

Service #5: Targeted Testing for TB
(Tuberculin Skin Test and Interferon-Gamma Release Assays)

I. Background about targeted testing for TB

A. Targeted testing is an essential TB prevention and control strategy that is used to identify, evaluate, and treat persons who are at high risk for LTBI or at high risk for developing TB disease once infected with TB. Identifying persons with LTBI is important to the goal of TB control and elimination because treatment of LTBI can prevent infected persons from developing TB disease and stop the further spread of TB.

- All testing activities should be accompanied by a plan for appropriate follow-up medical evaluation and treatment
- Necessary medical evaluation and treatment resources need to be identified before testing activities begin
- Unfocused population-based testing is not cost-effective or useful and leads to unnecessary treatment. **Individuals without specific risk factors for TB infection or disease should not be tested.**
- TB testing activities should be conducted only among high-risk groups, with the intent to treat if LTBI is detected
- Once TB disease has been excluded, treatment of LTBI should be offered to patients regardless of their age, unless medically contraindicated

B. Currently, there are 2 testing methods available for the detection of M. tuberculosis infection in the United States:

- Mantoux tuberculin skin test (TST)
- Interferon-gamma release assays (IGRAs)

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

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

C. Identifying persons at risk for developing TB disease

Generally, persons at risk for developing TB disease fall into 2 broad categories:

- Those who have an increased likelihood of exposure to persons with TB disease
- Those with clinical conditions or other factors associated with an increased risk of progression from LTBI to TB disease

Persons at risk for exposure to persons with TB disease include the following:

- Known close contacts of a person with infectious TB disease
- Persons who have immigrated from TB-endemic regions of the world
- Persons who work or reside in facilities or institutions with people who are at high risk for TB, such as hospitals that care for TB patients, homeless shelters, correctional facilities, nursing homes, or residential facilities for patients with HIV infection/AIDS

Also at risk are those with certain conditions and other factors associated with progression from LTBI to TB disease. These conditions and factors include the following:

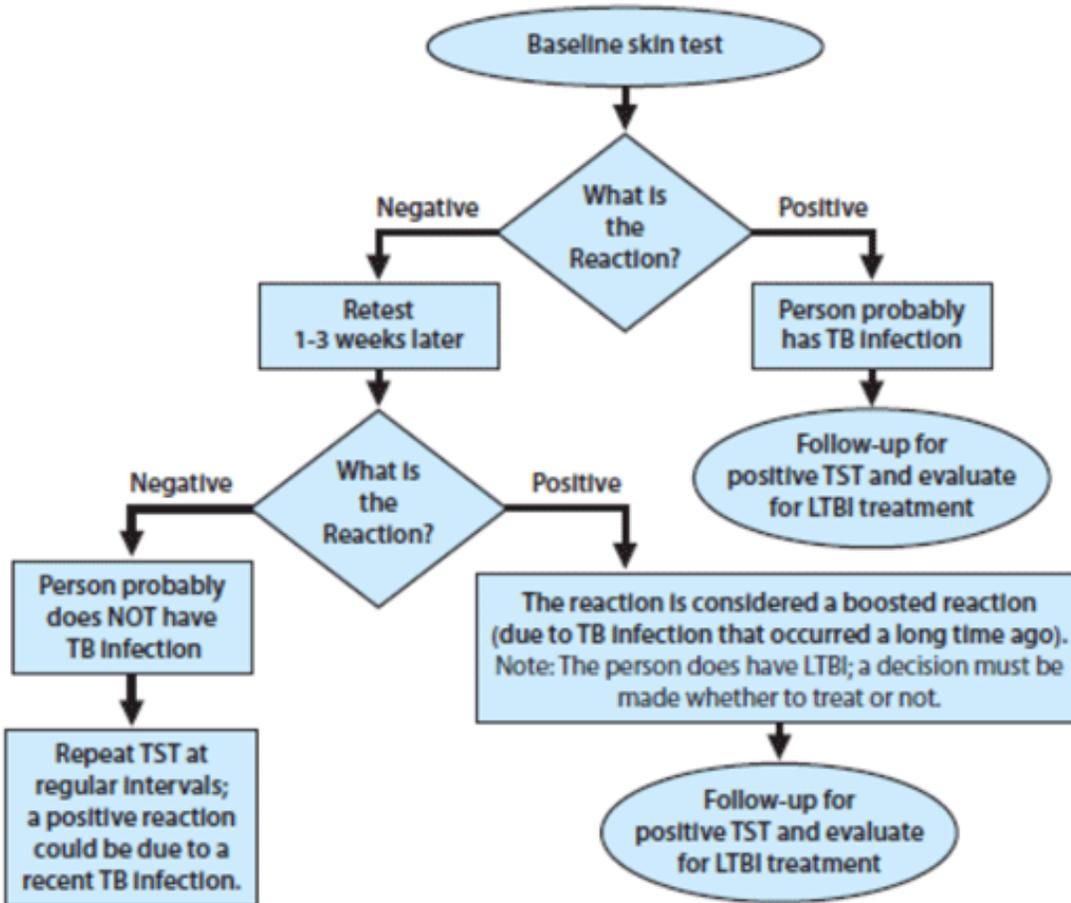
- HIV infection
- Injection drug use
- Radiographic evidence of prior healed TB
- Low body weight (10% below ideal)
- Other medical conditions, such as:
 - silicosis
 - diabetes mellitus
 - chronic renal failure or on hemodialysis
 - gastrectomy
 - jejunioileal bypass
 - solid organ transplant
 - head and neck cancer
 - conditions that require prolonged use of corticosteroids or other immunosuppressive agents such as TNF α antagonists
- Recent TST converters (that is, persons with baseline testing results who have an increase of 10 mm or more in the size of the TST reaction within a 2-year period)
- Infants and children under the age of five years who have a positive TB test result
- Note: the risk of progression is greatest in the first 1 or 2 years after infection.

II. Tuberculin Skin Test (TST)

- A. The skin test is administered intradermally using the Mantoux technique by injecting 0.1ml of 5 TU purified protein derivative (PPD) solution
- B. The reading and interpretation of TST reactions should be conducted within 48 to 72 hours of administration
- C. The TST should not be performed on a person who has written documentation of either a previous positive TST result or treatment for TB disease

- D. Only a trained health care professional should measure TST results; patients or family members should never measure TST results.
- E. Interpretation of the TST result is the same for persons who have had BCG vaccination because a majority of BCG cross-reactivity wanes with time
- F. A TST that was not measured and recorded in millimeters (mm) of induration must be repeated
- G. The “two-step method” is recommended at the time of initial testing for individuals who may be tested periodically (e.g., health care workers)
- If the first TST result in the two-step baseline testing is positive, consider the person infected and evaluate and treat the person accordingly
 - If the first test result is negative, the TST should be repeated in 1–3 weeks
 - If the second test result is positive, consider the person infected and evaluate and treat the person accordingly
 - if both steps are negative, consider the person uninfected and classify the TST as negative at baseline testing (see Figure 1).

Figure 1: Two-Step TST Testing



III. Interferon-Gamma Release Assays

A. IGRAs are used to determine if a person is infected with TB by measuring the immune response to TB proteins in whole blood. Specimens are mixed with peptides that simulate antigens derived from *M. tuberculosis* and controls. In a person infected with TB, the white blood cells recognize the simulated antigens and release interferon-gamma (IFN- γ); results are based on the amount of IFN- γ released.

B. Key points

- **There is no preference for the use of one IGRA or the other**
- Advantages of IGRAs include the following:
 - Requires a single patient visit to conduct the test.
 - Does not cause booster phenomenon. When IGRAs are used for serial testing, there is no need for a second test because boosting does not occur.

- Laboratory test not affected by health care worker perception or bias.
- Results can be available within 24 hours.
- Unaffected by BCG and most environmental mycobacteria.
- Limitations of IGRAs include the following:
 - Blood sample must be processed within 8-30 hours after collection.
 - Limited data exist on use in groups such as children younger than 5 years of age, persons recently exposed to TB, immunocompromised persons, and those who will be tested repeatedly (serial testing).

IV. Selecting a test to detect TB infection

A. Based on recommendations from the DSHS 2012 Tuberculosis Expert Panel, **IGRAs should be the standard test for diagnosis of TB infection in Texas, except in groups for which it is contraindicated or not indicated (such as children under 5 years old)**. IGRAs are the preferred method of testing for (not in priority order):

- Congregate settings, for employees and residents (e.g., correctional facilities, nursing homes, shelters, and transitional living environments)
- Persons with diabetes or dialysis patients
- High risk individuals who have previously received a dose of BCG
- Immunocompromised persons (e.g., chemotherapy or transplant patients)
- Persons undergoing contact investigations
- Persons who work with TB patients
- Persons about to receive TNF-alfa inhibitors or biologic response modifiers
- Persons who have low rates of returning for TST readings

Note: IGRA should be done *unless*

- Phlebotomy is refused
- Phlebotomy is impractical (e.g. no veins, very young child)
- Patient is in on a Friday or day before a holiday and completion of processing of specimen would be required on a weekend or a holiday; the patient cannot return for phlebotomy during the specified hours

B. TST is the preferred method for testing for:

- Children under the age of 5 years

C. Note: Routine testing with both TST and IGRAs is NOT recommended; however, there are certain situations where results from both tests may be useful. Consult the treating physician.

V. Interpretation of test results

A. Interpretation of TST results is based on the measurement of the reaction in millimeters, the person's risk of acquiring TB infection, or the risk of progression to disease if infected. See the risk stratification below.

A TST reaction of **≥5 mm of induration** is considered positive in:

- HIV-infected persons
- Recent contacts of a person with infectious TB disease
- Persons with fibrotic changes on chest radiograph consistent with prior TB
- Patients with organ transplants and other immunosuppressed patients (including patients taking the equivalent of ≥15 mg/day of prednisone for 1 month or more or those taking TNF- α antagonists)

A TST reaction of **≥10 mm of induration** is considered positive in the following individuals:

- Recent arrivals to the United States (within last 5 years) from high-prevalence areas
- Injection drug users
- Residents or employees of high-risk congregate settings (e.g., correctional facilities, long-term care facilities, hospitals and other health care facilities, residential facilities for patients with HIV infection/AIDS, and homeless shelters)
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that increase the risk for progression to TB disease
- Children younger than 5 years of age
- Infants, children, and adolescents exposed to adults in high risk categories

A TST reaction of **≥15 mm of induration** is considered positive in the following individuals:

- Persons with no known risk factors for TB
- Interpretation of IGRA results

B. The interpretation of IGRAs is based on the amount of INF-g released, in QFT, or on the number of cells that release INF-g, in T-SPOT®.TB. Laboratories should provide both the qualitative and quantitative results.

Qualitative results are reported as positive, negative, indeterminate or borderline.

Quantitative results are reported as numerical values that include a response to the TB antigen and 2 controls, nil and mitogen. Quantitative results may be useful for clinical decision making in

individual cases, in combination with risk factors.

VI. TB control action

TST or IGRA Result	TB Control Action
Positive	<i>M. tuberculosis</i> infection likely Action: if CXR, form TB-202 or other evidence suggests active disease, see service #4, otherwise treat for LTBI (see service #2)
Negative	<i>M. tuberculosis</i> infection unlikely, but cannot be excluded 1. if patient is a contact to a TB case, the test must be repeated at 8-10 weeks after break in exposure. Evaluate for eligibility for window prophylaxis (see service #2) 2. if TB infection unlikely, close chart & give clearance card 3. if TB infection cannot be excluded, especially if: 1. patient has TB signs or symptoms or 2. patient has a high risk for developing TB disease once infected then rule out active TB disease (see service #4 and consult the treating physician)
Indeterminate	Test failure – cannot be interpreted. Consult the treating physician.

VII. Documentation

A. TST:

- Record name of antigen, manufacturer, lot number, expiration date, date of testing, and date of reading
- Record site of application of test if applied at site other than the left volar surface
- Record the size of induration in millimeters (mm)
- Record whether the result is considered positive or negative
- Document instructions given to the patient regarding care of the injection site

B. IGRA:

- Results are to be reviewed as they would for any blood test
- Place paper copy of the results in the patient's chart and notify the treating physician of the results
- Document results on TB400 and/or TB340 - documentation should include date of blood draw, results (TB antigen detected, not detected, or indeterminate)