

Divisive drug-resistance

A new battle line in tuberculosis control has been drawn where antibiotic misuse and mismanagement have their origins – in weak and dysfunctional health-care systems. Jane Parry looks at how countries in Asia are rising to the challenge.

Even in places where tuberculosis control has seen the greatest progress, such as many of the countries in WHO's Western Pacific Region, the fight against drug-resistant tuberculosis faces huge challenges.

"In most of the high-burden countries in the region, MDR-TB is either managed outside the public health sector or in the public sector, but outside the national tuberculosis programme" says Dr Pieter van Maaren, regional adviser for Stop TB in WHO's Western Pacific Region, adding that treatment outside national programmes tends to be poor.

"In many countries public health is under a different department to curative services, and it's difficult for national tuberculosis programmes to control what is happening in hospitals. As a result all kinds of poor management of MDR-TB are happening."

Multidrug-resistant tuberculosis (MDR-TB) refers to strains of the tuberculosis *bacillus* that are resistant to at least the two most efficacious drugs (rifampicin and isoniazid), while a sub-set of MDR-TB, extensively drug-resistant tuberculosis (XDR-TB), refers to strains that are resistant to nearly all current tuberculosis drugs,

and is considered to be virtually incurable. Growing drug resistance is largely the consequence of decades of mismanagement of antibiotics. Quality of antibiotics also contributes, although in the case of tuberculosis the true extent of this is unknown.

Efforts to control drug-resistant forms are hampered by deep divisions in health-care systems. One division is between those with and without access to health care, others are the divides between public health and curative services, between private and public health-care providers and between health-care and other sectors.

“The causes of M/XDR-TB are a reflection of weak health-care systems.”

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In countries where hospital treatment is offered on a fee-for-service basis, such in China, this can create a major barrier to referral for treatment under the national tuberculosis pro-



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Medicines for tuberculosis. The drugs for the lengthy treatment of MDR-TB can cost more than 100 times that of the drugs to treat common tuberculosis strains.

grammes. For countries with a strong private sector, such as the Philippines, the cost of treatment is prohibitive for most patients with MDR-TB. "Many patients start treatment then drop out," says van Maaren.

China and India account for half of the world's estimated MDR-TB cases and are among the 27 countries where 85% of these cases have been found globally.

"The causes of M/XDR-TB are a reflection of weak health-care systems," agrees Dr Ernesto Jaramillo, TB drug resistance team leader at WHO's Stop TB Department.

"For example, one of the major barriers to access to treatment is the limited health-care work force that is properly trained," Jaramillo says, adding that this is a problem related to the dynamics of the labour market in general. "Ministries of health have limited capacity to affect those market forces," he says.

Efforts to control MDR-TB are particularly vulnerable to such pressures because of the high level of human resources needed to diagnose and treat patients effectively. "To treat someone with MDR-TB takes two years of daily work, the drugs need to be directly observed and taken five or six days a week. The drugs are quite toxic and people develop intolerance quickly. If a patient starts to self-select the drugs they take, it amplifies the resistance within as little as one month," says Jaramillo. "You can deal with drug-susceptible TB with fairly simple health-care infrastructure, when it comes to MDR-TB what you need is more sophisticated."



WHO/Nick Otto

Patient with MDR-TB is given medicine in China.

Since the World Health Organization (WHO) began systematically surveying drug resistance to tuberculosis treatments in 1994, it has observed a continual increase in drug resistance. But the idea of tackling MDR-TB head-on has been a more recent development.

"In the 1980s the common wisdom was that MDR-TB was impossible to diagnose and treat," says Jaramillo. "There were some centres in the United States [of America] and Europe, where a few experts were treating MDR-TB, but it was very complicated and no-one dared to think about treating it in very low-resource settings like, for example Lesotho or Timor-Leste."

Then in 2000, WHO and its partners, including *Médecins Sans Frontières* and the Harvard-based non-governmental organization Partners in Health, formed the Green Light Committee to address the three barriers to tackling MDR-TB: the high cost of drugs, lack of policy and lack of access. "The Green Light Committee Initiative negotiated with the pharmaceuticals industry to get a 95% reduction in the cost of drugs, and the WHO worked with its partners to pilot the complex public health interventions of delivering these drugs to patients in low-resource settings," says Jaramillo. By 2005, the Green Light Committee Initiative had accumulated enough evidence to pave the way for a new WHO policy on treating MDR-TB in poor settings.

In 2006, tackling MDR-TB became a core component of the new Stop TB Strategy. More recently, the fight against M/XDR-TB received a significant boost with the Ministerial Meeting of the 27 High M/XDR-TB Burden Countries held in Beijing in April 2009, closely followed by a resolution passed at the World Health Assembly (WHA) the following month on the prevention and control of M/XDR-TB.

"The call for action endorsed by the ministers of health at the Beijing meeting, and the WHA resolution, reflect the notion that M/XDR-TB is a health system problem, instead of one limited to patient behaviour. Insufficient investment has resulted in lack of access to drugs," says Jaramillo.

China's Ministry of Health's decision to host the meeting gave the country a good opportunity to focus attention at provincial level on the pressing problem of M/XDR-TB, according



WHO/Nick Otto

Working with tuberculosis samples.

to Dr Cornelia Hennig, a Beijing-based medical officer with WHO's Stop TB Department. "Inviting high-level political leaders from the provinces to this high-profile international meeting, which was opened by Vice Premier Li Keqiang, communicated the message that M/XDR-TB is very high on the agenda," she says.

Pilot projects financed by the Global Fund to Fight AIDS, Tuberculosis and Malaria are already under way in various countries including projects in parts of China that institute collaboration between the public health and hospital systems.

"Drug-susceptible TB patients can be managed on an outpatient basis but the sick and those with M/XDR-TB need to be cared for in hospital, so you need good collaboration between the two systems," explains Hennig. "The outcome is advantageous for both partners: the TB programme is strengthened because it can offer care for all its patients. The hospitals learn from the TB programme and institute a more rational use of resources through the introduction of standards and guidelines; this results in an overall strengthening of the health system."

For countries that already have a high M/XDR-TB burden, the challenge is huge. The target is 80% detection and treatment by 2015, against an estimated current 5% detection rate and only 3% of cases being treated according to WHO-recommended standards. Cost is still an issue. The drugs for the lengthy treatment of MDR-TB can cost

more than 100 times that of the drugs to treat common tuberculosis strains. Furthermore, while much is already known about the M/XDR-TB burden overall, for populations at risk for co-infection with other diseases such as HIV, the outlook is still unknown.

"We know there are 1.4 million new incident cases of TB also infected with HIV, with nearly 80% of the burden in sub-Saharan Africa," explains Haileyesus Getahun, TB/HIV team leader in WHO's Stop TB Department. "But how many of those cases are MDR-TB? We don't know, we need more research and drug surveillance efforts that included HIV testing as an integral part. The critical thing is we don't know the magnitude of HIV/MDR-TB co-infection. But what we know is that the outcome of such a combination is deadly to patients".

In addition to surveillance and treatment, training is crucial to the fight against M/XDR-TB. This is under way at a WHO collaborating centre in Latvia where national tuberculosis programme staff are trained in the management of MDR-TB, and a similar centre is being set up in the Philippines. "There should be cause for optimism regarding MDR-TB," says van Maaren. "We are only at the beginning of trying to intervene in this problem, and very few people are being treated in the way they should be, but there is a clear willingness of countries to get a grip on this problem." ■