New WHO plan targets the demise of sleeping sickness

A meeting of experts and African health officials sets in motion a campaign spearheaded by WHO to free Africa from the grip of sleeping sickness. John Maurice reports.

17 so-called neglected tropical diseases have been sitting for decades on the to-do list of WHO. Together they bring physical, social, and economic suffering to more than 1 billion people, according to WHO. A decade or so ago, WHO and its partners decided to pull these diseases out of the closet and to find the resources needed to finish what has too long been unfinished business. "These diseases are now being brought to their knees with stunning speed", WHO Director-General Margaret Chan told an international meeting in London last year.

Bringing diseases "to their knees" can mean, in health-speak, either eradication (incidence is permanently reduced to zero cases worldwide and no further action is needed); or elimination (incidence is reduced to zero cases worldwide or in a defined geographical area but action might be needed to keep it that way); or elimination as a public health problem (incidence is reduced to a defined level). Until now, of the 17 neglected tropical diseases only two-quineaworm disease and vaws-have been slated for eradication. Only three, blinding trachoma, leprosy, and lymphatic filariasis, are headed for worldwide elimination. Plans eliminate a fourth disease, sleeping sickness (human African trypanosomiasis), have recently been agreed on by experts at a WHO meeting held in December, 2012.

Theoretically, sleeping sickness could be eradicated but the parasite that causes the disease (a subspecies of *Trypanosoma brucei*) is transmitted by a fly, the tsetse fly: eradicating the disease would call for eradication of the fly, a formidable task. The fact, too, that animals can be infected by the parasite and might constitute a

reservoir of infection also casts doubt on eradicability of the disease.

Sleeping sickness, however, is certainly a strong candidate for elimination. "What we are aiming for", says Pere Simarro, head of WHO's human African trypanosomiasis programme, "is to bring the disease down to zero cases, to stop transmission, and to keep it that way indefinitely. It means using all the tools at our disposal to find infected people, to rid them of the infection,

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to stop the infection spreading, and to prevent it from resurging". There are, he believes, good reasons for making these efforts: "For one thing, it's a lethal disease. If you get infected and you don't get treatment, death is almost certain. For another, it's a disease that hits people at the most productive period of their lives and thus represents a serious economic burden on many African countries."

Achieving the zero-cases-zerotransmission target, the WHO meeting participants agreed, will not be easy. Hunting for cases is difficult in the remote jungle villages where most patients—and most tsetse flies-live. Screening for cases and diagnosis of the disease are hampered by the absence of specific signs or symptoms in the early months or years of the infection. During this period, the parasite is still in the patient's blood and lymph and hasn't yet passed into the central nervous system where it will produce a host visible symptoms—behaviour changes, drowsiness, and other neurological changes. The available drugs are effective but notoriously toxic and difficult to administer. There is a lack of field-friendly diagnostic tests. Efforts to stop transmission by killing the fly vector by spraying its forest haunts and animal hosts with insecticide or by trapping methods have, up to now, been too costly to deploy on a large scale. A further complication is the fact that there are two distinct forms of sleeping sickness, a west African (gambiense) form, which accounts for about 96% of sleeping sickness cases, and an east African (rhodesiense) form, which is essentially a zoonotic disease involving cattle and wildlife. The two forms differ biologically, clinically, and epidemiologically and call for quite different control strategies.

Yet, despite these difficulties, the meeting participants expressed few doubts about their ability to reach the zero-case target, at least for the west African form of the disease. One reason for optimism is that the target was almost reached in the past. Sleeping sickness first achieved recognition in the medical literature



A nurse checks for signs of sleeping sickness during a WHO campaign in Chad, 2002



Lumbar puncture test for sleeping sickness

at the end of the 19th century, shortly before the "invasion" of Africa by European colonisers and the upheaval they caused over the next two or three decades in the lives of the Indigenous populations. Many people were uprooted from their homes, conscripted into workforces, and obliged to move into the interior as new lands were opened up to mineral mining and other industries. A good number of these new lands were infested with the tsetse fly. The result was a repeated onslaught of sleeping sickness epidemics that killed thousands of people, including those working for the colonisers. In 1906, Britain's Colonial Undersecretary, Winston Churchill, returned from a visit to Lake Victoria in Uganda to announce to the House of Commons that Uganda had lost a third of its population because of sleeping sickness.

By the early 1930s, annual reported cases in west and central Africa had reached a record 50 000. Two decades later, the number had decreased to about 3000, thanks to mass campaigns undertaken by the colonial administrations and involving systematic screening, treatment, and follow-up of millions of people throughout west and central Africa. By 1962, experts

triumphantly declared the disease well and truly conquered. For the newly independent governments it was no longer a priority and sleeping sickness control programmes could be dismantled.

The triumph, however, was short-lived. Over the next four decades, with armed conflict preventing health workers from reaching endemic villages, with the drug supply unreliable, and with almost no support from the international health community, the disease resurged. By the turn of the century reported cases of sleeping sickness exceeded 30 000 annually (in 1995 a WHO expert committee estimated the true number to be more than 300 000).

Today, 70 million people are still living in areas where they risk being infected with sleeping sickness. Nearly two-thirds of these people are in the Democratic Republic of the Congo, which currently accounts for 85% of the total cases reported in Africa. However, new reported cases number less than 7000 (a 75% decrease over the past decade) while estimated cases are around 21000 (a 90% decrease).

Jose Ramon Franco Minquell, medical officer with WHO's neglected tropical disease team, attributes success in slashing case numbers since 2000 to a combination of factors: "First and foremost, we launched a large-scale advocacy campaign that put sleeping sickness back on the international radar screen. Then WHO assembled a powerful coalition of charitable and humanitarian institutions, pharmaceutical companies, bilateral country partnerships, non-governmental organisations, and research centres to fight the disease. We also got strong commitment from the African countries where the disease is endemic. We now know more about the dynamics of the disease and where exactly we must look for cases, thanks to a huge mapping exercise we have done that covered 29 000 villages and unearthed 175000 new cases in all countries reporting cases in the last decade. And, thankfully, there are now far fewer areas where conflict could prevent health workers from reaching patients. I think we can be optimistic about reaching our elimination target."

Anne Moore, who chaired the WHO meeting and is a medical epidemiologist with the US Centers for Disease Control and Prevention, in Atlanta, GA, USA, agrees that "the plan to eliminate sleeping sickness is looking very good".

"We have a really effective strategy for controlling the disease. We screen the whole population of a village, confirm diagnosis in suspected cases, hospitalise, and treat, and get them to come back every 2 years for a followup test. That strategy can reduce the prevalence of the disease by threeto-four fold with just one round. It worked for the colonial powers, although it took them 30 years to reach near-elimination of the disease. With the experience and better, if not perfect, tools we now have, and by adapting the strategy to different epidemiological contexts, it should take us less time."

The new drugs and new diagnostic tests in the pipeline, she believes, are added reasons for optimism. One serious omission, though, that the colonial powers made and that the current sleeping sickness combatants want to avoid was the failure to put in place a surveillance programme to prevent resurgence of the disease. This measure, says Moore, "is going to be a key factor in reaching our targets".

Before the WHO meeting broke up, it unanimously gave the green light to bringing down the incidence of the disease, by 2020, to less than 1 case per 10 000 of the population in at least 90% of the areas where cases exist. Thereafter, efforts will continue to bring the incidence of the disease to zero and to ensure that sleeping sickness will never again awaken to plague the African continent.

John Maurice