THE DOCTOR'S WORLD

Rise of a Deadly TB Reveals a Global System in Crisis

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Mike Hutchings/Reuters

A tuberculosis patient in rural Tugela Ferry, South Africa.

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LOS ANGELES — The spread of a particularly virulent form of tuberculosis in South Africa illustrates a breakdown in the global program that is supposed to keep the disease, one of the world's deadliest, under control.

Karin Weyer/South African Medical Research Council

During a tuberculosis outbreak in South Africa, patients often infected one another in clinics not designed to allow a quick quarantine.

The program was intended to detect tuberculosis cases, make sure patients were taking their antibiotics, test patients for resistance to those drugs and monitor the spread of the disease.

But international tuberculosis experts say the system is in deep trouble for an array of reasons: misuse of antibiotics; other bad medical practices, like failing to segregate high-risk patients in hospitals and clinics; and cuts in government spending for such basics as adequate supplies of drugs and laboratories to do the testing.

Such factors have led to the rise of drug-resistant tuberculosis bacteria, a menace the world has only begun to appreciate.

Mycobacterium tuberculosis, the microbe that causes the disease, was discovered 125 years ago this month. Today, the bacteria infect 8.8 million people a year and cause 1.6 million deaths. They are spread in tiny droplets when patients cough.

Tuberculosis is curable, as long as the bacteria are susceptible to antibiotics. It becomes deadlier when it attacks people who are also infected with H.I.V., the AIDS virus. And when the tuberculosis bacteria become extremely drug-resistant, the death rate soars.

That was the case in Tugela Ferry, a rural town in KwaZulu-Natal province in South Africa, when an outbreak of extremely drug-resistant tuberculosis — XDR-TB for short —

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killed 52 of its 53 victims, all of whom were also infected with H.I.V. The outbreak was detected in 2005, but it did not receive international attention until it was reported at the international AIDS meeting in Toronto last August.

The World Health Organization calls the extremely drug-resistant form "a grave public health threat" because of its potential explosiveness among the millions of H.I.V.-infected people in poor countries. It seems to be a lesser threat among people who do not have H.I.V., though it could be dangerous to the millions with weakened immune systems from treatment for cancer and other diseases.

XDR-TB is defined as tuberculosis that is resistant to the two most important antituberculosis drugs (isoniazid and rifampin), along with two other drugs: a member of the fluoroquinolone class and at least one of three others (capreomycin, kanamycin and amikacin).

A step lower on the resistance scale is a form of the disease called MDR-TB, for multidrug-resistant tuberculosis. An outbreak of that form struck in New York City in the early 1990s, and cost at least $1 billion in emergency measures to control and manage tuberculosis patients.

Experts say the tuberculosis outbreak in South Africa is the deadliest one that they can recall.

Although South African officials, who have known about the outbreak for a year, promised a prompt and full investigation, even experts there acknowledge that efforts are lagging.

"Unfortunately, we do not know much more than a year ago" mainly because "a systematic survey in each of the provinces has not yet started," Dr. Karin Weyer of the South African Medical Research Council told the Conference on Retroviruses and Opportunistic Infections here recently.

Dr. Weyer said in an interview that she had hoped that rapid surveys and screening tests would have been completed by now to show better the geographic extent of the disease.

Using statistics from recent years, Dr. Weyer said her team estimated that 6,000 new cases of multidrug-resistant tuberculosis occurred in South Africa each year and that the rate of treatment failure was about 10 percent. Assuming that most failures were due to the extremely drug-resistant form, a conservative estimate is 600 cases of XDR-TB in her country each year, Dr. Weyer said.

In data that her team examined, about 85 percent of patients infected with XDR-TB and H.I.V. died, she said. The fatality rate in H.I.V.-negative patients seemed lower, but could not be determined until they complete long-term therapy.

What is known is that the deadly XDR-TB strain has been found in more than 40 hospitals in all nine provinces of South Africa, she said.

The rest of sub-Saharan Africa is at risk, she went on, because "control of airborne infection is either totally inadequate or even absent" in virtually all of those countries.

The outbreak is not limited to Africa. Dr. Paul Nunn, a tuberculosis expert at the World Health Organization, told the meeting here that one or more cases of XDR-TB had been found in at least 28 countries. Extrapolating from data about the multidrug-resistant form of tuberculosis, Dr. Nunn estimated that two-thirds of the XDR-TB cases were from China, India and Russia.

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The recipe for spreading the disease is the same throughout the world: inappropriate use of antibiotics. When first-line drugs fail to kill the disease, Dr. Nunn said, doctors turn to a second group of drugs that are less widely used, and, they hope, more effective because the bacteria have not had a chance to become resistant to them.

“The little evidence we have suggests that this is not so much spread of resistant strains, but the creation of similar patterns of resistance in different strains around the world,” Dr. Nunn said, “because the drugs used are more or less the same everywhere, and unfortunately, so are the defects in the performance of TB control.”

South Africa has more laboratories to test tuberculosis strains for susceptibility to first- and second-line drugs than other sub-Saharan countries, Dr. Nunn said. He added, “Most African countries do not have a laboratory capable of carrying out first-line drug susceptibility tests, let alone for second-line drugs, which is technically more demanding.”

For those and other reasons, like a lack of doctors, health officials say they fear that tuberculosis may be spreading silently in other countries.

Experiments performed years ago have led some experts to speculate that drug-resistant tuberculosis bacteria are poorly transmissible. But that theory seems weakened by new studies from South African researchers working with colleagues from Harvard and the Centers for Disease Control and Prevention in Atlanta.

The researchers put caged guinea pigs in a ventilation stream leading from rooms housing patients with multidrug-resistant tuberculosis and possibly the extremely drug-resistant form. Skin tests showed that 80 percent of the animals were newly infected after four months, Dr. Weyer said.

XDR-TB may be just as infectious as regular tuberculosis and may be highly transmissible. And that is worrisome, Dr. Weyer said, because “most public health facilities in the developing world lack airborne infection control procedures.”

How the guinea pig findings translate to humans is uncertain because other studies have not been done or completed.

In one study, South African researchers tested 1,694 relatives and friends who had contact with 386 XDR-TB patients identified in Tugela Ferry. Among those contacts, only 12 cases of multidrug-resistant tuberculosis were found, and none of XDR-TB, Dr. Weyer reported.

The findings suggested that significant spread was not occurring in the community. But it was too soon to know, because even a drug-susceptible tuberculosis infection usually remains silent for years before it causes illness, Dr. Weyer said.

“This is the kind of exercise that we would like to see happening” in other areas and for longer periods to get a better understanding of the risk of transmission and getting sick, Dr. Weyer said.

The risk that the initial tuberculosis infection will progress to illness is compounded at 10 percent a year for those with H.I.V., compared with a lifetime risk of 10 percent among those who do not have the virus.

In medical journals and at scientific meetings, some doctors in South Africa and elsewhere have advocated enforced confinement of XDR-TB patients. But civil liberties aside, many experts say, these advocates have not thought through the practical aspects of such isolations. Enforced isolation “is much more difficult to implement than one

would think," Dr. Weyer said.

Because XDR-TB is believed to be incurable, such patients could be detained for life or until they die. All the while, infected patients may spread the disease to others.

Moreover, the disease is an occupational hazard for the health workers caring for patients; 4 were included among the 53 in the Tugela Ferry outbreak. Two additional cases in health workers were identified later.

So Dr. Weyer raised these questions, among others: What facilities would be used? Who would volunteer to take care of XDR-TB patients? How would these workers be protected? And without getting permission, how would health officials legally detect the many health workers who are infected with H.I.V.?

She offered no answers. And earlier this month, as if to illustrate the logistical hazards of caring for XDR-TB patients, 100 people walked out of a hospital in East London, South Africa, after paramedics wearing head-to-toe protection brought in eight patients with the disease.

Some South African hospitals are using engineering- and infection-control practices, like installing ultraviolet lights to kill tuberculosis microbes. Management studies show that health care facilities must be redesigned to prevent unnecessary contact between tuberculosis and H.I.V. patients in crowded clinics, X-ray departments, waiting lines and other areas, Dr. Weyer said.

On April 1, she said, South Africa plans to start field-testing 40,000 patients to determine the effectiveness of two new rapid tests to detect drug-resistant tuberculosis, and whether the results will lead to improved treatment outcomes. Elsewhere, researchers will test 60,000 patients under the direction of the Foundation for Innovative New Diagnostics in Geneva, Dr. Weyer said.

About 20 experimental drugs are being tested. But even if one is found effective in large-scale trials, it is unlikely to be marketed for a decade.

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