Virtually incurable TB warns of impending disaster

Like something out of a horror movie, a lethal strain of tuberculosis blazed in 2005 across Tugela Ferry, a small village in South Africa, striking down nearly everyone it touched.

The strain, dubbed XDR for extensively drug-resistant, doesn't respond to known TB drugs and killed 52 of 53 infected individuals—all those tested found to be HIV-positive—and all of them within weeks of diagnosis (*Lancet* **368**, 1575–1580; 2006).

Even among experts, the strain was cause for alarm. "The epidemic situation is very unusual, patients dying so rapidly," says Salim Karim, director of Caprisa, a Durban-based consortium of AIDS and TB researchers.

What is less unusual, however, isn't more reassuring.

XDR strains of TB have appeared in every part of the world, although they aren't all as virulent. Between 2000 and 2004, 20% of TB strains worldwide were found to be resistant to first-line drugs, and a tenth of those were XDR (*MMWR* **24**, 301–305; 2006).

"When we start looking in countries where multidrug resistance (MDR) is a serious problem, where second-line drugs have been used, I think we'll find XDR," says Chris Dye, coordinator for TB monitoring and evaluation for the World Health Organization's Stop TB program.

The former Soviet Union, China and India are all prime candidates, Dye says. "It remains to be seen how big the XDR problem is in these countries."

TB affects mostly young adults in their productive years; more than 50% of TB deaths occur in Asia

Elena Korenbaum

The answers won't be easy to come by. Most countries don't have the resources and labs to screen people for drug resistance. Even when people are diagnosed by culturing the bacteria, infected individuals can spread the disease during the ten days it takes to get the results.

The South African strain has already been found in other provinces and is very likely to have spread beyond to the neighboring countries of Lesotho, Swaziland and Mozambique.

Multidrug-resistant TB (MDR-TB) is a form of TB that does not respond to the standard drug treatment and is present in virtually all countries recently surveyed.

Extensively drug-resistant TB (XDR-TB) occurs when resistance to second-line drugs develops; it is extremely difficult to treat and cases have been confirmed worldwide.

South Africa has an unhappy mix of conditions that foster TB: the disease thrives in poor, overcrowded townships or mining communities and among those infected with HIV. At 5.3 million, South Africa has an HIV burden second only to India's.

Although South Africa is in many ways better equipped than its neighbors to handle the crises, the government is notoriously negligent toward these concerns and, according to experts on the ground, has done little to protect its citizens from TB or to take full stock of the problem. For example, government clinics don't provide preventive drugs for TB to those on antiretroviral therapy, even though individuals with AIDS are at particular risk of infection.

South Africa's Medical Research Council has been evaluating the country's program for dealing with MDR-TB. "For the large part, the MDR program is unsupervised," says Richard Chaisson, director of the Johns Hopkins Center for TB Research in Baltimore. "It's an invitation to create XDR-TB, no surprise."

Apoorva Mandavilli, New York

Spotlight on... Ken Duncan

Ken Duncan began the year with a new job to fight an old foe.

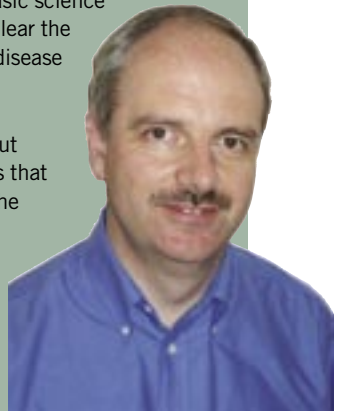
In January, he became a senior program officer for the Bill & Melinda Gates Foundation's tuberculosis (TB) program, where his job will be to shepherd the development of new drugs for the disease.

Duncan's main goal is to help foster drugs that might cure TB in a matter of weeks rather than in months. There have been no new drugs for TB in nearly 40 years, and existing ones must be taken for at least six months.

A veteran of TB research, Duncan directed GlaxoSmithKline's Action TB Initiative, which funded research in the UK, US and South Africa, from 1994 to 2004. He is putting to use the expertise he gained then in integrating basic science and drug discovery across the academia-industry divide to clear the hurdles in TB drug development—a poor understanding of disease pathogenesis and a lack of effective tools to study it (see page 272).

Linking research and drug discovery is a tricky process, but based on his long experience with the industry, Duncan says that certain advances, such as finding biomarkers for cure and the application of imaging technologies to TB research, would encourage companies to develop shorter treatment. "Being able to visualize the disease in real time and *in situ* would have the effect of making it possible to study new drugs much more rapidly than we can at the moment," he says.

Alisa Opar, New York



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