

## INFECTIOUS DISEASE

# Elusive Pathogen Cornered at Last

Françoise Portaels has finally answered the question she began to study in 1969 as a Ph.D. student in the Congo. She and her colleagues have discovered an environmental hiding place for the bacteria that cause a devastating disease known as Buruli ulcer. As they report in the March 2008 issue of *PLoS Neglected Tropical Diseases*, Portaels, now a microbiologist at the Institute of Tropical Medicine in Antwerp, Belgium, and her team have cultured the disease-causing organism, *Mycobacterium ulcerans*, from an aquatic insect from Benin. The accomplishment comes at the 10th anniversary of the World Health Organization's (WHO's) Global Buruli Ulcer Initiative and marks a major milestone in efforts to understand and control one of the world's most neglected tropical diseases.

Australian doctors first described Buruli ulcer and *M. ulcerans* in 1948. Although it belongs to a well-known genus that includes the bacteria responsible for tuberculosis and leprosy, the life cycle of *M. ulcerans* has remained mysterious. The infection begins as an innocent-looking bump under the skin that, in several months, opens into a painless lesion. The ulcer gradually spreads over the body, demolishing skin, soft tissue, and sometimes bone, leaving behind severe scars that cause both immobility and social stigma. The disease affects several thousand people each year, mostly in Africa and Australia. The infection is not transmitted person to person but always occurs near slow-moving water, leading researchers to suspect that aquatic insects might harbor and transmit the disease. But without a live culture as evidence, no one could be sure.

Ten years ago, Portaels resumed the search she had abandoned after her frustrating dissertation. "The big problem is that *M. ulcerans* is a very slow grower," she explains. It takes 6 weeks to cultivate a colony of *M. ulcerans* even from a human lesion in which it is abundant and active.

To keep fast-growing competitors from overrunning *M. ulcerans* in culture, Portaels's team used an unconventional growth medium: mice. They ground up five different water bugs collected from Benin and Togo and treated the samples to kill everything except mycobacteria. Then they injected the cultured mycobacteria into the

paws of mice, where harmless species, not suited for life in a mammalian host, slowly perished but *M. ulcerans* took hold. After passing through three different mice over the course of about 2 years, an *M. ulcerans* lineage from a single water strider began to grow in culture. Nearly 40 years after her first trip to the Congo, Portaels had, for the first time, isolated *M. ulcerans* from the environment.

"It's a significant contribution," says Kingsley Asiedu of WHO's Buruli Ulcer Initiative. But there's a catch: The water strider, *Limnogonus hypoleucus*, doesn't bite people, so it can't transmit the disease. Pamela Small, a microbiologist at the University of Tennessee, Knoxville, and an author of the study, suspects



**Scarred.** Bacteria that cause the disfiguring Buruli ulcer disease have been cultured from an African water strider.

that *M. ulcerans* thrives in another aquatic niche and had to pass through several links in the food chain before infecting the water strider. "Eventually, we will find where this organism is replicating," she says.

Portaels, Small, and dozens of other researchers will assemble in Geneva, Switzerland, on 31 March at WHO's 10th annual meeting on Buruli ulcer. Asiedu says the initiative's most notable success has been the development of antibiotic remedies for the disease—but much remains to be done: There is a need for earlier diagnosis, faster treatment, and better understanding of transmission. For the latter, Asiedu says Portaels's work is a boon. "This is the first time it's been proven beyond any doubt that *M. ulcerans* [occurs] in aquatic insects," he says. "It will stimulate interesting discussions." —**ELSA YOUNGSTEADT**

## Last Collider Standing

Next month, U.S. particle physicists will be down to their last particle smasher. On 7 April, the Stanford Linear Accelerator Center in Menlo Park, California, will shut down the PEP-II collider, 5 weeks after Cornell University's CESR collider took its last data. That leaves only the Tevatron at Fermi National Accelerator Laboratory (Fermilab) in Batavia, Illinois, still running—and it will shut down in 2010 at the latest.

The United States is not pulling out of particle physics; more than 1200 U.S. physicists are working on experiments that will run at the Large Hadron Collider (LHC), which will power up this summer at the European laboratory for particle physics, CERN, near Geneva, Switzerland. That's more than any other country in the world, but Abolhassan Jawahery of the University of Maryland, College Park, worries that after LHC, "it's a question" of how the U.S. program can thrive without a domestic collider. American physicists hope the answer lies in hosting the proposed International Linear Collider at Fermilab. But there's competition from Europe and Japan, and Congress has reduced funding this year for research on that multibillion-dollar machine. —**ADRIAN CHO**

## Fund Urged for Tropical Diseases

Developed countries should set up a special fund to fight neglected tropical diseases (NTDs) such as intestinal worms, schistosomiasis, elephantiasis, and river blindness, five influential researchers from around the world say in the current issue of *PLoS Neglected Tropical Diseases*. While the world is waging a multibillion-dollar attack against three major infectious killers through initiatives such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria, NTDs have received scant attention—a "tragic oversight," the group writes. The researchers, who hope government leaders will launch the fund at this summer's G8 summit in Toyako, Japan, put the cost at \$2 billion for the first 5 years. —**MARTIN ENSERINK**

## Gates Is Rainmaker for Drought Research

The Bill and Melinda Gates Foundation announced last week a joint \$47 million donation with the Howard G. Buffett Foundation to help develop drought-tolerant corn in Africa. The International Maize and Wheat Improvement Center in Nairobi will work with technology from Monsanto and BASF. The African Agricultural Technology Foundation plans to distribute seeds royalty-free. —**ERIK STOKSTAD**