An Overview of Best Practice Guidelines for *Mycobacterium tuberculosis* Screening and Treatment

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KEYWORDS

- Active TB • Latent TB (LTBI) • Mantoux tuberculin skin test (TST)
- Interferon gamma release assay (IGRA) • Purified protein derivative (PPD)
- *Mycobacterium tuberculosis*

KEY POINTS

- For the tuberculosis (TB) elimination goal to be reached in the United States, screening for latent TB and active TB must be used and focused on high-risk populations, such as the homeless, immigrants from endemic areas, and prisoners.
- The appropriate choice of a screening test (TST vs IGRA) for latent TB takes into consideration the age of the patient, likelihood of returning for follow-up visits, cost of the test, and any underlying comorbidities.
- Treatment of latent TB is important in reducing the potential pool of convertors to active TB disease.
- Treatment of active TB disease is most successful when attention is paid to the number of doses of medication the patient receives and when it is administered following direct observation technique.

INTRODUCTION

In 2014, the Centers for Disease Control and Prevention (CDC) estimated an incidence rate for new tuberculosis (TB) cases reported in the United States to be 3.0 cases per 100,000 persons.[1] Although the number of cases of TB had declined from 2013 to 2014, the rate of decline was the smallest decrease in more than a decade.[1] The elimination goal of less than 1 case per 1 million persons was set in 1989 and reaffirmed in 1999. The present incidence rate has prompted the CDC to call for vigilant surveillance

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and active prevention measures, including screening and treating both latent tuberculosis infection (LTBI) and active TB.[1]

LATENT VERSUS ACTIVE DISEASE

Tuberculosis is caused by a group of 5 related species that form the *Mycobacterium tuberculosis* complex: *Mycobacterium bovis, Mycobacterium microti, Mycobacterium africanum, Mycobacterium canettii*, and *M tuberculosis*. In the United States, most TB cases are caused by *M tuberculosis.* In 1882, Dr Robert Koch discovered the TB bacillus.[1] A characteristic of *M tuberculosis* is the tendency to form dense clusters of bacilli. A defining characteristic of the bacilli in this genus is acid-fastness; the ability to withstand decolorization with acid-alcohol rinse after staining with carbolfuchsin or auramine-rhodamine. Because of this characteristic, *Mycobacterium* are referred to as acid-fast bacilli or AFB.[2] Mycobacterium are obligate aerobes, intercellular pathogens with slow growth rates. They are known to form granulomatous reactions in a normal host. TB transmission occurs almost exclusively from human to human. Most cases are acquired from individuals with acid-fast–positive sputum. Approximately 17% of cases can be spread by individuals with AFB-negative sputum.[2]

Most individuals exposed to *M tuberculosis* contain the illness and never acquire active disease.[2] They will have a positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) test, and are normally found to have a normal chest radiograph and sputum testing that is negative. TB in the body is present but inactive. This is known as latent disease.[3] Latent TB infection (LTBI) is not communicable, and patients are asymptomatic. Most cases of active disease are communicable. The definition of active disease includes symptoms of a cough for 3 or more weeks, hemoptysis, night sweats, unexplained weight loss, and extreme fatigue. The lifetime risk for someone with latent disease developing active disease ranges between 5% and 10%. The risk is inversely proportional to age at the time of infection, thus children with latent disease are at greater risk than older adults with latent infection of developing active TB. Those individuals who have LTBI and medical comorbidities, especially immunocompromising conditions such as human immunodeficiency virus (HIV) infection, recent bone marrow transplantation, or a malignant neoplasm, are also at increased risk of developing active disease.[3]

SCREENING TESTS

Before 2001, the TST was the only commercially available immunologic test approved in the United States for the screening of *M tuberculosis.* The IGRA was developed in response to some of the recognized problems of administration and reading the TST. The TST requires appropriate intradermal administration by the Mantoux method of 0.1 mL of purified protein tuberculin derivative (PPD). The injection is placed on the volar surface of the forearm. When correctly placed, the injection should produce a wheal 6 to 10 mm in diameter.[3] For the most accurate results, the patient must return to have the test read in 48 to 72 hours by an experienced health care worker (**Fig. 1**).[4] Test results can be influenced by previous vaccination of Bacille Calmette-Guerin (BCG) and previous exposure to nontuberculous mycobacterium.[5]

In 2001, the Quantiferon-TB test (QFT) became the first IGRA approved by the Food and Drug Administration (FDA) as an adjunct test to be used in the diagnosis of TB. The specificity of the QFT proved to be less than the TST, and in 2005, the test was taken off the market but other IGRA tests were developed that had improved specificity.[5] The CDC issued guidelines for the use of IGRAs initially in 2003.[5] As new IGRA testing became available, the CDC guidelines were updated, with the latest updates being