Editorial

Gambiense sleeping sickness: re-emerging and soon untreatable?

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Towards the end of the 1950s, sleeping sickness caused by *Trypanosoma brucei gambiense* was believed to be on the verge of eradication. Today, however, it has returned with a vengeance, mainly because of a deterioration of control activities, severe disruptions of health services, and population movements into high-risk areas. For example, over the last ten years, annual detection rates of the disease in the Democratic Republic of Congo have been similar to those of the late 1920s (*1*), and although more than 150 000 new cases have been found the problem is still largely ignored. The situation may be even worse in parts of Angola (*2*). Currently, Gambiense sleeping sickness is also a major public health problem in vast areas of the Central African Republic, Chad, Congo (Brazzaville), Côte d'Ivoire, Guinea, southern Sudan, and Uganda.

The combination of active case-detection and successful treatment is the cornerstone of prevention and control of the disease. However, implementation of this strategy is facing huge problems: very few donors are funding sleeping sickness control and antitrypanosomals are quite toxic, irregularly produced, and too expensive. Moreover, increased drug resistance has recently been reported from several countries.

The article by Pépin et al. in this issue of the *Bulletin* (pp. 1284–1295) describes the results of a multicentre clinical trial of the effectiveness of 7-day versus 14-day intravenous eflornithine on patients with second-stage Gambiense sleeping sickness. It was hoped that the 7-day course would work well and halve the drug costs. However, the 7-day course was sufficiently effective only for relapsing cases, while for new cases it was inferior to those with the 14-day regimen in the Congo, the Democratic Republic of Congo, and Côte d'Ivoire. The authors conclude that the 7-day course cannot be recommended for new patients and that the cost of a 14-day course is prohibitive. Thus, melarsoprol will remain the first-line drug for the foreseeable future.

Eflornithine is a sad illustration of the gap between scientific progress and its implementation in the field. Almost two decades ago, eflornithine was a rationally designed cytostatic drug in search of a disease — its expected activity in tumour chemotherapy having proved to be unsatisfactory. At that time, there was no adequate therapy for melarsoprol-refractory sleeping sickness, and eflornithine was first tried for compassionate treatment in 1981 (*3*) after it had been shown that it could eliminate trypanosomes in vivo (*4*). It was originally administered orally and worked well, but some relapses occurred, mainly among children. In an attempt to limit the number of relapses to a minimum, the intravenous regimen was introduced. Administration of the currently recommended 14-day intravenous regimen to large numbers of patients is unfeasible in rural areas, and the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) has begun to reassess the effectiveness and adverse effects of oral eflornithine.

Although eflornithine is the only registered drug for sleeping sickness that can cure the melarsoprol-refractory form of the disease, nifurtimox has also been used with good results for compassionate treatment of such cases (*5*). Moreover, nifurtimox is administered orally and is relatively cheap (ca US$ 20 per treatment) but its supply is no longer guaranteed.

The availability of melarsoprol and of the first-stage drugs pentamidine and suramin is also in question. It is ironic that at a time when there is increasing evidence of synergism between melarsoprol, eflornithine and nifurtimox, and that combination doses are likely to be more effective and possibly less toxic than monotherapy with any of them (*5*), the risk is real that they may no longer be available in the near future.

WHO has recently initiated a Sleeping Sickness Treatment and Drug Resistance Network involving public and private partners. One of its main objectives is to make pentamidine, suramin, melarsoprol, eflornithine and nifurtimox available and financially accessible to governmental and nongovernmental organizations. In view of the present dramatic resurgence and the fatal outcome of untreated sleeping sickness, the initiative must not fail. ■

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1. **Miaka Mia Bilenge C et al.** Sleeping sickness resurgence in the DRC: the past decade. *Tropical Medicine and International Health*, in press.
2. Data provided by the Angolan National Trypanosomiasis Control Programme.
3. **Van Nieuwenhove S et al.** Treatment of Gambiense sleeping sickness in the Sudan with oral DFMO (dl-alpha-difluoromethylornithine), an inhibitor of ornithine decarboxylase; first field trial. *Transactions of the Royal Society for Tropical Medicine and Hygiene*, 1985, **79**: 692–698.
4. **Bacchi CJ et al.** Polyamine metabolism: a potential therapeutic target in trypanosomes. *Science*, 1980, **210**: 332–334.
5. **Van Nieuwenhove S.** Present strategies in the treatment of human African trypanosomiasis. In: Dumas M, Bouteille B, Buguet A, eds. *Progress in human African trypanosomiasis, sleeping sickness.* Paris, Springer-Verlag France, 1999: 253–280.

