undetected and untreated, thus maintaining the human reservoir. The second stage starts when the parasite crosses the blood-brain barrier and invades the central nervous system, causing severe neurological disorders. The disease due to *T. b. rhodesiense* is much more virulent than that due to *T. b. gambiense*, and can progress to the second stage in a matter of weeks or months. For both forms, symptoms during the second stage include altered mental state, sensory disorders, difficulties in talking and walking, and changes in the sleep cycle. Untreated, the disease invariably progresses to body wasting, somnolence, coma and death.

COMPONENTS OF CONTROL: DETECTION AND TREATMENT

4. Improved control reduces both mortality and the size of the human reservoir of infection, thereby contributing to conditions favourable to disease elimination. The combination of active case detection and successful treatment forms the cornerstone of control. That approach, however, faces formidable obstacles. Early in infection when symptoms are few yet treatment has the greatest chance of success, patients are usually unaware of their infection, which remains undetected, especially as health services are usually poorly staffed and equipped or non-existent in the remote rural areas where human contact with the vector is greatest. Moreover, even when general health services are accessible, diagnosis relies on sophisticated procedures beyond the capacity of most. Further the disease is notoriously difficult to treat, particularly after the parasite has crossed the blood-brain barrier. Even when patients' infections are cured, neurological damage may prove irreversible. Treated children frequently suffer from permanent mental and psychomotor impairments.

5. Human African trypanosomiasis is one of the few infectious diseases where proactive systematic population screening is essential for control, especially for the form due to *T. b. gambiense* with its long, almost asymptomatic initial stage. The WHO-recommended control strategy therefore relies on systematic screening of at-risk populations to detect all cases of infection, in either stage of the disease. That requires, however, considerable resources, which are well beyond the capacity of most endemic countries; at present, of the 60 million people considered to be at risk, regular surveillance covers only four million.

6. Treatment, the second component of control, also presents considerable challenges. Most available medicines were developed long ago; they are expensive, difficult to administer and toxic – sometimes lethal: an estimated 3% to 5% of patients treated in the second stage of infection die from the treatment itself. In addition, resistance to currently used drugs is a serious and growing problem; in some parts of central Africa, as many as 30% of patients show resistance to melarsoprol, the only drug available to treat the advanced stage of *T. b. gambiense* and *T. b. rhodesiense* disease.

PROSPECTS FOR CONTROL

7. Several international collaborations have been started and public-private partnerships formed in recent years to combat African trypanosomiasis. All contribute to the management of a disease with multiple determinants and a broad socioeconomic impact, and two are specifically designed to improve control of human disease.

8. In 1999, WHO launched the Treatment and Drug Resistance Network for Sleeping Sickness which links institutes and agencies engaged in research and control. Apart from establishing a system for sentinel surveillance of treatment failure and drug resistance, it ensures, as one of its main objectives, that drugs are available and financially affordable to governments and nongovernmental organizations. In 2001, a collaboration with Aventis Pharma and other pharmaceutical companies was established to deal directly with the crisis created by the disappearing arsenal of therapeutic drugs; the companies would donate drugs, provide cash to improve infrastructure and support logistics for drug delivery in endemic countries.

9. Thanks to these two initiatives, drugs for treatment are available free of charge. A system of drug distribution and tracking of all shipments, administered by WHO, is now fully operational. In the first 18 months of the collaboration, sufficient drugs were distributed for complete treatment of more

than 46 000 patients in 21 African countries. Reagents for the serological card agglutination trypanosomiasis test were made available throughout Africa.

10. WHO has worked with countries in which the disease is endemic to provide specialized training at field level and to establish national control programmes; as a result, about 80% of those countries now have such programmes. In 1999, WHO established a decentralized office in Africa to intensify national support to teams bringing services to remote areas; in 2003, the number of staff in the Trypanosomiasis Unit at the Regional Office for Africa was increased. The availability of free drugs has substantially boosted national control, as the cost of drugs has traditionally been one of its most expensive components, and national programmes can now devote more resources to case detection and treatment.

11. In addition, because of the highly focal epidemiology of trypanosomiasis, with disease outbreaks occurring in circumscribed ecological zones, satellite imagery and geographical information systems are being used to map geographical foci and thus to target active screening to populations at risk. Such applications, which draw on pioneering work by the interagency Programme Against African Trypanosomiasis, give yet another boost at country level to the introduction of active screening and treatment. Where human and animal disease overlap in specific ecological zones, WHO acts in collaboration with FAO, the International Centre of Insect Physiology and Ecology, the African Union, and others working on vector control as a powerful way to decrease transmission.

12. To support the drive to improve control, WHO has introduced a strategic approach stratified according to epidemiology and locally available resources. Its three levels comprise: low-prevalence countries with few resources, where intercountry teams are used to maximize resources and maintain a high level of technical expertise; areas of presumed medium prevalence, where standardized control activities are introduced together with epidemiological assessments; and areas facing an epidemic with numerous geographical foci, where reliance on regional networks and nongovernmental organizations facilitates emergency responses.

13. In recent months, intensified collaboration with countries has taken the form of missions to identify sentinel surveillance sites, epidemiological assessments to map geographical foci and assess prevalence, investigation of treatment failure, training of specialized staff, and the introduction of systems for computerized data collection and analysis. Within the context of the drug-donation collaboration, WHO has also provided funding for mobile teams, the rehabilitation of treatment centres, and the purchase of vehicles and laboratory equipment. In addition, sustainable protective measures (surveillance and/or vector control) are being formulated; in countries with low endemicity, surveillance systems are being set up to detect imported cases and prevent potential epidemic spread.

14. Focused screening campaigns are particularly important. In some instances, they have detected a large number of cases in countries where the prevalence was presumed to be low. In other situations, campaigns have, for the first time in recent decades, screened people in all geographical foci, placing all at-risk persons under active surveillance and treating everybody with detected infection. However, in many newly detected cases the disease has progressed to the neurological phase, for which new drugs are badly needed to improve outcome.

15. Recent advances in control have been considerable. Commitment and momentum, as expressed in initiatives such as the Pan African Tsetse and Trypanosomiasis Eradication Campaign, are high. Nonetheless, expansion of control activities lags behind the continuing resurgence of this disease, pointing to the urgent need for better control tools.

THE SEARCH FOR BETTER TOOLS

16. The UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) categorizes African trypanosomiasis as an emerging or uncontrolled disease, for which the main need is for new knowledge and new control tools. Through that Programme, WHO ensures that the research agenda is directly linked to the needs of disease control; strategic research has resulted in several promising advances, including the elaboration of a simple non-invasive field test for diagnosis, investigation of shorter treatment regimens, and results of combination therapy trials that indicate fewer side-effects and lower failure rates. Progress has been made in mapping the parasite genome and a specimen bank has been set up to facilitate drug discovery, a research activity also supported by recent public-private partnerships. Another strategic objective is the development of a simplified field test for determining the stage of disease.

17. The greatest need at present is for better therapeutic drugs, especially for advanced disease. An ideal drug would be effective in both stages of infection, non-toxic, relatively inexpensive, and safe to administer orally. Its availability would allow the rapid mass treatment of all at-risk populations, in a strategy similar to those underpinning highly successful efforts to eliminate onchocerciasis and, more recently, lymphatic filariasis as public health problems.

ACTION BY THE EXECUTIVE BOARD

18. The Executive Board is invited to note this progress report.

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