

Fast action urged to halt deadly TB

Technology holds the key to many of the challenges presented by a particularly virulent form of tuberculosis that broke out in South Africa last year. Countries across the region are making progress in keeping the threat at bay, but not fast enough.

Two new rapid diagnostic tests for multidrug-resistant tuberculosis (MDR-TB) are to be piloted in South Africa, dramatically cutting diagnosis time from two or more months to just two days. It will be the first time new technology is used to tackle the crisis of drug-resistant tuberculosis in Africa.

A pilot study to evaluate the tests in 40 000 tuberculosis patients started on 1 April in five South African provinces and is expected to last for 12 months.

"This is an important breakthrough, as it cuts the time for a definite diagnosis of MDR-TB," said Dr Karin Weyer, tuberculosis research director at the South African Medical Research Council.

Treating patients earlier will save lives, reduce the time spent on inappropriate and ineffective treatment, and reduce the spread of MDR-TB within crowded hospitals and clinics. Perhaps most importantly, it will be possible to diagnose patients with extensively drug-resistant tuberculosis (XDR-TB) at a much earlier stage.

In recent years, doctors had seen isolated cases that were highly resistant to drugs. But in March 2006, the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention first reported XDR-TB as a serious emerging threat to public health and TB control.

XDR is defined as tuberculosis that is resistant to the two most important antitubercular drugs, rifampicin and isoniazid, as well as to any fluoroquinolone and at least one of three second-line injectable drugs: kanamycin, amikacin and capreomycin.

Rapid diagnosis of drug-resistant tuberculosis is crucial for patients infected with HIV. The HIV-positive patients infected with XDR-TB in last year's epidemic in Tugela Ferry, KwaZulu-Natal, survived a median of just 16 days from the time of sputum (matter coughed up from the lungs) collection.

Since September 2006, about 183 people, most of whom were HIV positive, have died from XDR-TB in

South Africa. XDR-TB could exacerbate the HIV/AIDS epidemic in South Africa, where about five million out of a population of 45 million people are HIV positive and as many as 1000 people die of AIDS-related complications every day.

Although the 2007 WHO report, *Global tuberculosis control: surveillance, planning, financing*, announced the good news that tuberculosis prevalence and death rates have been falling globally, the case load continues to grow in WHO's African, Eastern Mediterranean and South-East Asian Regions (www.who.int/tb/xdr/globaltaskforce_update_feb07). And while HIV testing for tuberculosis patients is increasing fast in the African Region, little effort has been made to screen HIV-infected people for tuberculosis even though this is a good method for case finding.

The Foundation for Innovative New Diagnostics (FIND), a non-profit organization based in Geneva, is behind the new rapid tests. Weyer said an interim analysis would be carried out six months into the 12-months pilot study. If the results are positive, Weyer said she hoped the Department of

Health would roll-out the tests to the remaining provinces.

Improved diagnosis was one of the priorities identified by the WHO Global XDR-TB Task Force last October. Following this, eight countries in southern Africa drew up a regional strategy to manage and prevent XDR-TB. Since then, each has delivered individual action plans to WHO and, in February, WHO released a 20-page report, *The Global Task Force on XDR-TB Update*, on XDR-TB in southern Africa.

Dr Mario Raviglione, director of WHO's Stop TB Department, said there has been some progress in the region. "Things are moving, but it is far too slow for the seriousness of the epidemic," he told the *Bulletin*. Weyer agreed: "I don't see any sense of urgency from the health authorities in tackling the problem in the serious way that the situation deserves."

Another priority identified by the task force was for countries to conduct rapid surveys to find out the true extent of XDR-TB.

Rapid surveys to determine the prevalence of resistance to second-line



Woman and child infected with multidrug-resistant tuberculosis receiving treatment at the Brooklyn Chest Hospital in Cape Town, South Africa. Cape Town has one of the highest incidences of tuberculosis in the world.

Lung Health Image Library/Gary Hampton

drugs in patients considered to be at high risk have been done in Lesotho and Botswana. Similar surveys are planned in Malawi, Mozambique, Namibia and Swaziland in the next few months.

Madagascar, Mozambique and the United Republic of Tanzania are doing nationwide surveys of resistance to antitubercular drugs, while Angola, Lesotho, Malawi, Namibia, South Africa and Zimbabwe plan to start such surveys later this year, or in early 2008.

Weyer said: "The department of health was supposed to start this last year in South Africa but it has not happened, which is very disappointing." The country's department of health has confirmed 269 cases of XDR-TB in South Africa to date, but Weyer believes the true figure is much higher.

"A previous survey showed 6000 cases of MDR-TB a year. If we estimate that up to 10% of these may be XDR-TB, then a conservative estimate is 600 cases." In the United States of America, 5% of MDR-TB cases are XDR; in Latvia, 19% of MDR-TB cases are XDR.

"For doctors on the ground the area most needing improvement is laboratory capacity, and perhaps sur-

prisingly, IT [information technology]," said Dr Mark Sonderup, specialist physician at Groote Schuur hospital in Cape Town. "Patients are mobile, so they move around between hospitals and between primary and secondary care. Tests are often duplicated or are lost in the system. We really need a central database of TB patients."

In the rest of southern Africa laboratory facilities tend to be even worse than those in South Africa. Researchers visiting Lesotho recently found the country's laboratory service was unable to diagnose drug-resistant forms of tuberculosis. FIND has sent technicians to help upgrade Lesotho's laboratory facilities, and these should be up and running in a few months. The Open Society Institute, founded by George Soros, donated US\$ 3 million

to help health-care workers in Lesotho treat people infected with drug-resistant tuberculosis and HIV/AIDS more effectively. The funds will also go towards developing the first global treatment guidelines for this deadly combination of diseases.

South Africa has made progress in infection control. Every province has identified one facility to treat patients

with drug-resistant tuberculosis, and these facilities are being upgraded and infection control procedures implemented. The South African Medical Research Council is running infection control training throughout the country.

An investigation by a team of epidemiologists, including WHO officials, into what happened at Tugela Ferry, started in March. Within a few months, it should be clear to what extent the epidemic arose out of poor infection control.

Could the epidemic in Tugela Ferry happen again? Weyer thinks so: "We are concerned that such outbreaks are happening all the time and are not detected. Deaths can be obscured by HIV and are not attributed to XDR-TB."

At the time of the Tugela Ferry epidemic, South African doctors had a limited drug armoury, as two of the nine antitubercular drugs were not available. However, the South African authorities have moved fast to ensure that capreomycin and *para*-aminosalicylic acid are now available.

But Raviglione cautioned: "Even if all the drugs are available, the important thing is to make sure these are delivered correctly, with patients counselled and supervised properly. In many areas basic TB control is lacking and if we don't have the basics in place, then the result is drug resistance." ■

Jacqui Wise, *Cape Town*

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Russian oblast is model in fight against TB

The chaos following the collapse of the Soviet Union in 1991 triggered a tuberculosis (TB) epidemic across the Russian Federation. A decade and a half later, the Russian "oblast" or region of Orel is reporting progress in fighting killer strains of *Mycobacterium tuberculosis* that are resistant to common TB drugs.

By the end of the 1990s, the tuberculosis epidemic had reached alarming proportions across the Russian Federation. Orel oblast, in the south-western part of the country, was no exception. "The TB situation in the region was very bad, especially from 1999 to 2000," said Dr Boris Kazyenny, chief doctor at Orel Oblast Tuberculosis Dispensary in the regional capital of Orel.

Kazyenny recalled how the supply chains of essential medicines for tuberculosis broke down and, with that, the quality of treatment.

"We didn't have enough essential drugs so we had to prescribe an incomplete course of chemotherapy and many patients did not adhere to the treatment regimen," Kazyenny told the *Bulletin*. "That's why after the beginning of the 1990s, many of our patients did not make a full recovery and continued to transmit bacteria."

Tuberculosis specialists have long known that erratic drug supplies and failure to make sure patients complete treatment lead to drug resistance.

But amid falling living standards, mass migration and a crumbling health

system after the 1991 collapse of the Soviet Union that resulted in drugs shortages, doctors in the Russian Federation had little choice but to administer ineffective and incomplete treatment.

In November 1999, the region introduced the World Health Organization (WHO)-recommended DOTS strategy and, in November 2002, it started implementing the DOTS Plus strategy to deal with drug-resistant tuberculosis.

"We introduced international diagnostic and treatment standards for the management of tuberculosis patients," Kazyenny said. "Thanks to all these measures, we managed to stabilize the tuberculosis epidemiological situation in Orel oblast. By 2006, incidence had decreased by 26.5%, mortality by 48.3% and prevalence by 44.5%."

DOTS originally stood for Directly Observed Treatment, Short course. Now