

## XDR tuberculosis can be cured with aggressive treatment



Multidrug-resistant (MDR) tuberculosis, once thought of as a problem largely confined to Russia and eastern Europe, has emerged as a substantial threat to treatment and control programmes for tuberculosis worldwide. Between 2002 and 2006, 81 countries reported cases of MDR tuberculosis, with about 490 000 cases emerging worldwide in 2006 alone.<sup>1</sup> Although MDR tuberculosis can be effectively treated with second-line regimens,<sup>2</sup> improvements in resistance testing have revealed what is now defined as extensively drug-resistant (XDR) tuberculosis,<sup>3</sup> with cases recorded in 45 countries.<sup>1</sup> XDR tuberculosis, defined as MDR tuberculosis with additional resistance to the two most important second-line classes (fluoroquinolones and the second-line injectable agents), is often referred to as untreatable, and as such has provoked fear among health staff, patients, and affected communities.<sup>4,5</sup>

The Russian Federation has one of the highest prevalences of MDR tuberculosis in the world, estimated at 19% of all tuberculosis cases and rising to 50% in prisoners with tuberculosis.<sup>1,6</sup> Unsurprisingly, a considerable proportion (about 7%) of these cases are found to have XDR tuberculosis when tested.<sup>1</sup> In today's *Lancet*, Salmaan Keshavjee and colleagues<sup>7</sup> report the outcome of treatment for 29 patients with XDR tuberculosis in part of a larger treatment programme for MDR tuberculosis in Tomsk, Russia. 14 (48%) patients were successfully treated in this setting.

Despite the small number of patients, there are lessons to be learnt from this experience. Patients with XDR tuberculosis were not differentiated from those who had MDR tuberculosis and enrolled in the treatment programme. All patients were treated with a regimen that aimed to include five effective antituberculosis drugs on the basis of in-vitro testing of drug susceptibility and previous treatment. Additionally, a fluoroquinolone (ofloxacin or levofloxacin), together with the second-line injectable capreomycin, was included in regimens even when drug resistance was found (although not counted as part of the five effective drugs). In Keshavjee and colleagues' study, this aggressive approach, which included the full range of available second-line agents from the outset, contributed to the successful treatment of two-thirds of patients with MDR tuberculosis but without the XDR form, and nearly half

of those with XDR tuberculosis. This result was achieved despite extensive disease and previous treatment, high consumption of alcohol and use of other illicit drugs, and high rates of current or previous imprisonment (all factors likely to complicate treatment of MDR tuberculosis). However, none of the patients with XDR tuberculosis and only 1% of the remaining patients with the MDR form had HIV infection in Tomsk.

The programme in Tomsk is the result of a partnership between regional tuberculosis and prison services, an international tuberculosis laboratory able to test for second-line drug susceptibility, and an international medical non-governmental organisation that provided good clinical support and resources. Such a partnership reveals the elements needed to effectively treat both forms of tuberculosis (MDR and XDR): ownership and commitment of local treatment services for tuberculosis, sufficient laboratory capacity, specific clinical skills, and dedicated resources.

Perhaps the most important lesson for drug-resistant programmes elsewhere is a commitment by tuberculosis services to provide the best possible care and treatment for individual patients. Although international organisations can provide technical assistance and help to mobilise funds, effective patient-centred treatment is up to governments to provide, because the only way to reduce further transmission of highly

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Guard at gate of ward for XDR tuberculosis, Brooklyn Infectious Disease Hospital, Cape Town

resistant strains will be to diagnose and successfully treat as many patients as possible.

XDR tuberculosis attained international prominence in 2006 after an outbreak in South Africa<sup>8</sup> in which all of the 53 reported cases eventually died. All patients with known HIV serostatus were positive. Although the overall proportion of MDR tuberculosis in tuberculosis cases is low in many settings with high HIV prevalence, the incidence of MDR and XDR tuberculosis might be very high because of much higher overall incidence of tuberculosis. On the basis of the latest worldwide estimates, the annual incidence of MDR tuberculosis in Russia is 26 per 100 000 population. By contrast, although MDR tuberculosis is estimated at only 2.6% of tuberculosis cases in South Africa, this equates to an incidence of 32 per 100 000 every year, of which an estimated 6% of patients have XDR tuberculosis.<sup>1</sup> In view of this high burden, Keshavjee and colleagues' results need to be urgently replicated in other settings, particularly for HIV-positive individuals.

At present less than 5% of the estimated 490 000 patients with MDR and XDR tuberculosis arising every year are likely to receive effective treatment, which highlights the urgent need to scale-up treatment worldwide.<sup>1,9,10</sup> Toxic effects of the drugs and long duration of treatment contribute to the problem, and the development of new drugs to treat both drug-susceptible and drug-resistant tuberculosis should be adequately supported.<sup>11</sup> Until these new drugs are developed, we are responsible for effective use of available drugs. Keshavjee and colleagues have shown that both MDR and XDR tuberculosis can be cured with aggressive treatment, with use of the most effective antituberculosis drugs available. Although we should

be cautious in our hope to attain such success rates in settings with a high prevalence of HIV, aggressive treatment is the logical strategy to provide the best chance of cure while avoiding the creation of additional drug resistance.

\*Helen Cox, Cheryl McDermid

Macfarlane Burnet Institute for Medical Research and Public Health, Melbourne, VIC 3004, Australia (HC); and Médecins Sans Frontières, Cape Town, South Africa (HC, CMcD) hcox@burnet.edu.au

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