CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

TUBERCULOSIS INFORMATION

- Diagnosis of Latent TB Infection and TB Disease

Tuberculin Skin Test

The Mantoux tuberculin skin test is used to determine whether a person is infected with *Mycobacterium tuberculosis*. Tuberculin skin testing is contraindicated only for persons who have had a necrotic or a severe allergic reaction to a previous tuberculin skin test. It is not contraindicated for any other persons, including infants, children, pregnant women, persons who are HIV infected, or persons who have been vaccinated with BCG. The Mantoux tuberculin skin test is the standard method of identifying persons infected with *M. tuberculosis*. Multiple puncture tests (MPTs) should not be used to determine whether a person is infected.

Administering the Tuberculin Skin Test

The Mantoux tuberculin test is performed by placing an intradermal injection of 0.1 ml of purified protein derivative (PPD) tuberculin containing 5 tuberculin units (TU) into the inner surface of the forearm. The injection should be made with a disposable tuberculin syringe, just beneath the surface of the skin, with the needle bevel facing upward. This should produce a discrete, pale elevation of the skin (a wheal) 6 mm to 10 mm in diameter. Institutional guidelines regarding universal precautions for infection control (e.g., the use of gloves) should be followed.

Interpreting Skin Test Results

The reaction to the Mantoux tuberculin skin test should be read by a trained health care worker 48 to 72 hours after the injection. The reading should be based on a measurement of induration (swelling), not on erythema, or redness. The diameter of the induration should be measured perpendicularly to the long axis of the forearm. All reactions, even those classified as negative, should be recorded in millimeters.

Classification of the Tuberculin Skin Test Reaction

An induration of **5 or more millimeters** is considered positive for	An induration of **10 or more millimeters** is considered positive for	An induration of **15 or more millimeters** is considered positive for persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.
S HIV-positive persons **S** Recent contacts of TB case **S** Persons with fibrotic changes on chest radiograph consistent with old healed TB **S** Patients with organ transplants and other immunosuppressed patients (receiving the equivalent of ≥ 15 mg/day of prednisone for ≥1 month)	**S** Recent arrivals (< 5 years) from high-prevalence countries **S** Injection drug users **S** Residents and employees of high-risk congregate settings: prisons and jails, nursing homes and other long-term facilities for the elderly, hospitals and other health-care facilities, residential facilities for AIDS patients, and homeless shelters **S** Mycobacteriology laboratory personnel **S** Persons with clinical conditions that place them at high risk* **S** Children < 4 years of age, or children and adolescents exposed to adults in high-risk categories.	

*HIV infection, substance abuse (especially drug injection), recent infection with *M. tuberculosis* (within the past 2 years), previous TB (in a person who received inadequate or no treatment), diabetes mellitus, silicosis, prolonged corticosteroid therapy, other immunosuppressive therapy, cancer of the head and neck, hematologic and reticuloendothelial diseases (e.g., leukemia and Hodgkin's disease), end-stage renal disease, intestinal bypass or gastrectomy, chronic malabsorption syndromes, low body weight (10% or more below the ideal)

Some persons who have positive skin test results may have TB disease. The possibility of TB disease must be ruled out before treatment of latent TB infection is begun.

False-Positive Reactions

The Mantoux tuberculin skin test is a valuable tool, but it is not perfect. Some persons may react to the tuberculin skin test even though they are not infected with *M. tuberculosis*. These false-positive reactions may be caused by infection with mycobacteria other than *M. tuberculosis* or by immunization with BCG. However, there is no sure way to determine the true cause of the reaction.

False-Negative Reactions

Some persons may not react to the tuberculin skin test even though they are truly infected with *M. tuberculosis*. These false-negative reactions can occur in several circumstances:

- When skin testing persons who were recently infected with *M. tuberculosis*.
  These persons may have a false-negative reaction because developing an immune response to tuberculin can take 2 to 10 weeks after infection. Therefore, persons who have been exposed to someone with infectious TB disease, but who have a negative reaction to the skin test, should be retested 10 to 12 weeks after the exposure ends.
- When skin testing persons who were infected with *M. tuberculosis* a long time ago.
  In some persons who are infected with *M. tuberculosis*, the ability to react to tuberculin may wane over time. When given a skin test years after infection, these persons may have a negative reaction. Two-step testing is used to determine whether these persons are truly infected.
- When skin testing persons who are anergic.
  Anergy is the inability to react to skin tests because of a weakened immune system.
- When skin testing is done after a recent live virus vaccination (e.g., measles).
  Tuberculin skin testing should be done on either the same day as vaccination with live-virus vaccines or 4-6 weeks after vaccination.

Two-Step Testing

In some persons who are infected with *M. tuberculosis*, the ability to react to tuberculin may wane over time. When given a skin test years after infection, these persons may have a negative reaction. However, this skin test may stimulate the immune system, causing a positive reaction to subsequent tests. This is called the booster phenomenon.

Two-step testing is used to distinguish between the booster phenomenon and new infection. If the reaction to the first test is negative, a second test is given 1 to 3 weeks later. If the reaction to the second test is positive, then it is probably a boosted reaction (usually from infection that occurred years ago) and should not be called a skin-test conversion (i.e., a new infection). Two-step testing can be useful for the initial skin testing of adults who are going to be retested periodically, such as health care workers or nursing home residents.

Anergy

Some persons may not react to the tuberculin skin test even though they are infected with *M. tuberculosis*. This may be because of anergy. Anergy is the inability to react to skin tests because of immunosuppression. Anergy is often caused by HIV infection, but it can also be caused by other medical conditions. Anergy is determined by administering two delayed-type hypersensitivity antigens, such as tetanus toxoid, mumps, or *Candida*, by the Mantoux method. Persons who do not react to any of these antigens, including tuberculin, are probably anergic. The use of anergy testing in conjunction with PPD testing is no longer recommended routinely for screening programs for *M. tuberculosis* infection conducted among HIV-infected persons in the United States.

Interpreting Skin Test Reactions in BCG-Vaccinated Persons

In persons vaccinated with BCG, sensitivity to tuberculin is highly variable, depending upon the strain of BCG used and the group vaccinated. The presence or size of a post-vaccination tuberculin skin-test reaction does not predict whether BCG will provide any protection against TB disease. Furthermore, the size of a tuberculin skin-test reaction in a BCG-vaccinated person is not a factor in determining whether the reaction is caused by *M. tuberculosis* infection or the prior BCG vaccination.

Tuberculin skin testing is not contraindicated for persons who have been vaccinated with BCG, and the skin-test results of such persons are used to support or exclude the diagnosis of *M. tuberculosis* infection. A diagnosis of *M. tuberculosis* infection and the use of treatment of latent TB infection should be considered for any BCG-vaccinated person who has a tuberculin skin-test reaction of 10 mm or greater of induration, especially if any of the following circumstances are present:

- The vaccinated person is a contact of another person who has infectious TB, particularly if the infectious person has transmitted *M. tuberculosis* to others;
- The vaccinated person was born or has resided in a country in which the prevalence of TB is high; or
- The vaccinated person is exposed continually to populations in which the prevalence of TB is high (e.g., some health care workers, employees and volunteers at homeless shelters, and workers at drug-treatment centers).

Treatment of latent TB infection should be considered for BCG-vaccinated persons who are infected with HIV and who are at risk for *M. tuberculosis* infection if they have a tuberculin skin-test reaction of $\geq$5 mm induration.

Diagnosis of Tuberculosis Disease

When to Suspect Tuberculosis (TB)

Pulmonary TB disease should be suspected in persons who have fever; chills; night sweats; fatigue; loss of appetite; weight loss; a productive, prolonged cough (duration of 3 weeks or longer); or hemoptysis. Persons suspected of having TB disease should be evaluated with a medical history, a physical examination, a Mantoux tuberculin skin test, a chest radiograph, and a sputum smear and culture. A positive culture for *Mycobacterium tuberculosis* confirms the diagnosis of TB. However, a positive culture is not always necessary to begin or continue treatment for TB. In addition, a negative tuberculin skin test does not rule out TB.

Persons with HIV infection and TB may have atypical chest radiographs, and they are more likely to have extrapulmonary TB than are persons without HIV infection. (However, pulmonary TB is the most common form of TB in all persons, including HIV-infected persons). The symptoms of extrapulmonary TB depend on the site affected.

Diagnostic Laboratory Tests

The presence of acid-fast bacilli (AFB) on a sputum smear often indicates TB. Acid-fast microscopy is easy and quick, but it does not confirm a diagnosis of TB because some acid-fast bacilli are not *M. tuberculosis*. Therefore, a culture is done to confirm the diagnosis. Culture examinations should be done on all specimens, regardless of AFB smear results.

Laboratories should report positive smears and positive cultures within 24 hours by telephone or fax to the primary health care provider.

For all patients, the initial *M. tuberculosis* isolate should be tested for drug resistance. It is crucial to identify drug resistance as early as possible in order to ensure appropriate treatment. Drug susceptibility patterns should be repeated for patients who do not respond adequately or who have positive culture results despite 2 months of therapy. Susceptibility results from laboratories should be promptly forwarded to the health department.

For More Information

For information about implementing CDC guidelines, call your state health department.

To order the following documents, call the CDC's Voice and Fax Information System (recording) toll free at (888) 232-3228, then press options 2, 5, 1, 2, 2 (Note: You may select these options at any time without listening to the complete message). Request the title or publication number of the document you would like to order. You may also visit the Division of TB Elimination's Web site at www.cdc.gov/nchstp/tb.

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