

What is Multidrug-Resistant Tuberculosis (MDR-TB)?

Tuberculosis, commonly referred to as TB, is often thought to be a “disease of the past.” But it has re-emerged as a global threat, with one third of the world’s population latently infected. There is a rapid increase due to HIV/TB co-infection (in some regions, 75 percent of HIV-positive patients are also infected with TB). Two million people die from TB every year, making this disease the second-leading cause among infectious diseases of adult deaths.

TB is an airborne bacterial infection (transmitted, for instance, by coughing) that can spread to any organ in the body, but is most often found in the lungs. The symptoms of TB include unexplained coughing for more than two to three weeks, fever, weight loss, chest pain, and night sweats.

Multidrug-resistant tuberculosis (MDR-TB) is a type of tuberculosis that often develops in patients who do not adhere to or complete the proper treatment for regular TB. This can occur when a physician does not prescribe a proper treatment regimen, or when a patient is unable to stick to the lengthy therapy. Once a strain of MDR-TB develops, it can be spread to other people just like “normal” TB.

The World Health Organization and the International Union Against Tuberculosis and Lung Disease have reported that in several regions around the world there is an MDR-TB prevalence of greater than 3 percent among newly diagnosed TB cases. Detection and treatment of all forms of drug-resistant tuberculosis must be an integral part of any TB- treatment program.

There are many challenges associated with the treatment of MDR-TB.

MDR-TB patients respond poorly to treatment with drugs for regular TB (first line drugs). MDR-TB requires a complex diagnosis, the use of second line drugs, and a much longer time commitment for treatment (up to 24 months, compared to 6 to 9 months for regular TB). Second line drugs are more expensive, and have more side effects. Additional barriers include extensive laboratory requirements to conduct culture and drug-susceptibility testing. This is why many programs choose hospitalization, at least for the initial portion of the therapy. Hospitalization, however, greatly increases the risk of transmission of MDR-TB to both staff and patients, especially those infected with HIV.

There is an urgent need for increased knowledge among health care professionals both in the public and private sector (physicians, nurses, and laboratory personnel) about early diagnosis, proper treatment, and monitoring of anti-microbial resistance.

XDR-TB

Recently, the Centers for Disease Control and the World Health Organization announced the worldwide emergence of XDR-TB—extensively drug-resistant tuberculosis. In Eastern Europe, 14 percent of MDR-TB patients have been diagnosed with XDR-TB. The phenomenon of XDR-TB gained international attention with the October 2006 outbreak in South Africa.

Just as MDR-TB is caused by improper or incomplete treatment with standard (first line) TB drugs, XDR-TB is caused by improper or incomplete treatment with MDR-TB (second line) drugs. XDR-TB is resistant to even more drugs than is MDR-TB, and treatment options are severely limited. The risk of the development of completely untreatable strains is high, so strict adherence to proper treatment of TB and MDR-TB is crucial.

The World Health Organization defines XDR-TB as tuberculosis that is resistant to any fluoroquinolone and at least one of three injectable second line drugs (capreomycin, kanamycin, and amikacin), in addition to isoniazid and rifampicin, the two most powerful first line drugs, to which MDR-TB is resistant.

Therapies for MDR-TB

Only a small number of second line (reserve) drugs are effective in curing MDR-TB, yet a treatment regimen needs to include at least four different drugs. MDR-TB treatment can be done either with standardized or individualized regimens depending on health care programs, facilities, and patient characteristics. The prolonged treatment period, with unpleasant and sometimes severe side-effects, often results in a lack of patient compliance and the need for supervised treatment, such as that outlined in the [World Health Organization's DOTS-Plus](#), (Directly Observed Treatment, short course) program ("Plus" referring specifically to MDR-TB) .¹

All TB treatment requires multi-drug therapy. Even some TB strains are now resistant to first line drugs, leaving only second line drugs, which are a last resort.

MDR-TB can be treated effectively with a combination of second line drugs, including two Lilly antibiotics: capreomycin (Capastat®) and cycloserine (Seromycin®).

- Capreomycin is a bactericidal agent used to treat pulmonary infections caused by capreomycin-susceptible strains of *M. tuberculosis* when the primary agents (isoniazid, rifampicin, ethambutol, para-aminosalicylic acid, and streptomycin) have been ineffective or cannot be used because of toxicity or the presence of resistant *tubercle bacilli*.
- Cycloserine is a bacteriostatic agent. It is indicated in the treatment of active pulmonary and extra-pulmonary tuberculosis (including renal disease) when the causative organisms are susceptible to this drug and when treatment with the primary medications (isoniazid, rifampicin, ethambutol and streptomycin) has proved inadequate.

MDR-TB

1. WHO Guidelines for MDR-TB Management