Diagnosis of Latent Tuberculosis Infection

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska TB Program guidelines to

- classify patients with latent TB infection (LTBI)
- diagnose LTBI

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.[1]

Evaluation and follow-up of contacts are covered in more depth in the Contact Investigation section **11.1**. For information on treatment, refer to the Treatment of Latent Tuberculosis Infection section **8.1**.

For detailed information on the diagnosis and treatment of latent tuberculosis infection in children, refer to the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 16 years of age) section **9.1**.

Policy

In Alaska, TB screening should be provided for:

- Individuals with risk factors for LTBI (See Table 2, 7.6).
- Persons with a greater risk to progress to active TB once infected with *M. tuberculosis* (i.e., those infected with HIV)[2]
- Persons who are contacts to an active TB case, as described in the Contact Investigation section **11.1**.

For roles and responsibilities, refer to the “Roles, Responsibilities, and Contact Information” topic in the Introduction **1.11**.

Forms

All required and recommended forms are available in the Forms section of this manual **18.1**.

Tuberculosis Classification System

The system for classifying tuberculosis (TB) is based on how the infection and disease develop in the body. Use this classification system to help track the status of TB in your patients and to allow comparison with other reporting areas.

Table 1: **TUBERCULOSIS CLASSIFICATION SYSTEM**[3]

Class	Type	Description
0	▪ No tuberculosis (TB) exposure ▪ Not infected	▪ No history of exposure and no evidence of TB infection or disease ▪ Negative reaction to the tuberculin skin test (TST) or interferon gamma release assay (IGRA)
1	▪ TB exposure ▪ No evidence of infection	▪ History of exposure ▪ Negative reaction to the TST or IGRA (given at least 8-10 weeks after exposure)
2	▪ TB infection ▪ No disease	▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) ▪ No clinical, bacteriologic, or radiographic evidence of TB disease
3	▪ TB disease ▪ Clinically active	▪ *Mycobacterium tuberculosis* (*M*tb) complex cultured (if this has been done) ▪ Clinical, bacteriologic, or radiographic evidence of current disease
4	▪ Previous TB disease ▪ Not clinically active	▪ History of episode(s) of TB ▪ Abnormal but stable radiographic findings ▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) ▪ No clinical or radiographic evidence of current disease
5	▪ TB suspect	▪ Signs and symptoms of active TB disease but medical evaluation not complete

Adapted from: CDC. Chapter 2: Transmission and Pathogenesis of Tuberculosis. *Core Curriculum on Tuberculosis (2013)* [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf . Accessed January 14, 2021.

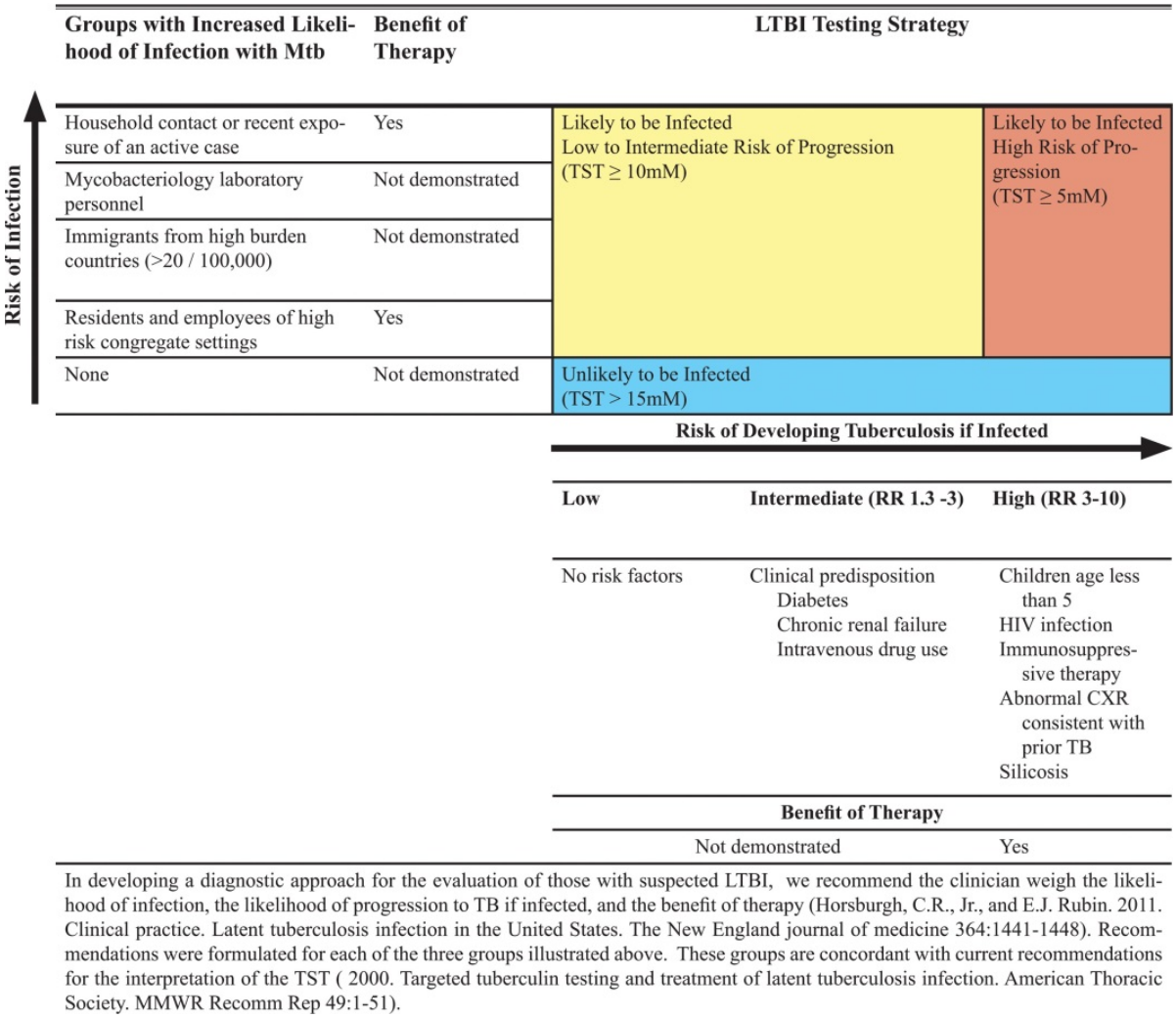
High-Risk Groups

Certain factors identify persons at high risk for tuberculosis (TB) infection and/or for progression to TB disease. Persons in the high-risk groups listed in Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease** are candidates for tuberculin skin testing in Alaska.

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 at much higher risk of having active TB than a US-born individual with HIV infection.

Alaska Native individuals, especially persons from the Southwest and Northern regions of the state, have an increased likelihood of TB infection.

Figure 1. **PARADIGM FOR EVALUATION OF THOSE WITH LATENT TUBERCULOSIS INFECTION (LTBI) BASED ON RISK OF INFECTION, RISK OF PROGRESSION TO TUBERCULOSIS, AND BENEFIT OF THERAPY**[4]



In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to TB if infected, and the benefit of therapy (Horsburgh, C.R., Jr., and E.J. Rubin. 2011. Clinical practice. Latent tuberculosis infection in the United States. The New England journal of medicine 364:1441-1448). Recommendations were formulated for each of the three groups illustrated above. These groups are concordant with current recommendations for the interpretation of the TST (2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. MMWR Recomm Rep 49:1-51).

Source: ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.

Table 2: **PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE**[5,6]

For Tuberculosis Infection	For Progression to Tuberculosis Disease[7]
▪ High-priority contacts such as housemates or coworkers or contacts of persons who have smear-positive pulmonary or laryngeal tuberculosis (TB) ▪ Infants, children, and adolescents exposed to adults in high-risk categories ▪ Recent immigrants (<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) ▪ Recent immigrants from Mexico ▪ Migrant workers ▪ Persons who have recently spent over 3 months in high-incidence countries ▪ American Indians/Alaska Natives ▪ Persons with high rates of TB transmission: • Homeless persons • Injection drug users • Persons with human immunodeficiency virus (HIV) infection • Persons living or working in institutions with individuals at risk for TB such as: ▪ Hospitals, especially staff in nursing, emergency departments, and laboratories ▪ Long-term care facilities ▪ Homeless shelters ▪ Residences for acquired immunodeficiency syndrome (AIDS) patients ▪ Correctional facilities	▪ Persons with HIV infection ▪ Infants and children aged <5 years ▪ Persons infected with *Mycobacterium tuberculosis* within the previous 2 years ▪ Persons with a history of untreated or inadequately treated TB disease ▪ Persons with radiographic findings consistent with previous TB disease ▪ Persons who use alcohol or illegal drugs (such as injection drugs or crack cocaine) ▪ Persons with any of the following clinical conditions or other immunocompromising conditions: • Silicosis • Diabetes mellitus • End-stage renal disease (ESRD)/chronic renal failure, hemodialysis • Some hematologic disorders (e.g., leukemias and lymphomas) • Other malignancies (e.g., carcinoma of head, neck, or lung) • Body weight ≥10% below ideal body weight • Prolonged corticosteroid use • Use of other immunosuppressive treatments (e.g., prednisone or tumor necrosis factor-alpha [TNF- α] antagonists) • Organ transplantation • Gastrectomy • Chronic malabsorption syndromes • Jejunoileal bypass

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 Tuberculosis Infection

The diagnosis of latent tuberculosis infection (LTBI) has traditionally been based upon results of tuberculin skin testing (TST). However, whole-blood interferon gamma release assays (IGRAs), are now increasingly available and may be the preferred option for detecting LTBI in many situations.

In December 2016, new *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* were published. These recommendations suggest performing IGRAs rather than TSTs in all individuals 5 years of age and older who are likely to be infected with *Mtb*, have a low or intermediate risk of disease progression, and in whom it been decided that testing for LTBI is warranted. The preferential use of IGRAs is most strongly recommended for those who have a history of BCG vaccination or who are unlikely to return to have their TST read. Many experts also approve the use of IGRA in children over the age of 2 years. A TST remains an acceptable alternative for TB testing, especially in situations where IGRAs are not available, too costly, or too burdensome.[8]

Figure 2. **SUMMARY OF RECOMMENDATIONS FOR TESTING FOR LATENT TUBERCULOSIS INFECTION (LTBI)**

Group	Testing Strategy	Considerations
Likely to be Infected **High** Risk of Progression (TST ≥ 5mM)	**Adults** **Acceptable**: IGRA OR TST Consider dual testing where a positive result from either result would be considered **positive** **Children ≤ 5 years of age** **Preferred**: TST **Acceptable**: IGRA OR TST Consider dual testing where a positive result from either would be considered **positive**[1]	Prevalence of BCG vaccination Expertise of staff and/or laboratory Test availability Patient perceptions Staff perceptions Programmatic concerns
Likely to be Infected **Low** to **Intermediate** Risk of Progression (TST ≥ 10mM)	**Preferred**: IGRA where available **Acceptable**: IGRA or TST	
Unlikely to be Infected (TST > 15mM)	**Testing for LTBI is not recommended** **If necessary:** **Preferred:** IGRA where available. **Acceptable**: Either IGRA OR TST **For serial testing**: **Acceptable**: Either IGRA OR TST Consider repeat or dual testing where a negative result from either would be considered **negative**[2]	

Figure 2. Summary of recommendations for testing for latent tuberculosis infection (LTBI). [1]Performing a second diagnostic test when the initial test is negative is a strategy to increase sensitivity. This may reduce specificity, but the panel decided that this is an acceptable trade-off in situations in which the consequences of missing LTBI (ie, not treating individuals who may benefit from therapy) exceed the consequences of inappropriate therapy (ie, hepatotoxicity). [2]Performing a confirmatory test following an initial positive result is based upon both the evidence that false-positive results are common among individuals who are unlikely to be infected with Mycobacterium tuberculosis and the committee's presumption that performing a second test on those patients whose initial test was positive will help identify initial false-positive results. Abbreviations: IGRA, interferon-γ release assay; LTBI, latent tuberculosis infection; TST, tuberculin skin test.

Source: ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.

Interferon Gamma Release Assays (IGRA) are not provided by or funded by the Alaska TB Program. Reference laboratories currently provide IGRA testing in many communities statewide.

Mantoux Tuberculin Skin Testing

The Mantoux method of tuberculin skin testing (TST) is used to detect infection with *Mycobacterium tuberculosis.*

In general, it takes 2 to 10 weeks after infection for a person to develop a delayed-type immune response to tuberculin measurable with the Mantoux TST.[9] During the test, tuberculin is injected into the skin. 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.

The size of the measured induration (a hard, dense, raised formation) and the patient's individual risk factors should determine whether TB infection is diagnosed.[10]

Based on the sensitivity and specificity of the purified protein derivative (PPD) TST and the prevalence of TB in different groups, three cut-points are used by CDC for defining a positive tuberculin reaction:

- Greater than or equal to 5 mm
- Greater than or equal to 10 mm
- Greater than or equal to 15 mm of induration[11]

For more information on cut-points for the TST, see the “Interpretation of the Tuberculin Skin Test” topic in this section.

In Alaska, because of our historic and continuing high rates of TB and latent TB infection, any person with a reaction of 10 mm or greater induration is considered TST positive.

Candidates for Mantoux Tuberculin Skin Testing

The Mantoux TST can be administered to all persons, including pregnant women,[12] persons who have previously been vaccinated with bacille Calmette-Guérin (BCG),[13] and human immunodeficiency virus (HIV)-infected persons. However, persons with a documented prior positive TST do not need another TST, and the Mantoux TST should not be administered until four weeks after vaccination with live-virus vaccines.

If the person being tested is a contact, follow the procedures outlined in the Contact Investigation section **11.1**.

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. Screen 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

Bacille Calmette-Guérin Vaccine

BCG vaccines are live vaccines derived from a strain of *Mycobacterium bovis.* Because their effectiveness in preventing infectious forms of TB has never been demonstrated in the United States, they are not recommended as a TB control strategy in the United States, except under rare circumstances. They are, however, still used commonly in other countries. A history of BCG vaccination is not a contraindication for tuberculin skin testing, nor does it influence the indications for a TST. Administer and measure TSTs in BCG-vaccinated persons in the same manner as in those with no previous BCG vaccination.

Diagnosis and treatment of LTBI should be considered for BCG-vaccinated persons with a TST reaction of equal to or greater than 10 mm induration, especially if they are

- continually exposed to populations with a high prevalence of TB (e.g., some healthcare workers, employees and volunteers at homeless shelters, and workers at drug treatment centers)
- born or have lived in a country with a high prevalence of TB; or
- exposed to someone with infectious TB, particularly if that person has transmitted TB to others.[14]

Evaluate these patients for symptoms of TB. If a patient has symptoms of TB disease, obtain chest radiography and collect sputum specimens.

One advantage of the IGRA testing is that persons with BCG vaccination will not have a positive IGRA test from BCG vaccination. For this reason, IGRA testing is preferred over TST for this population if feasible.

Anergy Testing

Anergy testing is not routinely recommended in conjunction with TST for HIV-infected persons in the U.S.[15]

Anergy testing is a diagnostic procedure used to obtain information about the competence of the cellular immune system. Conditions that may cause an impaired cellular immune system include HIV infection, severe or febrile illness, measles or other viral infections, Hodgkin's disease, sarcoidosis, live virus vaccination, and corticosteroid or immunosuppressive therapy. Persons with conditions such as these may have suppressed reactions to a TST even if infected with TB. However, there are no simple skin testing protocols that can reliably identify persons as either anergic or nonanergic and that have been proven to be feasible for application in public health TB screening programs.

Factors limiting the usefulness of anergy skin testing include the following:

- Problems with standardization and reproducibility
- Low risk for TB associated with a diagnosis of anergy

- Lack of apparent benefit of treatment for LTBI in groups of anergic HIV-infected persons

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 have a TB symptom assessment questionnaire administered to identify any symptoms of TB disease.[16] Persons who are symptomatic should receive a chest radiograph and evaluation including sputa collection. Routine chest radiographs are NOT indicated.

Use the *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* to document history and TB screening assessment. Forms are available in the Forms section of this manual **18.1.**

See the "Work or school clearance" topic in this section for additional information on clearing individuals with prior positive TSTs for work or school **7.21**.

Live-Virus Vaccines

The Mantoux TST can be administered safely in conjunction with all vaccines. However, the measles (MMR) vaccine—and possibly mumps, rubella, varicella, and live attenuated influenza vaccines—may transiently suppress the response to PPD.[17] Therefore, if a vaccine containing live virus (for example, measles, MMR, varicella, or live attenuated influenza vaccine) has already been given, the TST should be deferred until (or repeated) at least four weeks after the vaccine was administered.

When giving the TST and the live virus vaccine, one of the following three sequences should be used:

- Apply the TST at same visit as the live virus vaccine.
- Delay the TST at least four weeks if the live virus vaccine is given first
- Apply the TST first and then give the live virus vaccine when the TST is measured[18]

Multiple Puncture Tests

Multiple puncture tests (MPTs), such as the Tine test, should not be used. MPTs are not reliable because the amount of tuberculin injected intradermally cannot be precisely controlled and there is no standard for interpretation.

Administration of the Tuberculin Skin Test

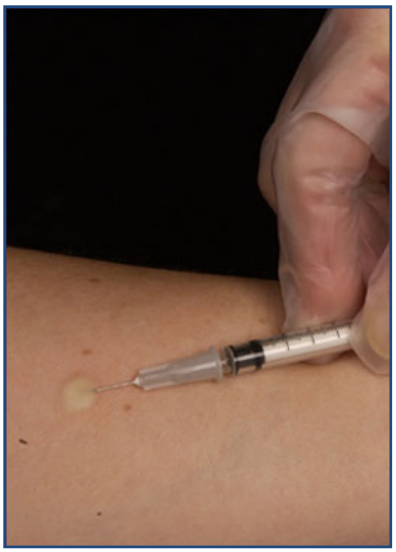
The TST should be placed by a healthcare worker who has received appropriate training and is following written protocols.

Table 3: **BEFORE YOU BEGIN TO ADMINISTER A TUBERCULIN SKIN TEST**

Before You Begin to Administer a TST	
Review Information	▪ CDC. *Mantoux Tuberculin Skin Test Facilitator Guide*. Available at: http://www.cdc.gov/tb/education/mantoux/pdf/mantoux.pdf ▪ Your agency's Infection control procedures
Gather Equipment	▪ Alcohol pads or alternative skin cleanser ▪ Safety needle ▪ Tuberculin syringe (Do not pre-draw tuberculin into syringes prior to test.) ▪ Purified protein derivative (PPD) (Tubersol® or Aplisol®: See the warning in the text below this table.) ▪ Sharps container ▪ Optional: gloves, depending on institutional policy **Note:** Opened PPD tuberculin vials must be dated and discarded after 30 days. See the package insert for appropriate storage information.

Read the PPD labels carefully before administering a TST. The packaging of tetanus toxoid-containing vaccines (TTCVs) is similar to Tubersol® and Aplisol®, and all are refrigerated. See CDC's "Inadvertent Intradermal Administration of Tetanus Toxoid--Containing Vaccines Instead of Tuberculosis Skin Tests" MMWR July 30, 2004 / 53(29);662-664 at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5329a5.htm

How to Administer a Tuberculin Skin Test



If the patient's written consent is required, obtain it per health department requirements.

1. Inject air into the vial air space (not into the solution). Injection of air into the air space in the vial prevents creation of negative pressure within the vial, allowing the antigen to be withdrawn easily. Injecting air into the solution creates bubbles and may interfere with withdrawing the correct amount of antigen.[19]
2. 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.
3. 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.
4. 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. Filled syringes should be kept cool and protected from light. If they are not used within an hour of being drawn up, they should be discarded.
5. The injection should produce a discrete, pale elevation of the skin (a wheal) 6 to 10 mm in diameter. **Note:** If a 6- to10-mm wheal is not produced, repeat the test on the opposite arm or the same arm, 2 inches from the original site.
6. 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 reason for testing according to clinic or agency protocol.[20]

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.[21]

- A positive reaction can be measured any time after 48 hours and may be read up to 7 days after placement.
- If the test is read more than 72 hours after placement and the test appears negative, the test should be repeated. It can be repeated immediately, or after one week, if two-step testing is required.

- On a case-by-case basis, TSTs may be read 2-3 hours early or late to avoid not reading them at all. This might occur, for example, when PHNs who itinerate to villages must read a TST when the patient is available or risk having the TST go unread.
- On occasion, TSTs read as negative between 48-72 hours develop measurable induration. If this occurs, call the Alaska TB Program at 907-269-8000 for guidance.

See “Two-Step Tuberculin Skin Testing” in the Infection Control section of this manual **17.11**.

Before you measure a TST, review information in the CDC’s *Mantoux Tuberculin Skin Test Facilitator Guide* at http://www.cdc.gov/tb/education/mantoux/pdf/mantoux.pdf .

How to Measure a Tuberculin Skin Test

1. Measure the TST site crosswise to the axis of the forearm.
2. Induration is a firm, dense, raised formation. Measure only induration (firmness) 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 and document the result.
4. Report adverse reactions to a TST (e.g., blistering, ulcerations, necrosis) to the FDA’s MedWatch Program at 1-800-332-1088, or via the Internet at http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm

Interpretation of the Tuberculin Skin Test

TSTs should be interpreted by a trained healthcare worker. Use Table 4 below to interpret TSTs.

Before you interpret a TST, review information in the CDC’s *Mantoux Tuberculin Skin Test Facilitator Guide* at http://www.cdc.gov/tb/education/mantoux/pdf/mantoux.pdf .

For questions or guidance regarding the interpretation of TSTs, call the Alaska TB Program at 907-269-8000.

How to Interpret a Tuberculin Skin Test

Use the table below to determine when a reaction is positive.

Table 4: **POSITIVE TUBERCULIN SKIN TEST REACTIONS IN ALASKA**

Induration Size	Considered Positive For:
5 mm or more	▪ Recent contacts of an infectious case of tuberculosis (TB) disease ▪ Persons with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) ▪ Persons with fibrotic lesions on chest radiograph consistent with healed TB ▪ Persons with organ transplants or other immunosuppressed persons (such as those receiving the equivalent of >15 mg/day of prednisone for >1 month) ▪ Persons receiving treatment with tumor necrosis factor-alpha (TNF-α) antagonists
10 mm or more	▪ **All others in Alaska**

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.

False-negative reactions may be due to the following:

- Anergy

See “Anergy Testing” under “Candidates for Mantoux Tuberculin Skin Testing” in this section **7.10**.

- 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, or yellow fever).

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” under “Candidates for Mantoux Tuberculin Skin Testing” in this section **7.11**.

- Some viral infections (measles, mumps, chickenpox, or HIV)
- Corticosteroids or other immunosuppressive agents given for two or more weeks

False-positive reactions may be due to the following:[22]

- Nontuberculous mycobacteria (NTM) or mycobacterium other than tuberculosis (MOTT)
- BCG vaccination

See “Bacille Calmette-Guérin Vaccine” under “Candidates for Mantoux Tuberculin Skin Testing” in this section.

Interferon Gamma Release Assays

TB blood tests are also called interferon-gamma release assays or IGRAs. Two TB blood tests are approved by the U.S. Food and Drug Administration (FDA) and are available in the United States: the QuantiFERON®–TB Gold In-Tube test (QFT-GIT) and the T-SPOT®.TB test (T-Spot).

A health care provider will draw a patient’s blood and send it to a laboratory for analysis and results.

- **Positive TB blood test:** This means that the person has been infected with TB bacteria. Additional tests are needed to determine if the person has latent TB infection or TB disease.
- **Negative TB blood test:** This means that the person’s blood did not react to the test and that latent TB infection or TB disease is not likely.

TB blood tests are the preferred TB test for:

- People who have received the TB vaccine bacille Calmette–Guérin (BCG).
- People who have a difficult time returning for a second appointment to have their TST read.[23]

The advantages of IGRA tests, compared with the TST, are that results can be obtained after a single patient visit, and that, because it is a blood test performed in a qualified laboratory, the variability associated with skin test reading can be eliminated.[24] In addition, the IGRA tests are unaffected by past BCG vaccination and may eliminate the unnecessary treatment of patients with BCG-related false-positive results.[25] However, the IGRA test also has practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory in time for testing. As with the TST, additional tests, such as chest radiography and bacteriologic examination, are required to confirm or rule out active TB disease. [26]

Persons with a positive IGRA or TST result, regardless the presence or absence of symptoms and signs, must be evaluated for TB disease before LTBI is diagnosed. At minimum, a medical examination should be performed and a chest radiograph should be done to look for abnormalities consistent with TB disease. [27]

Negative IGRA results should not be used alone to exclude *M. tuberculosis* infection in persons with symptoms or signs suggestive of TB disease. Medical evaluation of such persons should include a history and physical examination, chest radiograph, bacteriologic studies, serology for human immunodeficiency virus (HIV), and, when indicated, other tests or studies.[28]

CDC released new Interferon Gamma Release Assays (IGRA) guidelines on June 25, 2010, "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010" *(MMWR* 2010; 59 [No. RR-5];1-25) at http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf

Human Immunodeficiency Virus Screening

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

- 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 (or more frequent) HIV screening of patients known to be at high risk[29]

Follow-Up Activities

After testing, complete the following tasks:

If the person has signs or symptoms of TB, evaluate for TB disease as described in the "Diagnosis of Tuberculosis Disease" topic in the Diagnosis of Tuberculosis Disease section. **(5.11)**. Refer to Table 4: **When to Suspect Pulmonary Tuberculosis in Adults**.

If the person is a contact, follow the procedures for testing and evaluation in the Contact Investigation section **11.1**.

If the person is a participant in two-step screening, see the topic titled "Two-Step Tuberculin Skin Testing" in the Infection Control section **17.11**.

If the TST result is newly positive, a chest radiograph should be obtained for the patient, as specified in the "Chest Radiography" topic in this section **7.18**.

Chest Radiography

All individuals being considered for LTBI treatment should undergo a chest radiograph to rule out pulmonary TB disease. **Asymptomatic patients whose most recent chest radiograph was taken more than 2 - 3 months prior to starting treatment should have a repeat chest X-ray.** The Alaska TB Program may be able to provide partial reimbursement for patients in need of a chest x-ray but without insurance or financial resources to cover the cost.

Refer to Table 5 to determine when to obtain a chest radiograph and what follow-up is required for chest radiograph results.

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

PHNs or health care providers should request approval from the Alaska TB Program for partial reimbursement for a single view chest film (CPT 71010) for patients otherwise unable to pay **before** the x-ray is done. Call the Alaska TB Program at 907-269-8000 for an authorization number.

Authorize chest radiographs for patients otherwise unable to pay on the *Request and Authorization for TB Screening and Follow-up Services* **(18.1)** form and send the completed form to the service provider. All chest radiographs requested and authorized should be submitted to the Alaska TB Program for interpretation by our contract radiologist. Comparison films should also be included if available. Please submit all films or digital images and the completed *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* **(18.1)** to the Alaska TB Program at 3601 C St, Ste. 540, Anchorage, AK 99503.

Children younger than 5 years of age should receive posterior-anterior and lateral radiographs.[30]

For detailed information on the diagnosis and treatment of latent tuberculosis infection in children, refer to the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 16 years of age) section **9.1**.

For more information on chest radiography, refer to the Curry International Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians,2nd Edition* (Curry International Tuberculosis Center Web site; 2011) at http://currytbcenter.ucsf.edu/products/product_details.cfm?productID=EDP-04

For persons recently exposed to TB, follow the procedures for testing and evaluation in the Contact Investigation section **11.1**

Chest X-ray Interpretation and Treatment Recommendations

Treatment for LTBI should be prescribed by the patient's health care provider. **For patients without providers or the financial resources to obtain care, the Alaska TB Program recommendations from the Clinical Consultation Summary for LTBI treatment may be used as a prescription for LTBI treatment.** Such patients must be adequately evaluated and have a chest x-ray. The results of the TST or IGRA, review of symptoms, medical history and risk factors should be recorded on the *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* **(18.1)** and must be submitted to the Alaska TB Program with the chest radiograph for medical review and recommendations.

Table 5: **TARGETED TESTING FOR LATENT TUBERCULOSIS INFECTION: WHEN CHEST RADIOGRAPHS ARE REQUIRED AND HOW TO FOLLOW UP ON RADIOGRAPHY RESULTS**

Signs or Symptoms of TB Disease?	TST or IGRA Result?	Recent Exposure to Infectious TB?	Chest Radiograph?	Follow-up Action
Yes	Positive or negative	Yes or no	Normal or abnormal	▪ Evaluate for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.
No	Negative	No	CXR not recommended unless the patient has HIV infection or other forms of immunosuppression are present	▪ No further evaluation or treatment
No	Positive	No	Normal	▪ Treat for LTBI. Refer to the Treatment of Latent Tuberculosis Infection section.
			Abnormal: Noncalcified fibrotic lesions suggestive of old, healed TB; comparison film available and stable	▪ Consider evaluation for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.
			Abnormal: Consistent with TB disease; no comparison film	▪ Evaluate for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.

Definitions of abbreviations: CXR = chest radiograph; HIV = human immunodeficiency virus; IGRA = interferon gamma release assay; LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.

Work or School Clearance

Persons with newly positive TSTs or IGRAs may be cleared for work or school if they are low-risk by history, asymptomatic, and have a negative chest radiograph. Persons with prior positive TSTs may be cleared if they are asymptomatic. Routine chest radiographs are NOT indicated unless persons with prior positive TSTs or IGRAs become symptomatic for TB.

Use the *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* **(18.1)** to complete history and symptom screening. If history, symptom screening and chest x-ray are negative, the patient may be cleared for work or school by the PHN or provider. Complete the *Tuberculosis Screening and Clearance Card* to document clearance.

*Tuberculosis Screening and Clearance c*ards can be ordered from the Alaska TB Program by calling 907-269-8000.

Resources and References

Resources

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