



# Diagnosis of Latent Tuberculosis Infection

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## Introduction

### Purpose

Use this chapter to understand and follow recommendations for diagnosing latent TB infection (LTBI).

In the 2005 guideline, “Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America,” one of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the identification of persons with LTBI at risk for progression to TB disease, and treatment of those persons with an effective drug regimen.<sup>1</sup>

### Guidance



Contacts are mentioned within this chapter, but their evaluation and follow-up are covered in more depth in Chapter 10, “Contact Investigation.” For information on treatment of LTBI, refer to Chapter 8, “Treatment of Latent Tuberculosis Infection.”

### Forms



Required and recommended forms are available on the Tuberculosis Forms website

<http://healthandwelfare.idaho.gov/Health/DiseasesConditions/Tuberculosis/TuberculosisForms/tabid/854/Default.aspx> .



## Identifying High-Risk Groups Eligible for LTBI Testing

Certain factors identify persons at high risk for tuberculosis (TB) infection and/or progression to TB disease. According to the Centers for Disease Control and Prevention, persons in the high-risk groups listed in Table 1: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease** are candidates for LTBI testing. (This table can also be found in Chapter 3, “Targeted Testing for Latent Tuberculosis Infection” and Chapter 5, “Diagnosis of Tuberculosis Disease.”)

Persons with risk factors from both columns may be at much higher risk than those with risk factors in only one column. For example, an individual born in a high TB prevalence country with HIV infection is epidemiologically at much higher risk of having active TB than a U.S.-born individual with HIV infection.

In 2016, the United States Preventive Services Task Force (USPSTF) recommended screening for LTBI in populations at increased risk. Some clinicians may adopt these recommendations and initiate or expand LTBI screening for these persons. The USPSTF recommendation applies to asymptomatic adults who were born in, or are former residents of, countries with increased tuberculosis prevalence and persons who live in, or have lived in, high-risk congregate settings (e.g., homeless shelters and correctional facilities). The USPSTF did not review the evidence on screening in other populations that may be at high risk.<sup>2</sup>



TABLE 1: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE<sup>3</sup>

For Tuberculosis Infection	For Progression to Tuberculosis Disease <sup>4</sup>
<ul style="list-style-type: none"> <li>▪ High-priority contacts such as housemates or coworkers or contacts of persons who have smear-positive pulmonary or laryngeal tuberculosis (TB)</li> <li>▪ Infants, children, and adolescents exposed to adults in high-risk categories</li> <li>▪ Recent immigrants (&lt;5 years) from countries with high incidence of TB (Asian, African, Latin American, and Eastern European countries have TB rates 5–30 times higher than U.S. rates, and an increasing percentage of TB cases here are occurring among immigrants from those countries)</li> <li>▪ Migrant workers</li> <li>▪ Persons who have recently spent over 3 months in high-incidence countries (such as missionaries from the Church of Jesus Christ of Latter-Day Saints)</li> <li>▪ Native Americans</li> <li>▪ Persons with high rates of TB transmission:               <ul style="list-style-type: none"> <li>• Homeless persons</li> <li>• Injection drug users</li> <li>• Persons with human immunodeficiency virus (HIV) infection</li> <li>• Persons living or working in institutions with individuals at risk for TB such as:                   <ul style="list-style-type: none"> <li>▪ Hospitals, especially staff in nursing, emergency departments, and laboratories</li> <li>▪ Long-term care facilities</li> <li>▪ Homeless shelters</li> <li>▪ Residences for acquired immunodeficiency syndrome (AIDS) patients</li> <li>▪ Correctional facilities</li> </ul> </li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>▪ Persons with HIV infection</li> <li>▪ Infants and children aged &lt;5 years</li> <li>▪ Persons infected with <i>Mycobacterium tuberculosis</i> within the previous 2 years</li> <li>▪ Persons with a history of untreated or inadequately treated TB disease</li> <li>▪ Persons with radiographic findings consistent with previous TB disease</li> <li>▪ Persons who use alcohol or illegal drugs (such as injection drugs or crack cocaine)</li> <li>▪ Persons with any of the following clinical conditions or other immunocompromising conditions:               <ul style="list-style-type: none"> <li>• Silicosis</li> <li>• Diabetes mellitus</li> <li>• End-stage renal disease (ESRD)/chronic renal failure, hemodialysis</li> <li>• Some hematologic disorders (e.g., leukemias and lymphomas)</li> <li>• Other malignancies (e.g., carcinoma of head, neck, or lung)</li> <li>• <b>Body weight <math>\geq 10\%</math> below ideal body weight</b></li> <li>• Prolonged corticosteroid use</li> <li>• Use of other immunosuppressive treatments (e.g., prednisone or tumor necrosis factor-alpha [TNF-<math>\alpha</math>] antagonists)</li> <li>• Organ transplantation</li> <li>• Gastrectomy</li> <li>• Chronic malabsorption syndromes</li> <li>• Jejunioileal bypass</li> </ul> </li> </ul>

Source: Adapted from: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. MMWR 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6):7-9.



## Diagnosis of Latent TB Infection

Latent TB infection is usually diagnosed when tests indicate TB infection (see below) and the patient has no evidence of active TB disease.

### Diagnostic Testing Options

There are currently two methods available for the detection of *M. tuberculosis* infection in the United States. The two methods are:

- 1) Mantoux tuberculin skin test (TST; also known as a purified protein derivative (PPD) skin test)
- 2) Interferon-gamma release assays (IGRAs)<sup>5</sup>

The diagnosis of latent tuberculosis infection (LTBI) has traditionally been based upon results of tuberculin skin testing. However, interferon-gamma release assays (IGRAs) are now the preferred method in certain situations, such as when an individual has a history of BCG vaccination or is unlikely to return to have their TST read.<sup>6</sup> Some basic comparisons between the two methods are illustrated in the table below.

TST	IGRA
Tuberculin is injected under the skin and produces a delayed-type hypersensitivity reaction if the person has been infected with <i>M. tuberculosis</i>	Blood is drawn for testing; test measures the immune response to the TB bacteria in whole blood
Requires two or more patient visits to conduct the test	Requires one patient visit to conduct the test
Results are available 48 to 72 hours later	Results can be available in 24 hours (depending on the batching of specimens by the laboratory and transport)
Can cause booster phenomenon	Does <b>not</b> cause booster phenomenon
Reading by HCW may be subjective	Laboratory test <b>not</b> affected by HCW perception or bias
BCG vaccination can cause false-positive result	BCG vaccination does <b>not</b> cause false-positive result and infection with most nontuberculous mycobacteria does <b>not</b> cause false-positive result
A negative reaction to the test does <b>not</b> exclude the diagnosis of LTBI or TB disease	A negative reaction to the test does <b>not</b> exclude the diagnosis of LTBI or TB disease

Source: CDC. Chapter 3: Testing for Tuberculosis Infection and Disease. *Core Curriculum on Tuberculosis: What the Clinician Should Know* [DTBE website]. 2016: p 50. Available at: <https://www.cdc.gov/tb/education/corecurr/pdf/chapter3.pdf> Accessed November 6, 2018



Mantoux Tuberculin Skin Testing (TST; also known as a purified protein derivative (PPD) skin test)

The Mantoux method of tuberculin skin testing can be used to detect infection with *Mycobacterium tuberculosis*.

In general, it takes two to 10 weeks after TB infection for a person to develop a delayed-type immune response to the antigen tuberculin measurable with the Mantoux tuberculin skin test (TST).<sup>7</sup> To perform this test, tuberculin (also known as purified protein derivative, or PPD) is injected intradermally (between skin layers). The immune system of most persons with tuberculosis (TB) infection will recognize the tuberculin, causing a reaction in the skin. Repeated TSTs do not produce hypersensitivity.

Interpretation of a TST reaction considers the size of the measured induration (a firm, palpable swelling) and the patient's individual risk of acquiring TB infection or the risk of progressing to TB disease if infected.<sup>8</sup> Based on this risk stratification, there are three different cut-offs for defining a positive TST reaction:

- Greater than or equal to 5 mm of induration
- Greater than or equal to 10 mm of induration
- Greater than or equal to 15 mm of induration<sup>9</sup>



For detailed information about the interpretation of the TST, see the “Interpretation of the Tuberculin Skin Test” section of this chapter, below.

The Mantoux TST can be safely administered to all persons, including pregnant women,<sup>10</sup> persons who have previously been vaccinated with Bacille Calmette-Guérin (BCG),<sup>11</sup> and human immunodeficiency virus (HIV)-infected persons. However, the following should be noted:

- An IGRA (discussed below), if available, is preferred for people who have received a previous BCG vaccine.
- Persons with a documented prior positive TST do not need another TST, as it is likely to remain positive, even after treatment for LTBI.
- Persons with a previous allergic reaction to TST should not be retested; an IGRA should be used if testing is indicated.
- The Mantoux TST should not be administered until four weeks after vaccination with live-virus vaccines.
- Anergy testing in conjunction with TST is not helpful or recommended.



If the person being tested is a contact, follow the procedures outlined in Chapter 10, “Contact Investigation.”



## Bacille Calmette-Guérin Vaccine

BCG vaccines are live vaccines derived from a strain of *Mycobacterium bovis*. In many parts of the world where TB is highly prevalent, the vaccine is used to reduce the risk of severe disseminated TB and TB meningitis in young children.<sup>12</sup> For various reasons, including the low risk of severe TB disease in young children in the United States and variable efficacy of the vaccine in adults, BCG vaccine is generally not recommended in the United States, but may be used rarely for certain contacts of cases or healthcare workers traveling abroad to work in high-risk settings.<sup>13</sup>

A history of BCG vaccination is not a contraindication to tuberculin skin testing; however, a history of BCG vaccination can cause a false positive TST reaction (either initially or as a boosted reaction). For this reason, IGRA is the preferred testing strategy for individuals who have a history of BCG vaccination.<sup>14</sup> However, if IGRA testing is not available, TST testing can be administered to BCG-vaccinated individuals and interpreted in the same manner as in those who have no history of BCG vaccination.<sup>15</sup> For example, for an individual born in a country in which TB is common, the cut-off for a positive TST is 10 millimeters or more regardless of BCG vaccination history (unless other risk factors, such as HIV infection, are present that indicate a lower cut-off for a positive TST reaction).

Foreign born individuals being evaluated for LTBI may not know their personal BCG vaccination history. For assistance with determining if a patient may have received BCG in their country of origin, refer to: <http://www.bcgatlas.org/>

## Documented Prior Positive Tuberculin Skin Test

Persons who have tested positive in the past and can provide documentation of their status should not have another TST. Instead, they should be screened with a chest radiograph or have a TB symptom assessment questionnaire administered to identify any symptoms of TB disease.<sup>16</sup>

## Live-Virus Vaccines

Vaccines with live viruses (including measles, mumps, rubella, oral polio, varicella, yellow fever, and oral typhoid) may interfere with TST reactivity and cause a false negative reaction. To minimize false-negative TST reaction, TST should be done either on the same day that the live vaccine is administered or at least one month after vaccination. The decision on which approach to take should consider both the urgency of the TST as well as the likelihood that the individual will return in one month for an additional two visits (for administration and reading of the TST, respectively).<sup>17</sup>

## Booster Phenomenon and Two-Step Testing

Some people infected with *M. tuberculosis* may have a negative reaction to a single TST if many years have passed since they became infected. However, they may have a positive reaction to a subsequent TST because the initial test



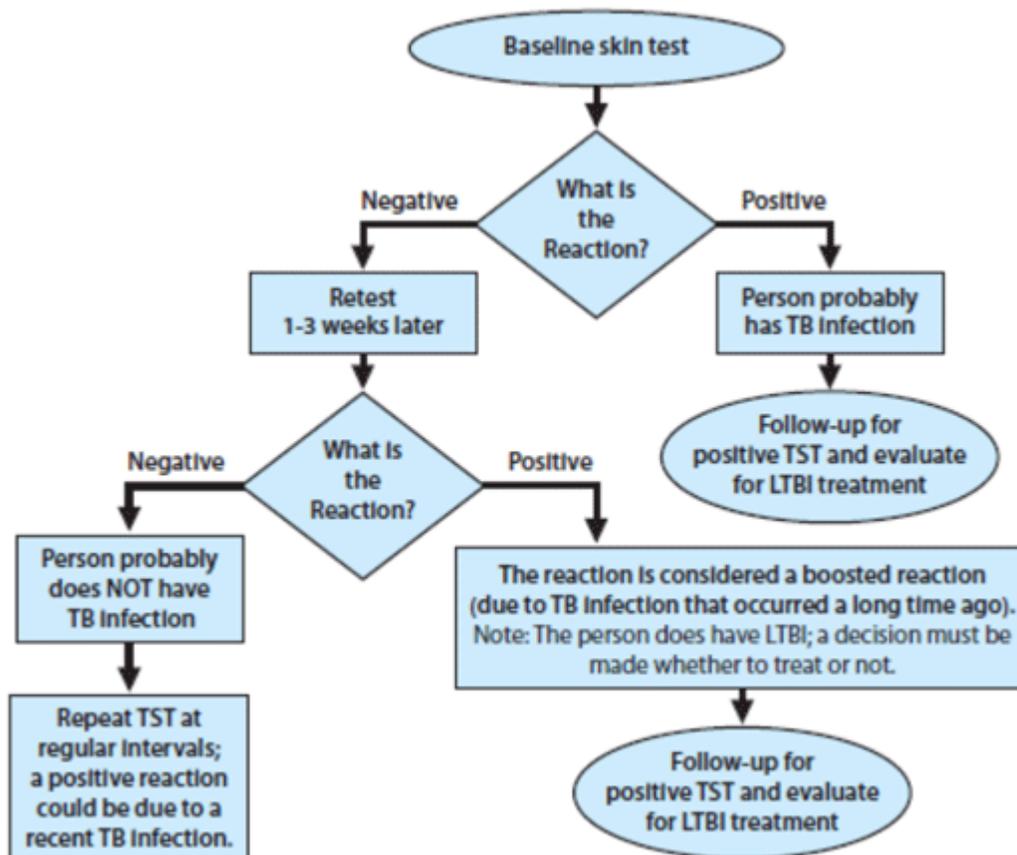
has stimulated their ability to react to the test. This is commonly referred to as the “booster phenomenon” and may incorrectly be interpreted as a skin test conversion (going from negative to positive).

For this reason, the “two-step method” is recommended at the time of initial testing for individuals who may be retested periodically (e.g., health care workers). The two-step method involves an initial TST for the individual. Next steps are as follows:

- If the first TST result is positive, consider the person infected and evaluate and treat the person accordingly.
- If the first test result is negative, the TST should be repeated in 1–3 weeks.
  - If the second test result is positive, consider the person infected and evaluate and treat the person accordingly
  - if both steps are negative, consider the person uninfected and classify the TST as negative at baseline testing ([see Figure 1](#)).<sup>18</sup>

When IGRAs are used for serial testing, there is no need for a second test because boosting does not occur.

Figure 1: Two-Step TST Testing





## Administration of the Tuberculin Skin Test

The TST should be placed by a healthcare worker who has received appropriate training and is following written protocols.

### How to Administer a Tuberculin Skin Test

1. Review the CDC “*Mantoux Tuberculin Skin Test Facilitator Guide*” at: <http://www.cdc.gov/tb/education/Mantoux/default.htm>
2. Gather equipment/supplies including: gloves, alcohol swabs or other skin cleanser, single-dose disposable tuberculin syringe, purified protein derivative (PPD) (Tubersol® or Aplisol®), sharps container.
3. If the patient’s written consent is required, obtain it per health department requirements.
4. Provide patient education about the test, including the requirement that the patient must return in 48-72 hours to have the test read. If the patient is unable to return within the 48-72 hour time period, do not administer the test.
5. Wash hands using appropriate hand-washing technique. Follow your institution’s standard precautions for infection control.
6. The injection should be placed on the palm-side-up surface of the forearm, about two to four inches below the elbow. Your local institutional policy may specify the right or left forearm for the skin test. The area selected should be free of any barriers to placing and reading the skin test, such as muscle margins, heavy hair, veins, sores, tattoos, or scars.
7. After choosing the injection site, clean the area with an alcohol swab by circling from the center of the site outward. Allow the site to dry completely before the injection.
8. Using a disposable tuberculin safety needle and syringe, inject 0.1 ml of PPD tuberculin containing 5 tuberculin units (TU) intradermally with the needle bevel facing upward. Because some of the tuberculin solution can adhere to the inside of the plastic syringe, the skin test should be given as soon as possible after the syringe is filled.
9. The injection should produce a discrete, pale elevation of the skin (a wheal) 6 to 10 mm in diameter. Note: If a 6 to 10 mm wheal is not produced, repeat the test on the opposite arm or the same arm, 2 inches from the original site.
10. Record the date and time of TST administration, location of injection site, dose, name of person who administered the test, name and manufacturer of tuberculin product used, lot number, expiration date, and the reason for testing.<sup>19</sup>

### Measurement of the Tuberculin Skin Test

A trained healthcare worker should read the TST 48 to 72 hours after the intradermal injection. **Patients should never be allowed to read their own TSTs.**<sup>20</sup>

- A positive reaction is considered valid even if it is read more than 72 hours after intradermal injection.



- If the results appear negative and more than 72 hours have passed, the test should be repeated. It can be repeated immediately, or after one week, if two-step testing is required.



A topic entitled “Two-Step Tuberculin Skin Testing” topic can be found in Chapter 16, “Infection Control” of this manual.

### How to Measure a Tuberculin Skin Test

1. Measure the TST site crosswise to the axis of the forearm (from the thumb side of the arm to the little finger side of the arm or vice versa).
2. Induration is a hard, dense, raised formation. Measure only induration hardness and not swelling around the site of the injection. **Do not measure erythema (redness).** A TST with erythema, but no induration, is nonreactive.
3. Record the test result in mm, not as "positive" or "negative." An exact reading in mm may be necessary to interpret whether conversions occur on a subsequent test. Record a TST with no induration as "0 mm." Where there is induration, do not round off the reading, but record it exactly as read.
4. Report adverse reactions to a TST (e.g., blistering, ulcerations, necrosis) to the FDA's MedWatch Program at 1-800-FDA-1088, or via the Internet at this hyperlink: <http://www.fda.gov/medwatch/>.





## Interpretation of the Tuberculin Skin Test

TSTs should be interpreted by a trained healthcare worker.



Call the Idaho State TB program at (208) 334-5939 for consultation regarding TST reactions for which interpretation and medical follow-up are unclear.

### How to Interpret a Tuberculin Skin Test

Use the table below.

TABLE 2: POSITIVE TUBERCULIN SKIN TEST REACTIONS

Induration Size	Considered Positive For:
5 mm or more	<ul style="list-style-type: none"> <li>▪ Persons with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS)</li> <li>▪ Recent contacts of an infectious case of tuberculosis (TB) disease</li> <li>▪ Persons with fibrotic lesions on chest radiograph consistent with prior TB</li> <li>▪ Persons with organ transplants or other immunosuppressed persons (such as those receiving the equivalent of <math>\geq 15</math> mg/day of prednisone for <math>\geq 1</math> month)</li> <li>▪ Persons receiving treatment with tumor necrosis factor-alpha (TNF-<math>\alpha</math>) antagonists</li> </ul>
10 mm or more	<ul style="list-style-type: none"> <li>▪ Foreign-born persons recently arrived (within 5 years) from countries with a high TB incidence or prevalence (e.g., most countries in Africa, Asia, Latin America, Eastern Europe, Former USSR), or from refugee camps</li> <li>▪ Persons who inject drugs or use other high-risk substances, such as crack cocaine</li> <li>▪ Residents and employees in high-risk, congregate settings (e.g., correctional institutions; long-term residential care facilities such as nursing homes, mental institutions, etc.; hospitals and other healthcare facilities; homeless shelters; and refugee camps)</li> <li>▪ Mycobacteriology laboratory personnel</li> <li>▪ Persons with other medical conditions that increase the risk of TB disease (such as silicosis, diabetes mellitus, chronic renal failure, certain types of cancer, and certain intestinal conditions)</li> <li>▪ Children younger than 5 years of age, or children and adolescents exposed to adults in high-risk categories</li> </ul>
15 mm or more	<ul style="list-style-type: none"> <li>▪ Persons with no known risk factors for TB</li> </ul>

Adapted from CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6): p24 found at: <https://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>

When interpreting TST results, be aware of the following:

**Skin test conversions:** For persons previously skin tested, an increase in induration of 10 mm or more within a two-year period is classified as a conversion to positive. For example, a person with a previous reading of 4mm who now is 14mm is considered positive, even if they have no known risk factors for TB.<sup>21</sup>



**False-negative reactions** may be due to the following:

- Anergy (the inability to react to a TST because of a weakened immune system)
- Recent TB infection (within the past 10 weeks)
- Very young age (less than 6 months of age because the immune system is not fully developed)
- Overwhelming TB disease
- Vaccination with live viruses (e.g., measles, mumps, rubella, varicella, oral polio, and yellow fever). Note: TB skin testing should be done either on the same day as vaccination with live virus or at least four weeks after vaccination. (See “Live-Virus Vaccines” in the section “Candidates for Mantoux Tuberculin Skin Testing” of this chapter.)
- Some viral infections (measles, mumps, chickenpox, and HIV)
- Corticosteroids and other immunosuppressive agents given for two or more weeks

**False-positive reactions** may be due to the following:<sup>22</sup>

- Nontuberculous mycobacteria (NTM) or mycobacterium other than *M. tuberculosis* (MOTT) infection
- History of BCG vaccination (See “Bacille Calmette-Guérin Vaccine” in the section “Candidates for Mantoux Tuberculin Skin Testing” of this chapter.)

## Interferon-Gamma Release Assay (IGRA) Testing

IGRAs are used to determine if a person is infected with *M. tuberculosis* by measuring the immune response to TB proteins in whole blood. Blood specimens are mixed with peptides that simulate antigens derived from *M. tuberculosis* and controls. In a person infected with *M. tuberculosis*, the white blood cells in the person’s blood specimen recognize the simulated antigens and release interferon-gamma (IFN-  $\gamma$ ); results are based on the amount of IFN-  $\gamma$  released.<sup>23</sup>

The U.S. Food and Drug Administration (FDA) approved IGRAs commercially available in the United States include:

- QuantiFERON®-TB Gold-in-Tube test (QFT-GIT) or QuantiFERON-TB Gold Plus (QFT-Plus)
- T-SPOT® TB test

### **Populations in which IGRAs are preferred for testing:**

- Persons who have received BCG (either as a vaccine or for cancer therapy); and
- Persons from groups that historically have poor rates of return for TST reading.

According to the American Academy of Pediatrics, TST is preferred over IGRAs for testing children less than 2 years of age.<sup>24</sup>



### **Interpretation of IGRA Results**

The interpretation of IGRAs is based on the amount of IFN- $\gamma$  released (QFT-GIT), or on the number of cells that release IFN- $\gamma$  (in T-SPOT®). TB laboratories should provide both the qualitative and quantitative results.

- Qualitative results are reported as positive, negative, indeterminate or borderline.
- Quantitative results are reported as numerical values that include a response to the TB antigen and 2 controls, nil and mitogen. Quantitative results may be useful for clinical decision making in individual cases, in combination with risk factors.

The antigens, testing methods, and interpretation criteria for IGRA results are outlined in Table 1.

**Table 1: Differences in Currently Available IGRAs**

	<b>QFT-GIT</b>	<b>T-Spot</b>
<b>Initial Process</b>	Process whole blood within 16 hours	Process peripheral blood mononuclear cells (PBMCs) within 8 hours, or if T-Cell Xtend® is used, within 30 hours
<b><i>M. tuberculosis</i> Antigen</b>	Single mixture of synthetic peptides representing ESAT-6, CFP-10 & TB7.7.	Separate mixtures of synthetic peptides representing ESAT-6 & CFP-10
<b>Measurement</b>	IFN- $\gamma$ concentration	Number of IFN- $\gamma$ producing cells (spots)
<b>Possible Results</b>	Positive, negative, indeterminate	Positive, negative, indeterminate, borderline

Source: <https://www.cdc.gov/tb/publications/factsheets/testing/igra.htm>

Routine testing using both TST and IGRAs in the same patient is NOT routinely recommended, though there are certain situations where results from both TST and IGRA may be considered:

When the initial test is **negative** and:

- The risk for infection, progression to disease, and/or a poor outcome is high (e.g., HIV-infected persons or children under 5 years of age who are exposed to a person with infectious TB) and suspicion for *M. tuberculosis* infection is high.



- There is clinical suspicion for TB disease (e.g., signs, symptoms, and/or radiographic evidence suggestive of TB disease) and confirmation of *M. tuberculosis* infection is desired prior to initiating treatment.

When the initial test is **positive** and:

- Additional evidence of infection is required to encourage acceptance and adherence to treatment (e.g., foreign-born persons who believe their positive TST is due to BCG).
- The person has a low risk of both infection and progression from infection to TB disease. Requiring a positive result from the second test as evidence of infection increases the likelihood that the test reflects infection. An alternative is to assume, without additional testing, that the initial result is a false positive or that the risk for disease does not warrant additional evaluation or treatment, regardless of test results.

In addition, repeating an IGRA or performing a TST might be useful when the initial IGRA result is indeterminate, borderline, or invalid and a reason for testing persists.

Remember, even multiple negative results from any combination of these tests cannot entirely exclude *M. tuberculosis* infection.

## Human Immunodeficiency Virus Screening

The risk of progression from LTBI to active TB disease is 7% to 10% each year for those with both LTBI and untreated HIV infection. Those with LTBI who are not HIV-infected have a 10% risk over their lifetime. Thus, the risk of progression to TB disease is much higher for those who are HIV infected. This risk is reduced with antiretroviral therapy for HIV, but is still higher than that in HIV-negative persons with LTBI.<sup>25</sup>

HIV-infected persons should be tested for LTBI as soon as their HIV status becomes known. A negative TST or IGRA result does not exclude LTBI as they may have a compromised ability to react to tests for TB infection. Annual testing should be considered for HIV-infected persons who are TST or IGRA negative on initial evaluation, and who have a risk for exposure to *M. tuberculosis*. The usefulness of energy testing in HIV-infected individuals or others has not been demonstrated; therefore, it is not recommended.

After the initiation of antiretroviral therapy (ART), repeat testing for LTBI is recommended for HIV-infected persons previously known to have negative TST or IGRA results. This is because the immune response may be restored by adequate treatment.

The Centers for Disease Control and Prevention (CDC) recommends:

- Routine HIV screening for all patients ages 13–64 seeking health care for any reason, without regard to patient's known risks for HIV infection
- Annual HIV screening of patients known to be at high risk<sup>26</sup>



## Pregnancy

Tuberculin skin testing is entirely safe and reliable for pregnant women, and pregnant women at high risk for TB infection or disease should be tested. Consider screening pregnant women for TB infection if they have any of the following conditions:

- Symptoms suggestive of TB disease
- HIV infection
- Behavioral risk factors for HIV
- Medical conditions other than HIV infection that increase the risk for TB disease
- Close contact with a person who has pulmonary or laryngeal TB disease
- Immigration from an area of the world where incidence of TB is high

## Follow-Up Activities

After TST or IGRA testing, complete the following tasks:

- **If the person has signs or symptoms of TB**, evaluate for TB disease as described in the Chapter 5, “Diagnosis of Tuberculosis Disease.” Refer to Table 3: **When to Suspect Pulmonary Tuberculosis in Adults.**
- **If the person is a contact**, follow the procedures for testing and evaluation in Chapter 10, “Contact Investigation.”
- **If the person is a participant in two-step screening**, see “Two-Step Tuberculin Skin Testing.”
- **If the tuberculin skin test (TST) or IGRA result is positive**, but does not have signs or symptoms of active TB disease, a chest radiograph should be obtained and treatment of LTBI should be considered. (See Chapter 8, “Treatment of Latent TB Infection.”)

## Chest Radiography

Chest x-rays help differentiate between LTBI and pulmonary TB disease in individuals with positive tests for TB infection. All individuals with a positive TST or IGRA being considered for LTBI treatment should undergo a chest radiograph to rule out pulmonary TB disease even in the absence of symptoms.<sup>27</sup>

A posterior-anterior radiograph of the chest is the minimum standard view used for the detection and description of chest abnormalities in adults. In most instances, a lateral view is obtained; other views (e.g., lordotic) or additional studies (e.g., computed tomography [CT] scans) may be necessary.



Children younger than five years of age should always receive posterior-anterior and lateral radiographs.<sup>28</sup>



For more information on chest radiography, refer to the Francis J. Curry National Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians* (Francis J. Curry National Tuberculosis Center Web site; 2006) at:

[http://www.nationaltbcenter.ucsf.edu/products/product\\_details.cfm?productID=EDP-04](http://www.nationaltbcenter.ucsf.edu/products/product_details.cfm?productID=EDP-04) .

For persons recently exposed to TB, follow the procedures for testing and evaluation in Chapter 10, "Contact Investigation."

## Sputum Examination for AFB Smear and Culture

Sputum examination is usually indicated for persons with positive test results for TB infection and either an abnormal chest radiograph or the presence of respiratory symptoms of greater than three weeks' duration (even when the chest radiograph is normal).<sup>29</sup>

## Physical Examination and Medical History

Physical examination and medical history should be done as part of the evaluation for latent TB infection. The history should include:<sup>30</sup>

- previous positive tests for TB infection
- previous treatment for LTBI or TB disease
- previous severe pulmonary disease
- risk assessment for liver disease
- drug allergies

Written documentation of a previously positive TST or IGRA result is required in order to forego testing someone with an indication for TB testing; a patient's verbal history is not sufficient.<sup>31</sup> If no written documentation is available, the test should be repeated, unless a history of severe allergic reaction to a previous TST is given, in which case an IGRA should be done.



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## Resources and References

### Resources

(For easy access to references, hyperlinks are provided for online references in the list below.)

- CDC. Self-Study Modules on Tuberculosis (2016) at: <http://www.cdc.gov/tb/education/ssmodules/default.htm>
- CDC. Core Curriculum on Tuberculosis (2013)at: <http://www.cdc.gov/tb/education/corecurr/index.htm>
- CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* (2013) at: <https://www.cdc.gov/tb/publications/ltbi/pdf/TargetedLTBI.pdf>
- Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children, *Clinical Infectious Diseases*, 2017;64(2) at: <https://academic.oup.com/cid/article/64/2/e1/2629583>

### References

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<sup>1</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54 (No. RR-12):15.

<sup>2</sup> *Clinical Summary: Latent Tuberculosis Infection: Screening*. U.S. Preventive Services Task Force. January 2017. <https://www.uspreventiveservicestaskforce.org/Page/Document/ClinicalSummaryFinal/latent-tuberculosis-infection-screening> Accessed November 7, 2018

<sup>3</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):7–9, 22.

<sup>4</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):8-9.

<sup>5</sup> CDC. Chapter 3: Testing for Tuberculosis Infection and Disease. *Core Curriculum on Tuberculosis: What the Clinician Should Know* [DTBE website]. 2016: p. 49. Available at: <https://www.cdc.gov/tb/education/corecurr/pdf/chapter3.pdf> Accessed November 6, 2018

<sup>6</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p 11. Available at: <https://www.cdc.gov/tb/publications/ltbi/pdf/TargetedLTBI.pdf> Accessed November 7, 2018.

<sup>7</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):11; CDC, NTCA. Guidelines for the investigation of contacts of persons with infectious tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):13; County of Los Angeles Tuberculosis Control Program. *Tuberculosis Control Program Manual: 2003 Edition:2-1*. Available at: <http://www.lapublichealth.org/tb/TBManual/TBmanual.pdf> . Accessed March 4, 2010.

<sup>8</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Providers* [DTBE website]. 2013. Available at: <https://www.cdc.gov/tb/publications/ltbi/default.htm>

<sup>9</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):1–2.

<sup>10</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):49.

<sup>11</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):50.

<sup>12</sup> CDC. Chapter 3: Testing for Tuberculosis Infection and Disease. *Core Curriculum on Tuberculosis: What the Clinician Should Know* [DTBE website]. 2016: p 67. Available at: <https://www.cdc.gov/tb/education/corecurr/pdf/chapter3.pdf> Accessed November 6, 2018.

<sup>13</sup> CDC. Chapter 3: Testing for Tuberculosis Infection and Disease. *Core Curriculum on Tuberculosis: What the Clinician Should Know* [DTBE website]. 2016: p 67. Available at: <https://www.cdc.gov/tb/education/corecurr/pdf/chapter3.pdf> Accessed November 6, 2018



- <sup>14</sup> Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children, *Clinical Infectious Diseases*, 2017;64(2): p e1, <https://academic.oup.com/cid/article/64/2/e1/2629583>.
- <sup>15</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p. 9 Available at: <https://www.cdc.gov/tb/publications/tbi/pdf/TargetedLTBI.pdf> Accessed November 6, 2018
- <sup>16</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):53.
- <sup>17</sup> CDC. Chapter 3: Testing for Tuberculosis Infection and Disease. *Core Curriculum on Tuberculosis: What the Clinician Should Know* [DTBE website]. 2016: p 56. Available at: <https://www.cdc.gov/tb/education/corecurr/pdf/chapter3.pdf> Accessed November 6, 2018
- <sup>18</sup> CDC. Chapter 3: Testing for Tuberculosis Infection and Disease. *Core Curriculum on Tuberculosis: What the Clinician Should Know* [DTBE website]. 2016: pp. 58-59 Available at: <https://www.cdc.gov/tb/education/corecurr/pdf/chapter3.pdf> Accessed November 6, 2018
- <sup>19</sup> CDC. Part two: reading the Mantoux tuberculin skin test. *Mantoux Tuberculin Skin Test Facilitator Guide* [DTBE Web site]. Available online at <http://www.cdc.gov/tb/education/Mantoux/default.htm> . Accessed March 4, 2010.
- <sup>20</sup> CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [DTBE Web site]. November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm> . Accessed March 4, 2010.
- <sup>21</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6): p24
- <sup>22</sup> CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [DTBE Web site]. November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm> . Accessed March 4, 2010.
- <sup>23</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p 10. Available at: <https://www.cdc.gov/tb/publications/tbi/pdf/TargetedLTBI.pdf> Accessed November 6, 2018
- <sup>24</sup> American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. American Academy of Pediatrics; 2018; 829-853. Available at: <https://redbook.solutions.aap.org/chapter.aspx?sectionid=189640207&bookid=2205#192304149> Accessed November 7, 2018.
- <sup>25</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p12. Available at: <https://www.cdc.gov/tb/publications/tbi/pdf/TargetedLTBI.pdf> Accessed December 17, 2018.
- <sup>26</sup> CDC. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. *MMWR* 2006;55(No. RR-14):1–17.
- <sup>27</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p. 14. Available at: <https://www.cdc.gov/tb/publications/tbi/pdf/TargetedLTBI.pdf> Accessed November 6, 2018
- <sup>28</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):25.
- <sup>29</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p 15. Available at: <https://www.cdc.gov/tb/publications/tbi/pdf/TargetedLTBI.pdf> Accessed November 6, 2018.
- <sup>30</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p 15. Available at: <https://www.cdc.gov/tb/publications/tbi/pdf/TargetedLTBI.pdf> Accessed November 6, 2018.
- <sup>31</sup> CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* [DTBE website]. 2013: p 15. Available at: <https://www.cdc.gov/tb/publications/tbi/pdf/TargetedLTBI.pdf> Accessed November 6, 2018.