Chapter II:
Testing for TB Infection

A. MANTOUX TUBERCULIN SKIN TEST (TST) 2

a. Skin testing of pregnant women 4

b. Contacts to active TB 4

c. Tuberculin skin testing of BCG-vaccinated persons 4

2. Administering the Tuberculin Skin Test 5

3. Reading the Tuberculin Skin Test Reaction 8

4. Classifying the Tuberculin Skin Test Reaction 8

5. Documentation of TST Results 10

B. INTERFERON GAMMA RELEASE ASSAY TESTS (IGRAS) 10

1. Description of the Test 10

2. How It Works 10

3. Advantages 11

4. Disadvantages 11

5. Using the Quantiferon-Gold In-Tube Test 11

6. How Test Results Are Reported 11

7. IGRA TESTING IN COLORADO 12

7. Anergy Testing 15

a. Common causes of anergy 15

b. Role of anergy testing 15

8. Two-Step Tuberculin Skin Testing 15

a. Background 15

b. Candidates and procedure for two-step testing 16

REFERENCES 17

A. Mantoux Tuberculin Skin Test (TST)

Mycobacterial infection causes an immunological response known as a cell-mediated or delayed hypersensitivity reaction. The tuberculin skin test uses this immunological response to detect when a person has been infected with *Mycobacterium tuberculosis (M. tuberculosis)*. When "tuberculin" (certain protein product extracts of *M. tuberculosis*) is injected into a person's skin, a delayed hypersensitivity reaction will be manifested as an area of induration at the injection site within 48 to 72 hours following the injection. This reaction indicates that the person's immune system recognizes the tuberculin antigen from previous exposure due to infection with *M. tuberculosis* or, less commonly, from exposure to similar antigens produced by other mycobacteria. A person who has not had previous mycobacterial infection will not show this immunological response and will not develop an area of induration. A person who has had infection with other mycobacteria may cross-react to *M. tuberculosis* tuberculin. This cross- reaction generally results in a smaller area of induration. As a general rule, the larger the reaction to tuberculin, the greater the probability that the reaction is specific for *M. tuberculosis*.

The Mantoux tuberculin skin test (TST) should be used for all TB skin tests. The Mantoux TST utilizes purified protein derivative stabilized with Tween 80 (PPD-S). PPD-S is a protein extract of the cell wall of the tubercle bacilli that is stabilized with a detergent (Tween 80) to reduce adsorption to glass and plastic. PPD-S should be used in 5 TU (tuberculin unit) strength. To order PPD-S, go to PPD Ordering Form to download the form for ordering Aplisol.

1. Candidates for Tuberculin Skin Testing

The TST screening should be focused on populations with the greatest risk for infection. In general, populations at low risk for TB infection should not be skin-tested because many reactions in these groups will be false-positives. A TST is not necessary for individuals with a documented previous positive TST.

Certain factors identify persons, who if they have been infected with TB, are at high risk for tuberculosis (TB) infection and /or for progression to TB disease. Persons in the high-risk groups listed in Table1: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease are candidates for tuberculin skin testing in Colorado.

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 burden country with HIV infection is at much higher risk of having TB than a US-born individual with HIV infection. Persons with a very high risk for progression, such as those with HIV infection are recommended for testing even without known risk-factors for prior exposure. For other conditions such as diabetes mellitus for which the progression risk is lower, testing for TB infection should be focused on patients with diabetes and risk for prior exposure, such as birth outside the United States.

Table 1: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE

For Tuberculosis Infection	For Progression to Tuberculosis Disease
▪ High priority contacts such as housemates or coworkers, or contacts of persons who have smear positive pulmonary or laryngeal tuberculosis (TB)	▪ Persons with HIV infection* ▪ Extremes of age (newborn or elderly) ▪ Persons infected with *Mycobacterium tuberculosis*

▪ Employees and residents of high risk congregate settings (e.g. correctional institutions, homeless shelters, drug/alcohol treatment facilities, long-term care facilities ▪ Health care workers in facilities that care for patients at risk for TB Immigration from endemic countries (Asian, African, Latin American, and Eastern European countries have TB rates 5-30 times higher than US rates, ▪ Infants, children and adolescents exposed to adults in high-risk categories ▪ Foreign birth or travel, or foreign visitors in and out of the home ▪ Persons who inject illicit drugs; any other substance abusers ▪ Some medically underserved, low-income populations as defined locally (e.g., homeless, transient populations ▪ Older individuals have a higher prevalence of tuberculosis infection to the greater cumulative years of possible exposure	within the previous two years ▪ Persons with a history of untreated or inadequately treated TB disease ▪ Persons with radiographic findings consistent with previous TB disease* ▪ Persons who abuse alcohol or illegal drugs (such as injection drugs, meth or crack cocaine)* ▪ Persons with any of the following clinical 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-a] antagonists*) • Organ transplantation* • Gastrectomy • Chronic malabsorption syndromes • Jujunoileal 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* 200;49(No.RR-6):7-9.
*Testing for tuberculosis infection is generally recommended for these condition even without risk factors for prior exposure. For others such as newborn children and diabetics, testing should be focused on those with exposure risks.

The TST is a valuable diagnostic tool in patients with clinical symptoms, x-ray evidence, or acid fast bacilli (AFB) smears that suggest TB disease. In these patients, a positive TST reaction indicates TB infection and helps support a TB diagnosis, but a negative immunologic test (TST or the newer IGRA) should never be used by itself to exclude the

diagnosis of active TB. Immuno-suppression associated with various medical treatments or other medical conditions, including severe TB, can cause a false-negative reaction.

a. Skin testing of pregnant women

TST screening is safe and reliable for pregnant women; no teratogenic effects have been documented. Routine TST screening of pregnant women is not indicated because pregnancy itself does not increase the risk for TB infection. However, pregnant women are relatively young and would meet criteria for treatment of TB infection (see Chapter V), and those at high risk for TB infection or disease should be tested. The most common and important criteria for testing pregnant women in Colorado of birth or residence in an area of the world where the TB burden is high, close contact with a person who has pulmonary or laryngeal TB disease and HIV infection. Refer to Table 1 for interpretation of other risks.

b. Contacts to active TB

All contacts to an active TB case should be evaluated for TB infection.

📖 For more information, see *Chapter X: Contact Evaluation and Management*.

c. Tuberculin skin testing of BCG-vaccinated persons

BCG (Bacille Calmette-Guérin) vaccine is a live, attenuated strain of *Mycobacterium bovis*. In many parts of the world, BCG vaccine is used routinely in an effort to prevent serious complications of TB, such as miliary TB and TB meningitis, in infants and children and in health care workers with frequent exposure to individuals with infectious TB.

Although the evidence is inconclusive, a large body of research indicates that BCG vaccination does not completely prevent TB infection or pulmonary TB. Some studies suggest that BCG vaccination does decrease the likelihood of disseminated TB and TB meningitis in infants. However, its efficacy in preventing TB in adults is variable and controversial. TST-positive persons from countries where TB is common are likely to be infected with TB and are at risk of developing TB disease, even if they have been BCG vaccinated.

In the United States, BCG vaccine is not recommended routinely for children and is not used as a control strategy against TB. It is also not recommended as a general preventive strategy for health care workers because it complicates the interpretation of TST reactions and because it has not been proven effective in preventing TB infection.

BCG vaccination complicates the interpretation of TST results because it can produce a false-positive reaction to the TST; especially if BCG was given after the age of one year (BCG given only at birth is less likely to be a significant cause of false-positive TST reactions). Other than testing with an IGRA as noted below, there is no way to distinguish between a positive reaction due to BCG vaccination and a positive reaction due to true TB infection. In BCG-vaccinated persons, however, sensitivity to tuberculin is highly variable and tends to wane over time.

Patients who are close contacts to an individual with pulmonary or laryngeal TB are considered TST positive if they have a reaction of 5 mm or more, regardless of BCG status. TST-positive contacts are candidates for treatment of latent TB infection (LTBI).

Patients who are recent arrivals from a high-burden country who have no other risk factors are considered TST positive if they have a reaction of 10 mm or more, regardless of their BCG status.

Patients who are *not* from a high-burden country and who have no other risk factors are considered TST positive if they have a reaction of 15 mm or more, regardless of their BCG status. However, LTBI treatment may not be

indicated *unless* the individual (1) has a TB risk factor, especially HIV infection, (2) has been in close contact with a person who has pulmonary or laryngeal TB disease, (3) has evidence of old, healed TB on a chest x-ray, or has a higher cumulative life-time risk for progression to active TB (Chapter V).

2. Administering the Tuberculin Skin Test

The TST should be placed by a healthcare worker who has received appropriate training and is following written protocols (see Table 2).

Algorithm for TST TB Testing

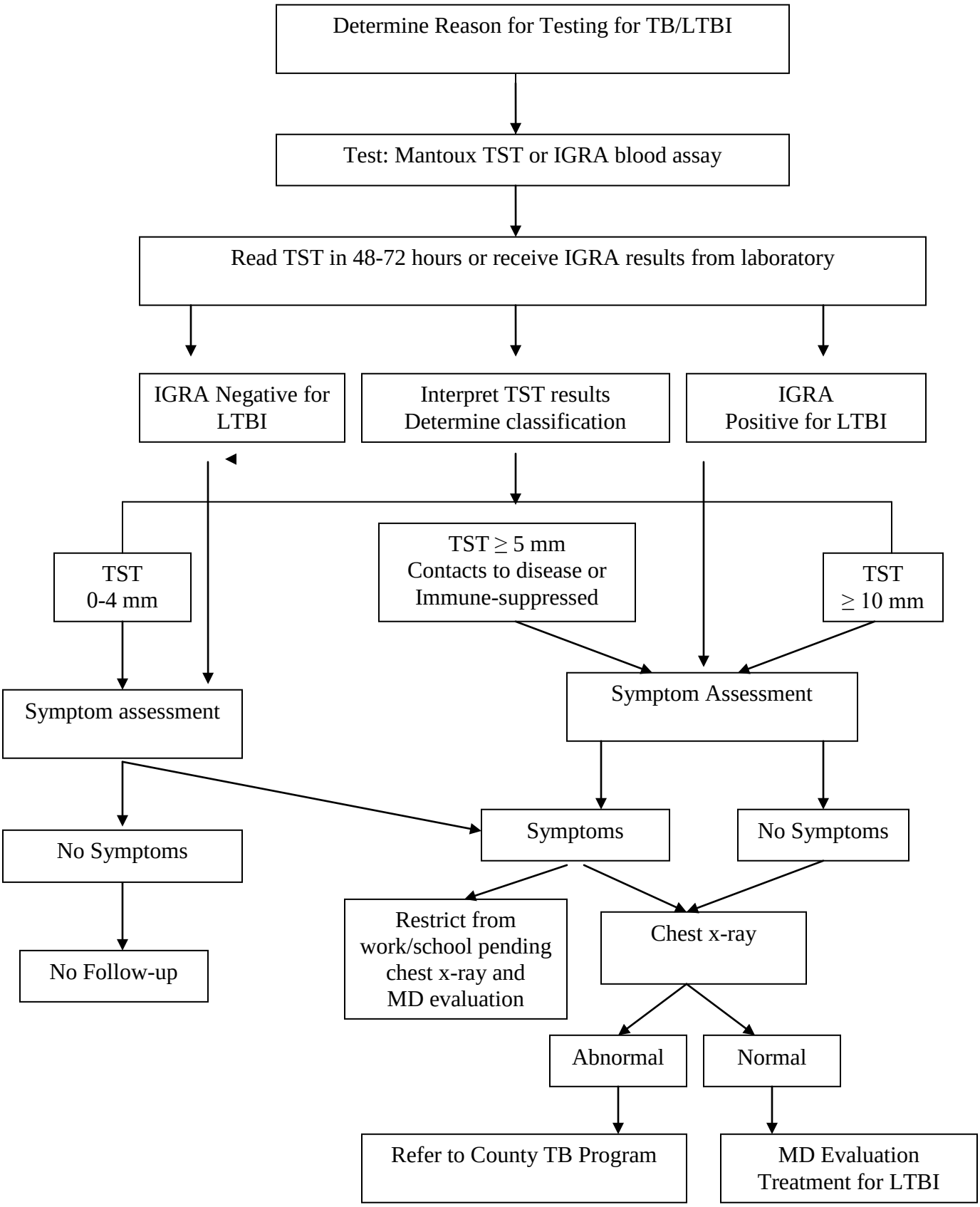


Table 2: BEFORE YOU BEGIN TO ADMINISTER A TUBERCULIN SKIN TEST

Before You Begin to Administer a TST	
Review Information	CDC's *Mantoux Tuberculin Skin Test Facilitator Guide* http://www.cdc.gov/tb/education/mantoux/guide.htm
Gather Equipment	▪ 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) ▪ Sharps container Note: Opened PPD tuberculin vials must be dated and discarded after 30 days. See the package insert for appropriate storage information.

The TST should be administered by the Mantoux technique, in which PPD tuberculin is injected intradermally with a needle and syringe. Multiple-puncture tests (e.g., the tine test) are not recommended by the CDC and should not be used, even in infants and children, because this type of test is not as well standardized as a correctly administered Mantoux.

Use the following procedure to administer a TST by the Mantoux technique:

- Inject 0.1 ml of tuberculin (5 tuberculin units) just under the top layer of skin on the upper, outer, lateral aspect of the left forearm. Use a short, disposable, 26-gauge needle, with the needle bevel facing upward. This should cause a discrete skin elevation (a wheal) 6 to 10 mm in diameter. The left forearm is the standard site for TB skin testing.
- Follow infection control procedures — including proper hand washing and use of a sharps container — for all injections. Gloves are not required but may be used under certain circumstances. When water is not available for hand washing, use an appropriate skin-cleaning product such as an antibacterial towelette.
- After administering the TST, the patient should be instructed not to rub, scratch, or put a band-aid on the test site. The area may be washed and patted dry.

(go to PPD Ordering Form to download the ordering form for Aplisol)

Viral infection or vaccination with a live virus vaccine (e.g. MMR–measles/mumps/ rubella or varicella) can cause a false-negative reaction to the TST. The TST should be administered either at the same time as, or a minimum of 6 weeks after, a live virus vaccine or illness.

3. Reading the Tuberculin Skin Test Reaction

Only a trained health care worker should read the test result; patients should never be allowed to read their own reaction. The following procedure should be used to read the reaction:

- Read the result 48 to 72 hours after administering the test; there is no evidence that reading the TST 2 to 3 days later is less accurate (this results in readings within 40 to 80 hours).
- Measure only the hard, swollen area known as induration. Do not measure any redness. Redness alone does not indicate TB infection.
- Measure the induration transversely at its widest point using a flexible ruler specific for reading a TST. Record the size of the induration in millimeters, not simply as "positive" or "negative." If there is no induration, record the result as "00 mm."

If the patient fails to return for the scheduled reading but returns up to a week after the test administration, examine the test site and measure any induration present. If it is large enough to be classified as positive, record the result. No further testing is needed. If there is no reaction or it is too small to be classified as positive, repeat the test.

You may choose to read TSTs placed by other providers if the patients come in with appropriate documentation and prior arrangements have been made with the other provider.

4. Classifying the Tuberculin Skin Test Reaction

Whether a reaction to the TST is classified as positive depends on the size of the induration and the person's medical and epidemiologic risk factors for TB. Patients who have a positive TST reaction should receive a clinical evaluation, including a chest x-ray, to rule out TB disease. See the following section on the use of IGRAs

📖 For more information, see the section on Tuberculin skin testing in *Chapter III: Evaluation for TB Infection and Disease*.

Table 3: Classifying the TST Reaction

Millimeters of Induration	Medical and Epidemiologic Risk Factors for TB
5 or more	• Close contacts to a person who has pulmonary or laryngeal TB disease • Persons with radiographic evidence of old, healed TB (e.g., stable, fibrotic upper lobe infiltrates)* • Immunosuppressive conditions or persons currently taking or planning to take certain medications: ▪ HIV-positive ▪ Congenital conditions causing immuno-suppression ▪ Certain malignancies (cancer of the head or neck, lymphomas, leukemias) ▪ Adults receiving the equivalent of >15 mg/day of prednisone for at least one month. (Children receiving 0.5 mg/kg/day of prednisone) Persons receiving inhaled steroids are not usually considered at increased risk unless unusually large doses are given ▪ Chemotherapy for cancer ▪ Tumor Necrosis Factor (TNF) blockers such as infliximab (Remicade) or etanercept (Enbrel) for arthritis or Crohn's disease ▪ Transplant patients (solid organ or bone marrow) on anti-rejection medication ▪ Other medications such as methotrexate or cytoxan
10 or more	▪ Children <4 years of age or children and adolescents exposed to adults in high-risk categories ▪ Persons who were born or lived in countries with a high TB burden (e.g., most countries in Africa, Asia, Latin America, Eastern Europe, Russia, or from any refugee camp, regardless of location ▪ Persons from medically underserved, low-income populations ▪ Employees or residents of congregate settings, such as hospitals, correctional facilities, homeless shelters, nursing homes, or drug treatment centers ▪ Persons with a history of drug injection or substance abuse (i.e., alcohol abuse or crack cocaine use) who are known to be HIV- negative ▪ Persons with medical risk factors for TB other than HIV infection, such as diabetes mellitus, silicosis, cancer of the head and neck, hematologic and reticuloendothelial disease (e.g., leukemia and Hodgkin's disease), chronic renal failure (dialysis), intestinal bypass or gastrectomy, chronic malabsorption syndromes, or low body weight (>10% below ideal) ▪ Health care providers or volunteers
15 or more	▪ Persons who meet none of the criteria for 5-mm or 10-mm cutoffs

📖 See "Candidates for Tuberculin Skin Testing, Priorities for Testing" section A.1 of this chapter.

*Those having an Immigration and Naturalization Service (INS) "change of status" exam are required to have a chest radiograph in order to detect those with fibrotic lesions, for whom > 5 mm or more is considered positive.

5. Documentation of TST Results

- Individuals should have their TST result documented in their medical record. You may also give documentation to the patient using the TB card developed by CDPHE, or on a card developed by your health department. To order TB cards please go to http://www.cdphe.state.co.us/dc/tb/tbhome.html under "Forms"
- TST results must be documented in TBdb
- Individuals with a positive TST should be referred for a chest x-ray. Each local health department shall identify a facility in their community that will perform chest x-rays and agree to be reimbursed at the current Medicaid rate.

📖 For more information, see section C.5 on TBdb in *Chapter XII: Miscellaneous Protocols.*

6. Next steps after Interpreting the Skin Test

The algorithm on the page 14 details the steps to take after interpreting whether a skin test is positive or negative.

B. Interferon Gamma Release Assay Tests (IGRAs)

1. Description of the Test

The Interferon Gamma Release Assay Tests (IGRAs) are blood tests designed to detect TB infection by measuring the cell-mediated immune response to selected TB proteins. PPD contains all proteins produced by growing *M. tuberculosis*. This is done by either a whole-blood assay or by using mononuclear white blood cells isolated from whole blood. These tests measure the amount of interferon gamma (IFN-g) produced from a small sample of a person's white blood cells after exposure to these proteins that are more specific from *M. tuberculosis*. High levels of IFN-g production are presumed to indicate infection with TB, and studies have shown the tests to be valid. There are 2 main types of IGRAs that have been developed, the QuantiFERON-TB Gold In-Tube (QFT-GIT) and the T-Spot, which are FDA approved. They differ in the specifics of the lab techniques but generally are very similar in their performance characteristics. The remainder of this section will reference the FDA approved QuantiFERON-Gold In-Tube, which is most-widely used IGRA in Colorado.

2. How It Works

Blood samples are collected in three small tubes, one of which contains a mixture of the specific TB proteins (early secretory antigenic target 6, or ESAT-6, culture filtrate protein 10, or CFP-10 and TB-&). The other tubes are a negative control (Nil) and positive control (Mitogen). Tubes are shaken to mix with antigens (protein substances that can produce an immune response) and incubated for 16 to 24 hours. Notably, the protein antigens used are absent in all BCG vaccine strains and in most non-tuberculous mycobacteria (NTM). For each patient, interferon gamma production is measured in the TB Antigen tube, Mitogen tube and nil control.

The QFT results are based on the interferon gamma measurement in the TB Antigen tube minus the nil tube. As with a TST, additional tests (such as chest radiograph) are needed to exclude TB disease and confirm the diagnosis of LTBI.

3. Advantages

- Only requires a single patient visit.
- Results can be available in 24 hours and are reproducible.
- Unaffected by BCG vaccination and nearly all non-tuberculous mycobacteria.
- Does not induce the booster phenomenon, which can happen with repeat tuberculin skin tests.
- A positive or negative result is available for > 90% of patients tested without relying on provider interpretation.
- The results can be recorded electronically with other lab results so the information is quickly retrievable.

4. Disadvantages

- Blood samples must be processed by the lab within 12 hours after collection.
- There is less laboratory and clinical experience with the QFT although this is growing.
- The ability of the QFT-GIT in predicting a patient's risk of progression to TB disease has not been evaluated.
- As with the TST, additional tests (such as chest x-rays) are needed to exclude active TB.

5. Using the Quantiferon-Gold In-Tube Test

CDC guidelines for the use of QFT-GIT were updated in June, 2010. http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf The test is approved as a diagnostic aid in the evaluation of any patient suspected of having active or latent TB. General considerations require that testing programs using the QFT-GIT should have ensured the ability to process and transport samples to a qualified lab, and should have the ability to perform the necessary follow-up medical evaluation and treatment as indicated. This includes obtaining contact information at the time a test is administered so the results can be communicated with the patient.

Note: the 2010 CDC guidelines for the use of IGRAs noted the performance of the QFT-GIT had not been fully evaluated in the following individuals, but published experience is steadily growing:

- persons with altered immune function due to HIV, diabetes, silicosis, or other immunosuppressive conditions (limitations of the tests believed to be similar to TST)
- individuals with a high likelihood of progressing from TB infection to disease (gaining widespread use)
- patients who have been treated for either LTBI or active TB (limited if any value for TST or IGRAs)
- persons younger than 17 years old (concern with age is large limited to children under 2 years of age now)
- pregnant women (widely used in Denver)

6. How Test Results Are Reported

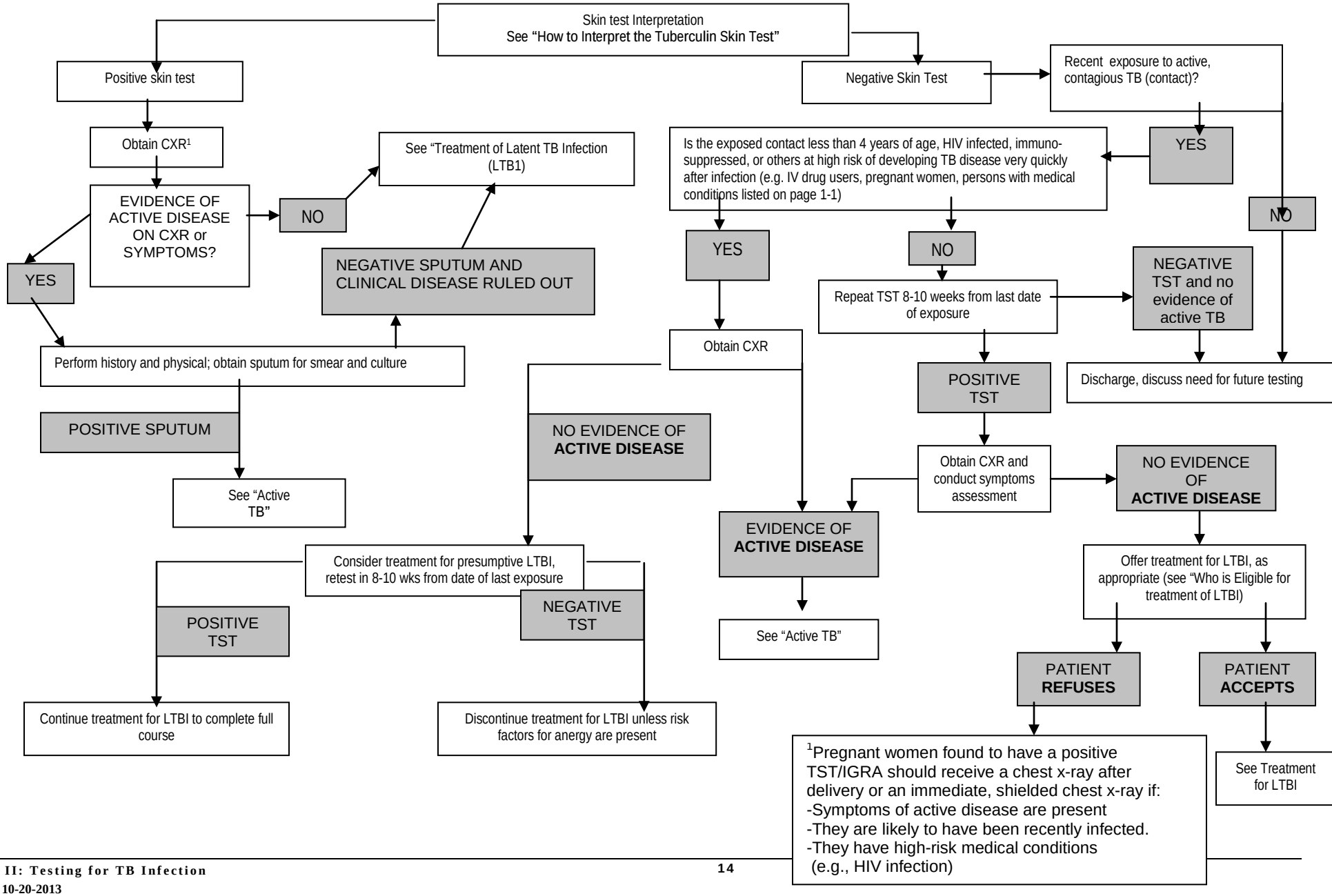
Test results for QFT are reported as positive, negative, or indeterminate. As with the TST, these results must be interpreted with consideration to the associated epidemiological, historical, medical, and other diagnostic information available. Due to the lack of a gold standard, the sensitivity and specificity of the QFT cannot be determined precisely. The sensitivity has been estimated to be between 78% and 89% with a specificity > 95%. False positive and false negative tests do occur as with the TST. False positive tests occur less often with the QFT than the TST among BCG-vaccinated persons, but repeat testing of low-risk health care workers results in false-positive rates of 2-4%, higher than the < 1% with TST after 2-step testing. Indeterminate results occur in 2-8% of tests and are attributed to: incorrect

specimen collection, transportation or processing, or abnormal IFN-g responses to the controls (due to excessive circulating IFN-g or cross-reacting antibodies).

7. IGRA Testing in Colorado

There are a limited number of hospital laboratories in Colorado that currently perform the QFT-GIT or T-Spot.TB. You may contact CDPHE for information related to IGRA testing sites. Please note, CDPHE will not reimburse for the IGRA unless previously approved.

What to Do After Interpreting The TB Skin Test



7. Anergy Testing

Anergy is the inability to mount a delayed-type, cutaneous, cellular immune response. Patients who are anergic may have a negative TST even if they have TB infection or active TB.

a. Common causes of anergy

Anergy can be due to any immunosuppressive therapy or condition. Other causes may include:

- Active TB, especially if overwhelming disease
- extremes of age (newborn or elderly)
- physiologic stress, such as surgery or burns
- certain viral infections (measles, mumps, chicken pox)
- bacterial infections such as typhoid fever, pertussis, brucellosis or Hansen's Disease (leprosy)
- medical conditions and/or treatment associated with immunosuppression (Table 1)
- clinical situations associated with substantial rapid weight loss or chronic under-nutrition
- recent (within 6 weeks) live-virus vaccinations such as MMR and varicella.

📖 For more information see section A.2 of this chapter, "Tuberculin Skin Testing, Individuals with Increased Risk of Progression to Active TB".

b. Role of anergy testing

Anergy testing in conjunction with TST testing is no longer recommended routinely for TB screening programs. If you think anergy may be involved, contact CDPHE's TB Program for assistance.

When making treatment decisions, signs and symptoms of TB disease should take precedence over anergy testing results. It is possible for a person to be TST negative and have active TB disease.

📖 For more information on anergy testing, see Slovis, Plitman and Haas, *The Case Against Anergy Testing as a Routine Adjunct to Tuberculin Skin Testing*, JAMA 2000; 283:2003-2007.

8. Two-Step Tuberculin Skin Testing

a. Background

In some TB-infected individuals, the ability to react to a TST diminishes over time. Thus, infected individuals who are skin tested many years after infection may have a negative TST reaction. However, if retested in the future,, they may have a positive reaction. This is called the booster phenomenon, and happens because the first TST "boosted" the immune response that had diminished over the years. Boosting can occur at any age but is most common in persons aged 55 and older, and can also occur in BCG-vaccinated persons.

However, repeated tuberculin skin testing itself rarely causes boost reactions in individuals without TB infection or BCG vaccination.

The booster phenomenon can complicate the interpretation of TST results in settings where testing is done repeatedly, because a boosted reaction to a second TST may be mistaken for a recent conversion. Thus, a TB infection, BCG vaccination or NTM exposure that occurred years ago may be interpreted as recent infection.

To eliminate boosted reactions as a cause of confusion, individuals who will be tuberculin skin tested repeatedly should undergo two-step testing the first time they are tested. With this type of testing, an initial TST is done; if the result is negative, a second TST is given one to three weeks later. The result of the second test is then used as the baseline. If it is positive, the patient is considered infected; if negative, the patient is considered uninfected.

b. Candidates and procedure for two-step testing

Two-step testing should be offered to individuals who cannot document a history of a negative TST reaction within the past year and who will be tested repeatedly, such as health care workers and employees or residents of congregate settings. The procedure is:

- If the reaction to the **initial** TST is negative, repeat the TST in one to three weeks, using the same dose and strength of tuberculin. Inject the tuberculin on the other forearm or at least 5 cm away from the original test site.
- If the reaction to the **second** TST is negative, classify the individual as uninfected (TB Class 0 or TB Class I).
- If the reaction to the **second** TST is positive, obtain a chest x-ray. If the chest x-ray is abnormal, classify the individual as Class V and evaluate for TB disease or another pulmonary disorder. If the chest x-ray is normal, classify the individual as Class II and evaluate for preventive treatment.
- If the reaction to the **initial** TST is positive, obtain a chest x-ray. If the chest x-ray is abnormal, classify the individual as Class V and evaluate for TB disease or another pulmonary disorder. If the chest x-ray is normal, classify the individual as Class II and evaluate for preventive treatment. A second TST is not necessary.

Individuals who can provide documentation of a negative reaction to a Mantoux TST given within the preceding year should be given an initial TST and classified on the basis of that result. A second TST is not necessary because the earlier test is, in effect, the first of a two-step test.

References

Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR*. 2000; 49(No.RR-6).

Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of persons with infectious tuberculosis and Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005; 54 (No. RR-15). http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Colorado Department of Public Health and Environment, TB Program. Tuberculosis Manual. http://www.cdphe.state.co.us/dc/TB/tbhome.html.

Denver Metro Tuberculosis Clinic. Department of Public Health and Preventive Medicine. *Tuberculosis Clinic Protocol Manual*. 1991.

Diagnostic Standards and Classification of Tuberculosis in Adults and Children. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. Am J Respir Crit Care Med.

2000 Apr;161(4 Pt 1):1376-95. Review. PubMed PMID: 10764337.

Horsburgh, CR. Priorities for the treatment of latent tuberculosis infection in the United States. *NEJM*. 2004; 350:2060-7.

New York City Department of Health. *Clinical Policies and Protocols, New York City Bureau of Tuberculosis Control*. 3rd ed. June 1999. http://www.ci.nyc.ny.us/html/doh/html/tb/tb.shtml.

Rieder HL, Cauthen GM, Comstock GW, Snider DE Jr. Epidemiology of tuberculosis in the United States. *Epidemiologic Reviews*. 1989; 11:79-98.

Slovis BS, Plitman JD, Haas DW. The case against anergy testing as a routine adjunct to tuberculin skin testing. *JAMA*. 2000; 283; 15:2003-2007.