

Southern Africa is moving swiftly to combat XDR-TB

Southern African leaders are working with WHO to fight a new health threat that is particularly dangerous for people with HIV/AIDS: extensively drug-resistant tuberculosis or XDR-TB.

Countries in southern Africa have moved quickly to draw up a regional strategy for managing and preventing extensively drug-resistant TB. This follows an outbreak in South Africa that demonstrated the high mortality of XDR-TB when associated with HIV infection.

The South African ministry of health called for an urgent meeting with WHO and representatives from other countries in the region in order to develop a regional approach to prevent and control TB, including XDR-TB. Representatives from South Africa, Lesotho, Malawi, Mauritius, Mozambique, Namibia, Swaziland and Zimbabwe contributed to the sub-regional framework, which builds on the recommendations produced in October by the WHO Global Task Force on XDR-TB.

Each of the eight countries was also asked to deliver individual action plans by 10 November. These included details of current status and key activities required in the following areas: basic TB control; clinical management of multidrug-resistant (MDR) and XDR-TB; laboratory capacity; second-line drug management; infection control; surveillance; and advocacy and communications. The action plans are also to outline any technical support needed from WHO and to include a budget for action. Most countries in the region have called for technical assistance in case management, data collection and infection control.

Worldwide attention was focused on South Africa when a research project publicized a deadly outbreak of XDR-TB in the small town of Tugela Ferry in

KwaZulu-Natal. Of 536 TB patients at the Church of Scotland Hospital, which serves a rural area with high HIV rates, some 221 were found to have multi-drug resistance and of these, 53 were diagnosed with XDR-TB.

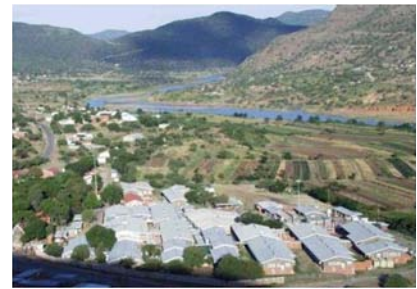
Fifty-two of these patients died, most within 25 days. Of the 53 patients, 44 had been tested for HIV and all 44 were found to be HIV-positive. The patients were receiving antiretrovirals and responding well to HIV-related treatment, but they died of XDR-TB. The study results were presented at the International AIDS conference in Toronto in August. Since the study, 10 more patients have been diagnosed with XDR-TB in KwaZulu-Natal. Only three of them are still alive.

“Tugela Ferry was a wake-up call that there were problems in the management of TB in southern Africa,” says Dr Mario Raviglione, WHO Stop TB Department Director. “It is vital that we now go back to Tugela Ferry to gather information about what went wrong so that we can learn any lessons from this.”

Dr Karin Weyer, TB Research Director at the South African Medical Research Council, warns: “We are afraid that this outbreak of XDR-TB might be the tip of the iceberg, as we haven’t really looked properly elsewhere.” She adds: “There are higher prevalence rates in pockets of eastern Europe and South-East Asia but we are particularly

worried in South Africa given our HIV problem, because of the rapid spread of XDR-TB amongst HIV patients and their rapid death.”

The incidence of TB is decreasing or stable in all regions of the world except for Africa, where it is on the



Church of Scotland Hospital in South Africa, where XDR-TB was found.

WHO

increase, with HIV fuelling TB. “Our big concern is that if we start seeing more XDR-TB cases in Africa we could see a major epidemic because of the high rates of HIV,” says Dr Raviglione. HIV fuels XDR-TB. Once someone is infected with TB there is a 5–10% lifetime risk of developing the disease, but in a person with HIV the risk is 5–15% a year. The Global Task Force has said that control of XDR-TB will not be possible without close coordination of TB and HIV programmes and interventions.

One of the priorities identified is to determine the magnitude of the problem of XDR-TB in the region. XDR-TB has now been reported in all provinces of South Africa, yet so far there have been no confirmed reports of cases in other countries in the region. Quick surveys are needed to determine where XDR-TB is and then longer-term surveillance needs to be put in place. Investment is urgently needed to strengthen the region’s laboratory capacity.

A key priority identified in the sub-regional framework is to strengthen basic TB control and so prevent drug resistance from occurring in the first place. If DOTS, the WHO-recommended treatment strategy for detection and cure of TB, is implemented properly it can prevent the development of drug resistance. Dr Anton Stoltz, Director of Infectious Diseases at the

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Foundation for Professional Development in Pretoria said: "In South Africa we are aiming at an 80% cure rate for TB but are only achieving a 50% cure rate, which is just not good enough. This is creating the problem of multi-drug-resistant TB."

"TB medicines must be taken for 6–8 months to kill off all the different organisms," Stoltz said. "The problem is that when people feel better they stop taking the drugs. Or in remote areas there may be a problem getting people to monitor the drug programme."

It makes economic sense to treat TB properly in the first place. It costs R400 (US\$ 52) to treat each patient with ordinary TB.

If a patient develops multidrug-resistant TB, the cost of treatment dramatically increases to R24 000 (US\$ 3168), which includes hospitalization and more expensive drugs.

No new TB drugs have been developed for four decades. There are several promising new candidates, but none will be available for at least five years. More investment in TB drug development is needed to guarantee future drugs supplies. A further complication is the interaction of antiretroviral drugs with TB medication, while little is known about the interaction between second-line TB drugs and antiretrovirals.

Second-line TB drugs are less effective and more toxic than the first-line options. "In some cases the side-effects are extremely severe. It can be a choice of going deaf or not being treated," said Weyer.

The strain of tuberculosis in KwaZulu-Natal is resistant to seven of the nine drugs that have been tested, and the remaining two drugs are not available in South Africa. A manufacturing plant to produce capreomycin sulfate is currently being built in South Africa, and the Medicines Control Council is fast-tracking the application for local registration of the drug. In the meantime, pharmaceutical company Eli Lilly has donated an emergency supply of capreomycin sulfate to the South African Department of Health.

XDR-TB has been defined by the WHO Global Task Force as resistance to at least rifampicin and isoniazidin in addition to any fluoroquinolone, and at least one of the three following injectable drugs: capreomycin, kanamycin and amikacin. The existence of XDR-TB was first mentioned in March 2006 in a report published by the US Centers for Disease Control and Prevention and WHO. XDR-TB has been found in all regions of the world but is rare. MDR-TB usually has to occur before XDR-TB arises. Experts believe that wherever second-line drugs to treat MDR-TB are being misused, there is a risk of XDR-TB.

Another priority is to improve diagnosis. "The world urgently needs new, safe and affordable diagnostics to simplify case detection," says Raviglione. "Despite scientific progress that is rapidly changing other fields, most of the world's TB patients have access only to conventional microscopy.

This method at times requires repeated testing, may miss cases, and is not adequate for many HIV co-infected patients who may have TB that is not detectable with sputum examination only." Plans have just been announced for the WHO Stop TB Department to col-

laborate with the Foundation for Innovative New Diagnostics (FIND) to start demonstration projects and introduce rapid-culture technology and new rapid drug-resistance tests in the southern African countries most affected. This will reduce the time needed to confirm a diagnosis of TB drug resistance from

as long as 3 months to just 2 weeks, thus speeding up treatment.

It is vital that infection control procedures are improved in hospitals to stop XDR-TB from spreading. Health workers in South African hospitals are starting to be trained in infection control procedures. One hospital in each province has been designated as an MDR centre where all such cases are to be sent. The policy is to hospitalize patients with MDR and keep them confined until they are no longer infectious. Efforts are being made to improve tracing of contacts to be able to find patients in an early stage of the disease before they start spreading it to other people.

TB experts at the Union World Conference on Lung Health in Paris on 31 October said that US \$95 million is urgently needed to address the threat of XDR-TB in 2007. Meanwhile, Raviglione and other TB and HIV leaders called on governments and funding agencies to provide resources to XDR-TB from spreading further. ■

Jacqui Wise, *Cape Town*

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Dr Mario Raviglione, WHO Stop TB Department Director.



TB/AIDS patients at Accra Teaching Hospital in a TB ward, Ghana.

WHO/TDR/Crump