

Tuberculosis Fact Sheet

Prepared by the Staff of the Center for Biosecurity of UPMC, June 8, 2007

Overview

- The World Health Organization (WHO) estimates that 1/3 of the world's population is currently infected with TB [see WHO Tuberculosis Fact Sheet].
- Globally, there are 8.8 million new infections and 1.6 million deaths per year from TB, (approximately 1,000 new cases per hour) [see WHO Tuberculosis Fact Sheet].
- Without treatment, approximately 5% to 15% of infected people will develop "active" TB at some point in their lives. The incidence of active disease is much higher in patients who are co-infected with HIV [see WHO Tuberculosis Fact Sheet].
- When TB is not treated, and precautions to prevent transmission are not taken, on average, each person with active TB spreads it to 10 to 15 other people. However, there is great variability in these numbers, as individuals with positive smears are highly infectious, and those who are positive only on culture are much less infectious [see WHO Tuberculosis Fact Sheet].
- In 2005, there were 14,000 new cases of TB reported in the U.S. [See CDC: TB Fact Sheets: Trends in TB, 2005–U.S.].
- In 2004, 662 people in the U.S. died from TB [See CDC: TB Fact Sheets: Trends in TB, 2005–U.S.].

Transmission and Infection

Tuberculosis (TB) is an infection caused by *Mycobacterium tuberculosis*. TB is transmitted by an infected ill person. The primary mode of transmission is respiratory droplet nuclei, which are infectious particles that are aerosolized by coughing, sneezing, or talking, that dry while airborne, remain suspended for long periods, and infect the terminal air passages in the lung of a susceptible person. The lung is the most commonly affected organ. A minority of patients, especially those who are immunosuppressed (e.g. from HIV infection) are at a higher risk of developing disseminated disease.

Most often, at the time of initial infection, a person's immune system contains the infection in his/her lung but does not eradicate the bacteria. People who are infected but do not manifest signs or symptoms of tuberculosis are referred to as having *latent* TB infection. The risk of developing active tuberculosis disease is highest in the first year after infection, but may also occur many years later. Malnutrition, alcoholism, and immunosuppression are among the factors that increase one's risk of developing active disease. Only individuals with active disease are contagious (that is, able to transmit the disease to others) [CDC Fact Sheets. Tuberculosis: General Information].

Drug Resistant TB

M. tuberculosis organisms may develop resistance to anti-tuberculosis drugs. Resistance develops primarily from improper use of the antibiotics used to treat TB, and may be the result of a patient's non-adherence to his/her prescribed treatment regimen, or of ineffective administration of effective medicines. Acute infection with an already resistant strain may also occur.

- **Multi-drug-resistant tuberculosis (MDR-TB)** refers to isolates that are resistant to at least the two main first-line TB drugs—isoniazid (INH) and rifampin.
- **Extensively-drug-resistant tuberculosis (XDR-TB)** refers to MDR-TB isolates that are also resistant to three or more of the six classes of second-line drugs. The designation XDR-TB does not mean that the organism is resistant to all antibiotics.
- Globally, WHO estimated that there were about 500,000 people infected with MDR-TB in 2004 [WHO. FAQ—XDR-TB].
- It is estimated that about 10% of drug-resistant TB cases meet the definition of XDR-TB, but these numbers vary widely from country to country. [Emergence of *Mycobacterium tuberculosis* with Extensive Resistance to Second-Line Drugs-Worldwide, 2000–2004. MMWR 2006;55;301-305.].

- Between 2000 and 2006, 922 cases of MDR-TB were reported in the U.S.; 17 of these (2%) were XDR-TB. [Extensively Drug-Resistant Tuberculosis-United States, 1993–2006. MMWR 2007;56;250-253].

Diagnosis

Latent infection with *M. tuberculosis* is diagnosed by a positive reaction to the purified protein derivative (PPD) test, which is commonly referred to as the TB skin test. The skin test may not turn positive until many weeks after the actual exposure.

Active pulmonary TB is indicated by an abnormal chest x-ray and the presence of *M. tuberculosis* organisms in the patient's sputum. Although sometimes organisms can be seen on microscopic examination of the sputum ("smear positive"), bacteriological cultures are often needed for detection. Since *M. tuberculosis* is a slow growing organism, cultures can take weeks to grow.

Identification of Drug Resistance

Once the organism has grown in cultures, antibiotic sensitivity testing is conducted to determine the bacteria's ability to grow in the presence of various antibiotics used to treat TB. If the organism grows in the presence of a drug, then it is resistant to that antibiotic. Depending on the method used to test for antibiotic susceptibility testing, this process can take many weeks. Newer diagnostic approaches have been and are being developed, but they must be standardized before they can be used widely.

Treatment

Active TB requires treatment for a prolonged period of time with multiple drugs to accelerate bacterial clearance and prevent the emergence of drug resistant mutations.

- Most common treatment regimens include the drugs isoniazid (INH), rifampin, ethambutol and pyrazinamide or a fluorquinolone (e.g., ciprofloxacin, ofloxacin, levofloxacin).
- Second line drugs include the injectable antibiotics amikacin, kanamycin, or capreomycin.
- Directly observed therapy (DOT) is recommended to enhance treatment compliance and ensure completion of treatment regimen.
- Treatment of latent TB infection is recommended for those who are at a relatively higher risk for development of active disease, and generally requires 9 months of therapy with INH or 4 months of therapy with rifampin.
- Treatment of drug resistant TB (MDR-TB and XDR-TB) requires therapy with multiple agents, including prolonged treatment with injectable antibiotics. Surgical removal of the part of the lung involved with drug resistant TB is often indicated.

For additional information on treatment of TB, see the following fact sheets from the CDC Division of Tuberculosis Elimination (DTBE):

- Treatment of Latent TB Infection (2006)
- Treatment of Latent Tuberculosis Infection: Maximizing Adherence (2005)
- Treatment Options for Latent Tuberculosis Infection (2005)
- Treatment of Drug-Resistant Tuberculosis (2005)
- Treatment of Drug-Susceptible Tuberculosis Disease in Persons Not Infected with HIV (2003)
- Treatment of Drug-Susceptible Tuberculosis Disease in HIV-Infected Persons (2003)

Is There a Vaccine for TB?

While the BCG vaccine has been used for more than 60 years throughout the world and is still used in some countries where TB is endemic, there is no vaccine for TB currently available in the U.S. BCG is not used in the U.S. because it does not provide high rates of immunity, and it interferes with the interpretation of the usual TB skin test as a marker of new infection.

There is no clear consensus on the efficacy of the BCG vaccine because of great variability in stock quality, in the health of the immunized population, and in retention of vaccination records. A recent meta-analysis suggests that, on average, the vaccine reduces the risk of tuberculosis by about 50%, and the immunity rates wane over time.

Several new vaccines are currently in development but are several years away from being licensed.

TB and Air Travel

Studies suggest that the risk of infection with *M. Tuberculosis* during air travel is similar to that associated with other activities in which contact with potentially infectious individuals may occur, such as train travel, bus travel, or any gathering in enclosed spaces. Transmission of TB has been documented in only a few passengers who were seated in the same section as and in close proximity to a passenger with infectious TB on a flight lasting longer than 8 hours. To date, no case of active TB has been identified as resulting from exposure on a commercial aircraft.

The WHO recommends that: People known to have infectious TB must not travel by public air transportation until at least two weeks of adequate treatment have been completed and patients with MDR-TB should not travel until they have been proved to be non-infectious (i.e. culture negative) [WHO: Tuberculosis and Air Travel. Guidelines for Prevention and Control, Second Edition, 2006; p. 16.]

Suggested Further Reading

Iseman, MD. Tuberculosis. In: Goldman L, Ausiello D, eds. Cecil Textbook of Medicine, 22nd ed. Philadelphia: Saunders, 2004;1894-1902.

Fitzgerald D, Hass DW. *Mycobacterium tuberculosis*. In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 6th ed. New York: Elsevier/Churchill Livingstone, 2005;2852-2885.

Blumberg HM, Burman WJ, Chaisson RE, et al: American Thoracic Society, Centers for Disease Control and Prevention and the Infectious Disease Society of America: American Thoracic Society/Centers for Disease Control and Prevention/Infectious Disease Society of America: Treatment of tuberculosis. Am J Respir Crit Care Med. 2003;167:603-662.