TUBERCULOSIS (TB)

Historically, how has TB affected people globally and in the U.S? What concerns remain?

Historically and today, TB remains one of the leading causes of death due to infectious disease. About two billion people are infected worldwide.

In the U.S., death rates dropped dramatically after anti-TB drugs were discovered in the 1940’s. There was a resurgence of deaths in the 1980’s due to reduced TB control, the HIV epidemic, immigration from countries where TB is common, and the transmission of multidrug-resistant (MDR) TB. Since the early 1990’s, TB cases have declined in the U.S.

TB affects racial and ethnic minorities disproportionately.

Multidrug-resistant (MDR) TB remains a problem.

What organism causes most TB in the U.S.? Where does the disease develop in the body?

*Mycobacterium tuberculosis* causes the vast majority of cases in the U.S. *M. tuberculosis* is also called tubercle bacilli.

Pulmonary TB develops in the lungs and is the most common.

Extrapulmonary TB occurs elsewhere in the body.

Miliary TB occurs when tubercle bacilli enter the bloodstream and are carried to all parts of the body.

How do latent TB infection (LTBI) and TB develop? What are risk factors?

TB infection begins when the tubercle bacilli multiply in the small air sacs of the lungs. A small number enter the bloodstream and spread throughout the body. The body’s immune system usually keeps the bacilli under control. This condition is referred to as latent TB infection (LTBI). LTBI has no symptoms and is not infectious.

TB develops when the immune system cannot keep the tubercle bacilli under control and the bacilli begin to multiply rapidly. This can happen very soon after infection or years later. Risk is highest in the first two years after infection. With HIV, the risk increases to 7-10% per year. TB is contagious and usually has symptoms.

How are LTBI and TB similar and different?

Test results are usually positive for both. LTBI has inactive tubercle bacilli; TB has active bacilli.

For LTBI, chest ex-rays are usually normal. Sputum smears and cultures are negative. There are no symptoms, and it’s not infectious.

For TB, chest x-rays are usually abnormal. Sputum smears and cultures may be positive.

Pulmonary TB symptoms include cough, chest pain with breathing, and coughing up sputum or blood. General TB symptoms include weight loss, fatigue, malaise, fever, and night sweats.
What are the different types of drug-resistant TB?

Drug resistant TB refers to *M. tuberculosis* resistant to at least one of the first-line treatment drugs. Monoresistant TB resists only one drug. Poly-resistant TB resists at least two drugs but not both isoniazid and rifampin. Multiple drug resistant TB (MDR TB) resists at least isoniazid and rifampin. Extensively drug-resistant TB (XDR TB) extends resistance to any fluoroquinolone and at least one injectable second-line drug.

Primary resistance refers to drug resistant TB transmitted from person-to-person.

Secondary resistance develops during TB treatment if the regimen is not appropriate or the patient does not follow it as prescribed.

How is TB spread? What factors increase the probability of transmission?

TB is spread from person-to-person through the air. A person with TB may expel tiny “droplet nuclei” through coughing, sneezing, speaking or singing. Droplet nuclei can remain suspended in the air up to several hours. Transmission may occur when another person inhales air containing droplet nuclei.

The probability of transmission depends on the:

- Infectiousness of the person with TB.
- Environment.
- Length of exposure.
- Virulence (strength) of the tubercle bacilli.

Although anyone can get TB, who is most at risk for TB exposure or infection?

- Contacts - people who spend a lot of time in enclosed spaces with people infected with TB, for example, family members, friends, roommates, or co-workers
- People who have come to the U.S. within the last 5 years from areas of the world where TB is common
- Low-income groups with poor access to healthcare, including the homeless
- Cigarette smokers and people who abuse drugs or alcohol
- Workers and residents in high-risk residential settings, such as nursing homes, homeless shelters, or correctional facilities
- Health care workers who serve high-risk clients
- High-risk racial or ethnic minority populations, as locally defined
- Infants, children, and adolescents exposed to adults in high-risk groups.
Who is most at risk for developing TB disease once infected?

- People living with HIV
- People infected with *M. tuberculosis* with the past 2 years
- People with medical conditions such as diabetes mellitus, severe kidney disease, certain cancers and intestinal conditions, and more
- Cigarette smokers and people who abuse drugs or alcohol
- Infants and children younger than four.

Targeted testing for TB infection helps identify persons at high risk for developing TB. What are the two most common tests?

The Mantoux Tuberculin Skin Test (TST) is the most commonly used. It uses a needle and syringe to inject tuberculin between layers of skin and requires a wait of 48-72 hours before the patient’s arm is examined for reaction. Certain factors can lead to false positives and false negatives.

Interferon-Gamma Release Assays (IGRAs) are blood tests that measure a person’s immune reactivity. White blood cells usually release interferon-gamma in response to TB infection. To conduct tests, fresh blood is mixed with antigens and controls. Results are available within 24 hours. Blood samples must be processed within 8-16 hours of collection. In contrast to TSTs, IGRAs do not produce false positives for the BCG TB vaccine.

What are the five components of a complete medical evaluation to diagnose TB?

A complete medical history requires checking for: TB symptoms, exposure to persons with TB or other exposure risk factors, previous TB infection or disease, risk factors for developing TB.

A physical examination cannot confirm or rule out TB but it can provide valuable information about the patient’s overall condition which affects appropriate treatment.

Testing for TB infection with a TST or IGRA can confirm TB in most cases.

Chest X-Rays cannot confirm TB. However, they can rule out pulmonary TB and identify other lung abnormalities.

Bacteriologic examination requires sputum for suspected pulmonary TB. When acid-fast bacilli are seen on a smear under the microscope, positive smears are considered infectious. Culturing a specimen is necessary to confirm the diagnosis of TB. Nucleic acid amplification (NAA) tests can be used, but they do not replace the need for a smear, culture, and clinical judgment. All patients should also have specimens tested for drug susceptibility.

What is the treatment regimen for Latent TB Infection (LTBI)? Why is it important?

LTBI treatment prevents the development of TB disease in people with TB infection. Generally, people who have already completed treatment for LTBI or TB disease do not need to be treated again.

The preferred regimen is isoniazid given daily for nine months. Patients should be evaluated monthly for signs of hepatitis or adverse reactions.
What is the treatment regimen for TB disease?

TB disease must be treated for at least six months with at least four drugs. The regimen must include at least two drugs to which the bacilli are susceptible in order to prevent drug resistance. Drug resistance can also develop when patients do not take treatment as prescribed.

A clinician should evaluate patients at least monthly during treatment for possible adverse reactions.

What considerations are involved in adhering to TB disease treatment?

Treatment for TB disease lasts longer and requires more drugs than treatment for other infectious diseases. In order to cure TB and prevent drug resistance, patients must follow the complete course of treatment.

Direct Observed Therapy (DOT) is the most effective strategy for adherence to treatment and the only way to assure adherence. DOT requires a health care worker or trained person to watch the patient swallow each dose.

Education is an important way to help patients understand the importance of their medicine and how TB is spread.

During the course of treatment clinicians should conduct clinical and bacteriologic evaluations to determine how the patient is responding.

Successful TB treatment is the responsibility of the medical providers and health care workers, not the patient. Case management is a strategy to help ensure success.