

## Good News on a Tropical Disease

**W**e sometimes use this space to complain, so we welcome the occasional opportunity to dole out good news and praise those responsible for it. Onchocerciasis is not a disease that troubles many *Science* subscribers—at least we hope not, because we want you to be able to read this. It is, however, a scourge in Africa and, to a lesser extent, in Latin America, having blinded a quarter of a million people and afflicted many millions more. For those who don't know, *Onchocerca volvulus* is the parasitic nematode that causes a disease called river blindness, so named because it is transmitted by several species of Simuliid flies (black flies) that breed in moving water. They pester temperate-zone fishermen but are much more than a nuisance in the tropics, where they can infect the humans they bite by introducing parasitic larvae that develop into adult worms. The female worms produce microfilaria that swarm under the skin, causing skin disease and itching; they can also migrate to their victims' eyes and slowly steal their sight.

The background for this feel-good story is that for 25 years, the World Bank and World Health Organization (WHO) have run a highly successful control program in West Africa focused on black fly vector control. (There is concern that the discontinuation of this effort, scheduled for this year, may lead to some recrudescence of the disease.) Another program, the African Programme for Onchocerciasis Control, emphasizes annual treatment with the antiparasitic drug ivermectin, of which Merck & Co. has donated well over 250 million doses (as Mectizan). A third program, the Onchocerciasis Elimination Program of the Americas, promotes twice-a-year ivermectin treatments. Together, these efforts have caused a dramatic decrease in the prevalence of skin and eye disease attributable to onchocerciasis.

This is where the remarkable work of the Carter Center comes in. In addition to monitoring elections, promoting Quality Protein Maize in the developing world, and closing in on the eradication of Guinea worm disease in most parts of Africa, Carter Center epidemiologists are working with the Pan American Health Organization and six afflicted countries in the Americas to establish "proof of concept" that transmission can be permanently stopped, and thus eradicated, by the use of ivermectin. Experts convened by the Carter Center and WHO in January 2002 reviewed the evidence and agreed that eradication could be achieved in most, perhaps all, of this hemisphere.

*Science* has a small oar in this water, because we recently published a very interesting paper [A. Saint André *et al.*, *Science* **295**, 1892 (2002)] in which the authors reveal a new culprit in river blindness. It turns out that there is, as a colleague once put it, "a bug in the bug in the bug." It seems that all stages of *O. volvulus* contain a symbiotic bacterium, *Wolbachia*, and the paper demonstrates, using a mouse model, that it is the bacterial endotoxin and not the parasites themselves that causes the ocular pathology. In the mice used in these experiments, doxycycline afforded significant relief from the ocular symptoms. Might antibiotic therapy lift this extraordinary Third World disease burden or provide a substitute for semiannual ivermectin treatment?

Not quite. Antibiotics may indeed relieve morbidity by killing *Wolbachia* in the microfilaria that enter the eyes, but delivering 6 weeks of daily doxycycline treatment in remote areas of Africa and the Americas looks like an unlikely logistical substitute for semiannual ivermectin. But more interesting to Carter Center epidemiologists is the emerging evidence that the adult worms can be themselves sterilized or killed when their *Wolbachia* symbionts are killed. The bacteria may supply a critical nutrient that the worms simply can't do without. If that were the case, eradication in the Americas would be much closer. But there's a problem: How do you determine whether antibiotic therapy kills the adult worms? If it does, can you find a single-dose or short-course therapy that is applicable to the mass distribution programs currently in place?

The next step is more research aimed at detecting and killing the bacteria in adult worms, and then perhaps an eradication project in Africa, where interruption of transmission will be much more difficult. That's because the disease is more widespread and the vectors more competent than in the New World. But the battle against river blindness may be edging toward completion, and that is welcome news. It is a reminder that good science can still make a big difference against an old problem in the developing world.



*Onchocerca volvulus*

Donald Kennedy