M/XDR-Tuberculosis: Therapy as Prevention

C. Lange[1, 2, 3, 4]

[1] Forschungszentrum Borstel
[2] Universität Lübeck
[3] Karolinska Institut, Stockholm, Schweden
[4] Universität von Namibia, Windhoek, Namibia

As the incidence of tuberculosis (TB) has been globally declining over the past decades the World Health Organization (WHO) is now proposing the elimination of TB in Europe. However, in the absence of an effective vaccine for the prevention of TB, elimination of TB will not be possible in the near future due to the emergence of drug-resistant strains of *Mycobacterium tuberculosis*. Forty-four percent of all patients identified with multidrug-resistant or extensively drug-resistant tuberculosis (MDR-TB, XDR-TB) worldwide live in the European Region of the WHO. Management and prognosis of patients with M/XDR-TB is dramatically different from patients with pan drug-susceptible TB in several ways.

While successful treatment outcome can generally be achieved in more than 80% of patients with pan drug-susceptible TB, a recent study from the European Centers for Disease Prevention and Control (ECDC) reported treatment success in patients with MDR-TB and XDR-TB of only 32 percent and 19 percent, respectively. Adverse drug effects often hamper adherence to M/XDR-TB therapy. Overall costs for the treatment of patients with MDR-TB and XDR-TB in the European Union have been estimated at 55.000 Euros and 168.000 Euros, respectively, compared to the costs of treating a patients with pan drug-susceptible TB of approximately 7.800 Euros in total. While the duration of combination drug therapy in drug-susceptible TB is 6 months (with 2 drugs for daily treatment in the continuation phase of treatment), current guidelines for M/XDR-TB recommend total treatment duration of at least 20 months (with at least 4 drugs for daily treatment in the continuation phase of treatment).

In this aspect mycobacterial diseases differ from most other bacterial infectious diseases where the duration of combination antibiotic therapy required to achieve relapse-free cure is substantially shorter. The optimal duration for treatment of TB likely differs between individuals and depends on a variety of variables, such as the extent of the disease, the immune status of the host and the virulence and the drug-resistance of the causative strain of *M. tuberculosis*. Personalization of the duration of treatment for TB by identification of bio-signatures that will eventually lead to individual recommendations for the duration of anti-TB therapy, especially for patients with M/XDR-TB, is highly desired.

However, the WHO estimates that less than 20% of patients with M/XDR-TB receive an adequate therapy at all.

Early detection of drug-resistant tuberculosis by molecular methods and initiation of an adequate treatment regimen is the most effective measure to stop transmission of drug-resistant strains of *M. tuberculosis* and an important step on the way to elimination of tuberculosis.

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Bibliography
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Correspondence
Christoph Lange
Forschungszentrum Borstel
Parkallee 35
23845 Borstel
clange@fz-borstel.de