

## A One-Two Punch Against Sleeping Sickness

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**NEW ORLEANS, LOUISIANA--**It's far from the ideal therapy, but scientists say a new combination of two old drugs is an important step forward in the fight against sleeping sickness, a long-neglected tropical disease. They hope the combo will help reduce the use of a 60-year-old, highly toxic drug that kills one in 20 patients.

Sleeping sickness, caused by two subspecies of the *Trypanosoma brucei* unicellular parasite and transmitted by tsetse flies, affects an estimated 50,000 to 70,000 people annually in Africa. In the late stages of infection, the parasites not only disturb the sleep cycle but also cause paralysis, behavioral changes, and eventually death. That's why scientists find its common name a bit too innocuous sounding; they usually call the affliction human African

trypanosomiasis (HAT).

Of the few existing medications that fight HAT, none are very good. A drug initially developed for cancer, called eflornithine, kills *Trypanosoma* and is reasonably safe, but the parasites are becoming increasingly resistant to it. Moreover, patients need 56 intravenous (IV) infusions over 14 days, a huge hassle in developing countries. (The sheer weight of the medication and other materials needed makes eflornithine very expensive to ship as well, says Pere Simarro of the World Health Organization.) As a result, 70% of patients in 2007 were still treated with melarsoprol, an arsenic-based compound developed in the 1940s that is very toxic.

An international consortium of researchers tested a new treatment in the Democratic Republic of the Congo and its neighbor, the Republic of the Congo. They enrolled 280 patients in a trial that compared the standard eflornithine regimen with one in which only 14 infusions of that drug were given over a week's time, combined with 10 days of nifurtimox, an oral drug licensed against Chagas disease--which is also caused by *Trypanosoma* parasites--but not considered active enough as a standalone HAT drug.

Finding, treating, and following patients in the most remote corners of both countries proved a huge challenge, says Gerardo Priotto, an epidemiologist with Doctors Without Borders in Paris. To make sure that the patients were really free of the parasite, for instance, they had to be persuaded to travel back to the study clinic and undergo painful lumbar punctures 6, 12, and 18 months after the trial--which isn't easy when patients no longer feel sick.

But it was worth the trouble. The combination works at least as well as eflornithine or melarsoprol alone, the researchers reported here yesterday at the annual meeting of the American Society of Tropical Medicine and Hygiene. And it had fewer side effects. That's an important step forward, says Peter Hotez, who studies HAT and other tropical diseases at George Washington University Medical Center in Washington, D.C. Giving two drugs rather than one should help prevent resistance, he says. And because just 14 instead of 56 eflornithine infusions are needed, the combination should help drive down the use of melarsoprol.

Still, better and cheaper drugs that do away with the need for IV drips altogether are desperately needed, says Simon Croft of the London School for Hygiene and Tropical Medicine. Thanks to a recent influx of money to the field, several are now in the pipeline; the combination treatment, says Croft, "will eventually be no more than a stopgap."