

Diagnosis of Latent Tuberculosis Infection

CONTENTS

Introduction.....	7.2	Candidates for Mantoux tuberculin skin testing	7.8
Purpose.....	7.2	Administration of the tuberculin skin test.....	7.11
Policy	7.2	Measurement of the tuberculin skin test	7.13
Forms.....	7.3	Interpretation of the tuberculin skin test	7.14
Tuberculosis Classification System.....	7.4	Human immunodeficiency virus screening.....	7.16
High-Risk Groups	7.5	Follow-up activities.....	7.16
Diagnosis of Latent Tuberculosis Infection.....	7.7	Interferon gamma release assays	7.16
Mantoux tuberculin skin testing	7.7	Chest radiography.....	7.17
		Resources and References.....	7.20

Introduction

Purpose

Use this section to understand and follow national and Arizona guidelines to

- classify patients with latent TB infection (LTBI)
- diagnose 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.¹



Contacts are mentioned within this section, but their evaluation and follow-up are covered in more depth in the Contact Investigation section. For information on treatment, refer to the Treatment of Latent Tuberculosis Infection section.

Policy

In Arizona:

- Targeted testing for LTBI should be conducted only among persons in groups with identified risk factors for LTBI and/or progression to TB disease.
- Contacts should be evaluated as described in the Contact Investigation section.



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

State Laws and Regulations

Arizona Laws/Rules Regarding Tuberculosis Control
Arizona Revised Statutes. Title 36: Public Health and Safety; Chapter 6:
Public Health Control; Title 6: Tuberculosis Control. (ARS§36-711
through §36-738)

ARS§36-711. Definitions.

ARS§36-712. Administration by the department.

ARS§36-714. Tuberculosis control officer.

ARS§36-715. Costs; removals; proceedings.

ARS§36-716. Payment of assistance.

ARS§36-717. Responsibility for care or treatment by counties.

ARS§36-718. Contracting for care of afflicted persons.

ARS§36-721. Rules.

ARS§36-723. Investigation of tuberculosis cases.

ARS§36-724. Voluntary control measures.

ARS§36-725. Orders to cooperate; emergency custody.

ARS§36-726. Petition for court ordered examination, monitoring,
treatment, isolation or quarantine.

ARS§36-727. Hearings; procedure; confidentiality.

ARS§36-728. Judicial action.

ARS§36-729. Amended orders for intervention and transport of afflicted
persons.

ARS§36-730. Appointment of guardian or conservator.

ARS§36-731. Confinement; selection; jails; prohibition.

ARS§36-732. Early release from court ordered treatment.

ARS§36-733. Choice of physician and mode of treatment.

ARS§36-734. Treatment; exemption.

ARS§36-735. Notification of rights.

ARS§36-736. Administrative procedures act; judicial review of
administrative procedures; exemption; appeals.

ARS§36-737. Violation; classification.

ARS§36-738. Qualified immunity.

Arizona Administrative Code. Title 9. Chapter 6. Department of
Health Services Communicable Diseases and Infestations.

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**²

Class	Type	Description
0	<ul style="list-style-type: none"> ▪ No tuberculosis (TB) exposure ▪ Not infected 	<ul style="list-style-type: none"> ▪ No history of exposure ▪ Negative reaction to the tuberculin skin test (TST) or interferon gamma release assay (IGRA)
1	<ul style="list-style-type: none"> ▪ TB exposure ▪ No evidence of infection 	<ul style="list-style-type: none"> ▪ History of exposure ▪ Negative reaction to the TST or IGRA
2	<ul style="list-style-type: none"> ▪ TB infection ▪ No disease 	<ul style="list-style-type: none"> ▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) ▪ No clinical, bacteriologic, or radiographic evidence of TB disease
3	<ul style="list-style-type: none"> ▪ TB disease ▪ Clinically active 	<ul style="list-style-type: none"> ▪ <i>Mycobacterium tuberculosis</i> complex cultured (if this has been done) ▪ Clinical, bacteriologic, or radiographic evidence of current disease
4	<ul style="list-style-type: none"> ▪ TB disease ▪ Not clinically active 	<ul style="list-style-type: none"> ▪ History of episode(s) of TB <li style="text-align: center;">Or ▪ Abnormal but stable radiographic findings ▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) <li style="text-align: center;">And ▪ No clinical or radiographic evidence of current disease
5	<ul style="list-style-type: none"> ▪ TB suspect 	<ul style="list-style-type: none"> ▪ Diagnosis pending

Adapted from: CDC. Classification system. In: Chapter 2: transmission and pathogenesis. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/pubs/corecurr/default.htm> . Accessed July 3, 2006.

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 Arizona.

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.

Table 2: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE³

For Tuberculosis Infection	For Progression to Tuberculosis Disease ⁴
<ul style="list-style-type: none"> ▪ 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 (such as missionaries from the Church of Jesus Christ of Latter-Day Saints) ▪ Native Americans ▪ Persons with high rates of TB transmission: <ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> ▪ Hospitals, especially staff in nursing, emergency departments, and laboratories ▪ Long-term care facilities ▪ Homeless shelters ▪ Residences for acquired immunodeficiency syndrome (AIDS) patients ▪ Correctional facilities 	<ul style="list-style-type: none"> ▪ Persons with HIV infection ▪ Infants and children aged <5 years ▪ Persons infected with <i>Mycobacterium tuberculosis</i> 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: <ul style="list-style-type: none"> • 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 $\geq 10\%$ below idea 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 • Jejunioileal 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 been traditionally based upon results of tuberculin skin testing. However, the QuantiFERON®-TB Gold test (QFT-G), a whole-blood interferon gamma release assay (IGRA), is now another option for detecting LTBI.

Use the Mantoux tuberculin skin test (TST) or the QFT-G to test for *Mycobacterium tuberculosis* infection. QFT-G can be used in all circumstances in which the TST is used, and the QFT-G usually can be used in place of (and not in addition to) the TST.⁵



For information on testing methods available in Arizona, refer to the Laboratory Services section.

Mantoux Tuberculin Skin Testing

The Mantoux method of tuberculin skin testing 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 tuberculin skin test (TST).⁶ 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.⁷ Based on the sensitivity and specificity of the purified protein derivative (PPD) TST and the prevalence of TB in different groups, three cut-points have been recommended 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 induration⁸



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

Candidates for Mantoux Tuberculin Skin Testing

The Mantoux TST can be administered to all persons, including pregnant women,⁹ persons who have previously been vaccinated with Bacille Calmette-Guérin (BCG),¹⁰ 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.

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, 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.¹¹

Evaluate these patients for symptoms of TB. If a patient has symptoms of TB disease, obtain chest radiography and (if the patient is coughing) collect sputum specimens.

Anergy Testing

Anergy testing is not routinely recommended in conjunction with TST for HIV-infected persons in the U.S.¹²

Anergy testing is a diagnostic procedure used to obtain information about the competence of the cellular immune system. Conditions that 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.¹³ Persons who are symptomatic should receive a chest radiograph.

Live-Virus Vaccines

The Mantoux TST can be administered 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.¹⁴ Therefore, if a vaccine containing live virus (e.g., measles, smallpox) 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 MMR, one of the following three sequences should be used:

- Apply the TST at same visit as the MMR
- Delay the TST at least four weeks if the MMR is given first
- Apply the TST first and then give the MMR when the TST is measured¹⁵

Multiple Puncture Tests

Multiple puncture tests (MPTs), such as the Tine test, should not be used. The 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	<p>CDC. <i>Mantoux Tuberculin Skin Test Facilitator Guide</i> at http://www.cdc.gov/tb/pubs/Mantoux/guide.htm</p> <p>Infection control procedures (including hand washing before and after the procedure and the use of gloves and a sharps container).</p>
Gather Equipment	<ul style="list-style-type: none"> ▪ Gloves ▪ 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 in this table.) ▪ Sharps container <p>Note: Opened PPD tuberculin vials must be dated and discarded after 30 days. See the package insert for appropriate storage information.</p>



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 the CDC's "Errors Involving Mix-up of Tuberculin Purified Protein Derivative and Vaccine Products" (*TB Notes Newsletter*, 2005;No. 1) at http://www.cdc.gov/tb/notes/TBN_1_05/Errors_mix_up.htm.

How to Administer a Tuberculin Skin Test

1. If the patient's written consent is required, obtain it, per health department requirements.
2. 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.¹⁶
3. 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.
4. 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.
5. 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.
6. 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.
7. 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.¹⁷

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.¹⁸

- A positive reaction can be measured anytime after 48 hours.
- 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.



See the topic titled “Two-Step Tuberculin Skin Testing” in the Infection Control section.



Before you measure a TST, review information in the CDC's *Mantoux Tuberculin Skin Test Facilitator Guide* at <http://www.cdc.gov/tb/pubs/Mantoux/guide.htm> .

How to Measure a Tuberculin Skin Test

1. Measure the TST site crosswise to the axis of the forearm.
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 <http://www.fda.gov/medwatch/> .

Interpretation of the Tuberculin Skin Test

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



Call the medical director regarding TST reactions when interpretation and medical follow-up are unclear.



Before you interpret a TST, review information in the CDC's *Mantoux Tuberculin Skin Test Facilitator Guide* at <http://www.cdc.gov/tb/pubs/Mantoux/guide.htm>.

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**

Induration Size	Considered Positive For:
5 mm or more	<ul style="list-style-type: none"> ▪ Persons with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) ▪ Recent contacts of an infectious case of tuberculosis (TB) disease ▪ 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	<ul style="list-style-type: none"> ▪ 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, Russia, or from refugee camps) ▪ Persons who inject drugs or use other high-risk substances, such as crack cocaine ▪ Alcoholics ▪ 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) ▪ Mycobacteriology laboratory personnel ▪ Persons with other medical conditions that increase the risk of TB disease ▪ Children younger than 5 years of age, or children and adolescents exposed to adults in high-risk categories

Induration Size	Considered Positive For:
15 mm or more	<ul style="list-style-type: none"> Persons with no known risk factors for TB

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.

- 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.

- 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:¹⁹

- 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.

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 HIV screening of patients known to be at high risk²⁰

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. 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 the Contact Investigation section.



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



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

Interferon Gamma Release Assays

An interferon gamma release assay (IGRA) is another method to test for *M. tuberculosis* infection. For patients with a previous documented positive TST reaction, an IGRA can be done. Refer to www.quantiferon.com for available test sites. Refer to the Celestis web-site <http://cellestis.com/> for additional information.

Blood assay for *Mycobacterium tuberculosis* (BAMT) is a general term referring to recently developed in vitro diagnostic tests that reveal the presence of infection with *M. tuberculosis*. This term includes, but is not limited to IGRAs. The IGRA currently approved by the Food and Drug Administration (FDA) and available on the market is QuantiFERON[®]-TB Gold (QFT-G), which can be used in all circumstances in which the TST is used. QFT-G usually can be used in place of the TST.²¹ Other cytokine-based immunoassays are under development and may also become useful in the diagnosis of *M. tuberculosis* infection. Future FDA-licensed products, in combination with CDC-issued recommendations, may provide additional diagnostic alternatives.²²

The advantages of IGRA, 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.²³ In addition, the QFT-G test appears to be less affected by past BCG vaccination than the TST and may eliminate the unnecessary treatment of patients with BCG-related false-positive results.²⁴ However, the QFT-G test has practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory in time for testing. For QFT-G tests, the blood must be incubated with the test antigens <12 hours after collection, while the lymphocytes are viable.²⁵ ²⁶ Refer to www.quantiferon.com for available test sites. Refer to the Celestis web-site <http://cellestis.com/> for additional information regarding a new QuantiFERON®-TB Gold In-Tube (IT) test that has recently been approved by the FDA.

Additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease.²⁷

Persons with a positive QFT-G result or a positive TST result, regardless of symptoms and signs, should be evaluated for TB disease before LTBI is diagnosed. At minimum, a chest radiograph should be examined for abnormalities consistent with TB disease.²⁸

Negative QFT-G 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.²⁹



For more information on IGRAs and the QFT-G test, see the CDC's "Guidelines for Using the QuantiFERON®-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States" (*MMWR*. 2005;54[No. RR-15]) at <http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf> .



For information on laboratories that provide QFT-G testing services for Arizona, go to www.quantiferon.com. For supplies to draw and ship the blood samples, see the "Specimen Collection and Shipment Supplies" topic in the Supplies, Materials and Services section.

Chest Radiography

All individuals being considered for LTBI treatment should undergo a chest radiograph to rule out pulmonary TB disease. For information on how to classify TB, see the "Tuberculosis Classification System" topic at the beginning of this section. 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.



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



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.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.

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	<ul style="list-style-type: none"> ▪ Classify as Class 5. ▪ 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	<ul style="list-style-type: none"> ▪ Classify as Class 0.
No	Positive	No	Normal	<ul style="list-style-type: none"> ▪ Classify as Class 2. ▪ Consider treatment 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	<ul style="list-style-type: none"> ▪ Classify as Class 4 or 5. ▪ Consider evaluating for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.
			Abnormal: Consistent with TB disease; no comparison film	<ul style="list-style-type: none"> ▪ Classify as Class 3 or 5. ▪ Evaluate for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.
<p>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.</p>				

Resources and References

Resources

- ATS, CDC, IDSA. "Diagnostic Standards and Classification of Tuberculosis in Adults and Children" (*Am J Respir Crit Care Med* 2000;161[4 Pt 1]). Available at: <http://www.cdc.gov/tb/pubs/PDF/1376.pdf> .
- CDC. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. November 2001. Available at <http://www.cdc.gov/tb/pubs/corecurr/default.htm> .
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 1999). Available at: <http://www.cdc.gov/tb/pubs/ssmodules/default.htm> .

References

- ¹ 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.
- ² CDC. Classification system. In: Chapter 2: transmission and pathogenesis. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/pubs/corecurr/default.htm> . Accessed July 3, 2006.
- ³ 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.
- ⁴ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):8–9.
- ⁵ CDC. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54 (No. RR-15):52.
- ⁶ 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 February 6, 2007.
- ⁷ Francis J. Curry National Tuberculosis Center. *Diagnosis and treatment* [Web page]. Available online at: http://www.nationaltbcenter.edu/abouttb/diagnosis_and_treatment.cfm . Accessed November 30, 2006.
- ⁸ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):1–2.
- ⁹ CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):49.
- ¹⁰ CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):50.
- ¹¹ CDC. Candidates for treatment of latent TB infection. In: Chapter 6: treatment of LTBI. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/pubs/corecurr/default.htm> . Accessed July 3, 2006.
- ¹² CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/pubs/corecurr/default.htm> . Accessed July 3, 2006.
- ¹³ CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):53.
- ¹⁴ CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, McIntyre L, Wolfe S., eds. 9th ed. Washington, DC: Public Health Foundation; 2006:24–25, 143.
- ¹⁵ CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, McIntyre L, Wolfe S., eds. 9th ed. Washington DC: Public Health Foundation; 2006:24–25, 143.

-
- ¹⁶ CDC National Center for Health Statistics. Skin test preparation steps: filling syringes. In: Skin Test Preparation Steps: Filling Syringes. *National Health and Nutrition Examination Survey (NHANES) Manual*. Hyattsville, MD: National Center for Health Statistics.
- ¹⁷ CDC. Part two: reading the Mantoux tuberculin skin test. *Mantoux Tuberculin Skin Test Facilitator Guide* [Division Tuberculosis Elimination Web site]. Available online at: <http://www.cdc.gov/tb/pubs/Mantoux/part2.htm> . Accessed November 30, 2006. *Manual* 2004;1.3.
- ¹⁸ CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/pubs/corecurr/default.htm> . Accessed February 6, 2007.
- ¹⁹ CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/pubs/corecurr/default.htm> . Accessed February 6, 2007.
- ²⁰ CDC. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR* 2008;55(No. RR-14):1–17.
- ²¹ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- ²² CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4.
- ²³ Francis J. Curry National Tuberculosis Center. *Diagnosis and Treatment* [Web page]. Available online at http://www.nationaltbcenter.edu/abouttb/diagnosis_and_treatment.cfm . Accessed November 30, 2006.
- ²⁴ Francis J. Curry National Tuberculosis Center. *Diagnosis and Treatment* [Web page]. Available online at http://www.nationaltbcenter.edu/abouttb/diagnosis_and_treatment.cfm . Accessed November 30, 2006.
- ²⁵ CDC. Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- ²⁶ CDC. Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- ²⁷ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR*. 2005;54(No. RR-15):52
- ²⁸ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR*. 2005;54(No. RR-15):52.
- ²⁹ CDC. Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR*. 2005;54(No. RR-15):52.
- ³⁰ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):25.