BACKGROUND ON MDR-TB

Tuberculosis (TB)

Tuberculosis (TB) is often thought to be a “disease of the past,” but about one-third of the world's population carries a latent strain of the disease. Two million people die from TB each year, one every 20 seconds, and the spread of the disease has been fueled by HIV/TB co-infection. HIV infection weakens the immune system. If a person’s immune system gets weak, TB infection can activate and become TB disease. In some parts of the world, 75 percent of HIV-positive patients also are infected with TB, and TB is also the leading killer of people with AIDS. TB is an airborne bacterium that can spread to any organ of the body, but most often is found in the lungs. Symptoms may include severe and prolonged coughing, fever, weight loss, chest pain and night sweats.

Multidrug-Resistant Tuberculosis (MDR-TB)

The World Health Organization (WHO) defines multidrug-resistant tuberculosis (MDR-TB) as resistance to at least rifampicin and isoniazid, two of the first line anti-TB medicines. It is a type of TB that often develops in patients who do not adhere to treatment for regular TB, have failed first-line treatment or contracted the disease unknowingly. Treatment for regular, first-line TB lasts six to nine months and is administered under the direct observation of a healthcare worker. In much of the developing world, people find it very difficult to adhere to such a long, rigorous course of treatment, which requires isolation from families and friends to prevent contamination.

WHO 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 three percent among newly diagnosed TB cases. Failure to comply with treatment for MDR-TB can lead to even more-virulent forms of the disease, including extensively drug-resistant tuberculosis (XDR-TB).

There are many challenges associated with the treatment of MDR-TB, which does not respond well to treatment with first-line medicines. MDR-TB is complex to diagnose, and the course of treatment can last up to 24 months. Significant human resources are required to oversee treatment and compliance in countries where healthcare workers are scarce. Patients choosing hospitalization for the initial treatment period can increase the risk of MDR-TB transmission to staff and patients, particularly those already compromised by HIV/AIDS. There is an urgent need for additional training of healthcare workers on the prevention of transmission of TB within healthcare facilities, as well as training in diagnosis, treatment and monitoring of resistance.

Therapies for MDR-TB

Current treatments can be effective in curing MDR-TB, but new, faster-acting medicines are needed. MDR-TB treatment is often supervised as part of the WHO DOTS program (Directly Observed Treatment, Short-course), and all TB treatment requires multidrug therapy. MDR-TB can be treated effectively with a combination of Lilly's two second-line 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 medicine and when treatment with the primary medications (isoniazid, rifampicin, ethambutol and streptomycin) has proven inadequate.

Extensively Drug Resistant Tuberculosis (XDR-TB)

The WHO defines XDR-TB as tuberculosis that is resistant to isoniazid and rifampicin, the two most powerful first-line anti-TB medicines; any fluoroquinolone; and at least one of three injectable second-line medicines (capreomycin, kanamycin and amikacin).

In 2006, the U.S. Centers for Disease Control and Prevention and the WHO announced the worldwide emergence of XDR-TB. In Eastern Europe, 14 percent of MDR-TB patients have been diagnosed with XDR-TB. It was the outbreak of XDR-TB in South Africa reported in 2006 that first focused international attention on the problem.

Diagnosis of XDR-TB is extremely complex and treatment options are limited.