

Policy for Tuberculosis Control in Substance Abuse Treatment Centers

**Massachusetts Department of Public Health
Bureau of Infectious Disease Prevention, Response and
Services
&
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EXECUTIVE SUMMARY

The scientific evidence of Tuberculosis (TB) risk to clients and staff in Treatment Centers has been well documented. Although TB is an airborne, infectious, transmittable disease, it is both treatable and curable with anti-TB medications. Latent tuberculosis infection (LTBI) is also treatable – reducing the risk of developing active TB disease in the future by over 90% in infected persons.

It is important that Treatment Centers have site-specific TB policies that include all of the following: TB history, TB risk assessment, TB symptom screen, referral, education, and follow up for persons who are on TB medication. Included in this document are the TB Division's recommendations for TB screening and targeted TB testing based on an individual's TB history and TB risk. As not all persons attending Treatment Centers are at equal risk for TB, a policy requiring universal TB screening is NOT recommended. Instead, a **targeted approach** to TB screening is recommended as the most effective mechanism and best practice to protect clients and staff at these Centers. Targeted TB testing of specific prioritized groups requires that Treatment Centers adhere to the following **minimal** standards:

- Obtain TB histories and TB risk assessments to identify those presumed to be at highest risk for developing TB disease
- Perform TB symptom screening for anyone with an identified risk or history of TB.
- Make TB referrals for medical evaluation and follow up for those identified persons
- Perform repeat screening and testing as indicated
- Provide TB education about symptoms and the need for immediate medical follow up should such symptoms develop.

Also included in this document, are recommendations for symptom screening, suspected active TB disease follow-up, screening pregnant clients, screening of children and adolescents, repeat client screening, and recommendations for staff. TB history and TB risk assessment forms are included, as well as flowcharts, which provide an overview of the recommendations discussed.

To allow for maximum flexibility for Treatment Centers with or without health care provider capacity, the procedures recommended below and in the appendices include both the minimal standards, as well as the complete range of TB services: risk assessment, administering tuberculin skin tests, making referrals, initiating and ensuring completion of LTBI treatment, and collaboration with the local board of health/health department in situations when a client on TB treatment is being discharged into the community.

CURRENT FEDERAL REQUIREMENTS OF TREATMENT CENTERS FOR TB SCREENING AND FOLLOW UP

The Substance Abuse and Mental Health Services Administration (SAMHSA), through its Center for Substance Abuse Treatment (CSAT), requires the **provision of (or arrangements for)** TB services for each individual receiving substance abuse services as a condition of federal funding. Those TB services include:

- Counseling the individual with respect to TB
- Testing to determine whether the individual is infected with TB
- Providing or referring the infected individual for appropriate medical evaluation and treatment

Treatment Centers are also expected to defer to state policies for TB control at these funded sites. (Public Law 102-321 45 CFR 96- rules and regulations, Section 96.121)

PROCEDURES FOR TB SCREENING AND TARGETED TESTING

NOTE: No set of procedures can cover all individual screening situations that may arise. Please consult with the MA Division of TB Prevention and Control (617) 983-6970, as needed.

CLIENTS

A. Obtain a TB history and TB risk assessment on ALL clients before admission. Use the Intake Form on page [5]:

1. All clients with **NO** identified TB history or TB risk may be admitted to the Treatment Center. **No further evaluation is necessary.**
2. Clients **WITH** an identified TB history or TB risk **must have a TB symptom screen documented.**

Follow Flowchart 1

Treatment Centers – Intake Form

Name: _____

Center: _____

Date: ____/____/____

TB History

↓ **If the answer is “yes” to any of the following questions, do a Symptom Screening below.** ↓

TB Risk Assessment

	Yes	No
1) Have you ever had a positive skin test for TB?	_____	_____
Do you have the results written down?	_____	_____
Date ___/___/___ result (in MM) _____		
2) Have you ever had a positive blood test for TB?	_____	_____
Date ___/___/___ result: _____		
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 10px auto;"> If the answer is “no” to all of the above, STOP </div>		
3) Do you have a chest x-ray result written down	_____	_____
Date ___/___/___ result: normal _____ abnormal _____		
4) Did you take medication for your positive skin test?	_____	_____
5) Have you ever been sick with TB disease?	_____	_____
If yes, did you take medication for your illness?	_____	_____

Risk Factors:	Yes	No
<div style="background-color: yellow; padding: 5px;"> There is no need to specify “yes” or “no” for each item listed below. Instead, circle above for “No” to all of the items OR “Yes” to one or more. </div>		
<u>A “YES” RESPONSE REQUIRES A “SYMPTOM SCREENING” BELOW.</u>		
1) Have you lived with or spent time with anyone who has been sick with TB in the last 2 years ?	_____	_____
2) Have you ever lived or traveled for more than a month in Asia, Africa, Eastern Europe, Middle East, Russia, Central or South America or the Caribbean?	_____	_____
3) Do you have AIDS or HIV infection or other immune-compromised condition?	_____	_____
4) Do you have (or have you had) other medical conditions such as:		
• Diabetes ?	_____	_____
• Cancer ?	_____	_____
• Kidney disease ?	_____	_____
• Rheumatoid arthritis ?	_____	_____
• Stomach or intestinal surgery ?	_____	_____

TB Symptom Screening

<u>Symptoms:</u>	Yes	No
1) Have you had a prolonged, unexplained cough lasting more than 3 weeks or a recent change in a chronic cough	_____	_____
<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 10px auto;"> If the answer to the question above is “no”, then STOP here </div>		
2) Have you recently lost weight of 10 pounds or more for no apparent reason?	_____	_____
3) Have you had a fever of more than 100 degrees F for over 2 weeks?	_____	_____
4) Do you sweat at night?	_____	_____
5) Have you felt unusually tired recently?	_____	_____

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SYMPTOMATIC CLIENTS: Follow Flowchart 2 [Screen for Symptoms]

Early identification of persons with **active, potentially infectious TB** is critical to preventing TB transmission. Educate all clients with a TB history or TB risk to recognize the signs and symptoms of active TB, (e.g. prolonged unexplained cough lasting more than 3 weeks or recent change in chronic cough, night sweats, recent unexplained weight loss \geq 10 lbs, fever of more than 100⁰F for more than 2 weeks, recent unexplained fatigue).

If symptoms suggest a possible case of active TB, Treatment Center staff should:

- At a minimum, isolate the client immediately (if possible) and have the client wear a mask.
- Refer the client to a health care provider, medical clinic or hospital emergency department for a prompt medical evaluation including a chest xray. Ensure that the client wears a mask during transport to the provider.
- If this medical evaluation results in active TB disease being ruled out then the client may be re-admitted.
- If this medical evaluation results in a diagnosis of suspected active TB disease, the following should occur:
 - The health care provider will report the suspect TB case to the Department of Public Health's Office of Integrated Surveillance and Informatics Services (ISIS).
 - TB case management for the client will begin in conjunction with the local board of health/health department public health nurse (PHN) case manager.
 - The PHN will assure that before the client is re-admitted to the Treatment Center, the client is on TB therapy, not infectious and is medically cleared.
 - The supervision of TB therapy for the client and follow-up examinations will be the responsibility of the health care provider and the PHN in collaboration with the TB Division.
 - Treatment Center staff may be asked by the TB Division and/or the local PHN to assist with performing directly observed therapy (DOT) of client TB medication doses if indicated by the health care provider, and if resources are available.
 - The PHN will conduct a contact investigation, if indicated, at the Treatment Center, in collaboration with the TB Division and Treatment Center.
 - All Treatment Center contacts to an infectious suspected TB case will be required to have a tuberculin skin test or, if available, a blood test for TB (if not

documented as being previously positive). (Appendix 1 & 2 Tuberculin skin test and TB blood test CDC fact sheets)

- If the contact's tuberculin skin test or blood test for TB is positive, or the contact has symptoms consistent with TB disease: the Treatment Center will need to ensure medical evaluation to rule out active TB disease.
- If the contact is prescribed a course of treatment for LTBI, assistance with DOT of all doses of LTBI treatment for the contact may be suggested, if resources are available.
- Upon discharge to the community, all clients on TB treatment (active TB disease or LTBI) must be referred to the PHN at the local board of health/health department where the client will reside.

**NON- SYMPTOMATIC CLIENTS:
Follow Flowchart 3 [Symptoms Absent]**

For non-symptomatic clients who have a TB history or TB risk and:

- *Have no documented history of a tuberculin skin test or TB blood test*
 - Admit to the facility and then assure that a TB test (tuberculin skin test or TB blood test) is done on site or by referral. See Appendix 3 for the TB Division on-site tuberculin skin testing protocol.
- *Have documentation of a past positive tuberculin skin test or TB blood test*
 - Admit to the facility. Repeat testing is NOT indicated.
 - Provide the client with the “What you need to know about the TB skin test” CDC fact sheet (Appendix 4) and “TB/HIV Connection” CDC pamphlet (Appendix 5), and provide education about TB symptoms.
- *Have documentation of a negative tuberculin skin test or TB blood test*
 - Admit to the facility if the negative tuberculin skin test or TB blood test was done LESS than 3 months before admission. Repeat testing is NOT indicated.
 - If the tuberculin skin test or TB blood test was done MORE than 3 months before admission, admit to the facility and then test (tuberculin skin test or TB blood test) on site or by referral.
 - **NO RETESTING is required throughout a continuous treatment episode (i.e. transfer between facilities/programs).**
 - Provide the client with the fact sheet on TB/HIV and a copy of their risk assessment form.

B. On-site TB testing: New positives:

Assure that any client tested on site, who is newly TST or TB blood test positive, has a medical evaluation. Report any positive TST or TB blood test identified through on-site testing to the Department of Public Health's Office of Integrated Surveillance and Informatics Services (ISIS) on the LTBI reporting form. (Appendix 6)

PREGNANT CLIENTS

The same admission and follow-up requirements apply: TB history, TB risk assessment, and TB symptom screen and medical follow up as appropriate. Pregnancy is not associated today with an increased incidence of TB infection or disease as it was in the past. However, high-risk pregnant women have been targeted for TB testing for several reasons: 1) a pregnant woman with untreated, active pulmonary TB can endanger her newborn baby at delivery; 2) active TB and treatment for active TB during pregnancy could, in unusual cases, endanger the pregnancy, or complicate the pregnancy because of adverse drug reactions; 3) pregnancy may be the first encounter for many women with the health care system, and it provides an opportunity for targeted testing and for treatment of latent TB infection for high-risk women.

The tuberculin skin test is the only test currently recommended for testing for TB infection during pregnancy; the new TB blood tests for TB infection have not been studied adequately in pregnant women.

- As with all clients, testing should be limited to women at high risk for TB infection and/or progression to active TB.
- Tuberculin skin testing is *not* contraindicated during any stage of pregnancy. Testing early in pregnancy, when indicated, provides greater opportunity for the medical evaluation, if the test is positive.
- Pregnancy has no effect on the performance of the tuberculin skin test.
- Shielded chest x-rays can be done at any time during pregnancy, but may be deferred in asymptomatic women until at least the 2nd trimester.
- Treatment of LTBI in high-risk women may be initiated during pregnancy, although in many cases it can be delayed until soon after the birth of the child.

(See Appendix 7 for the TB Division policy statement on TB in pregnancy)

CHILDREN AND ADOLESCENTS

Children or adolescents who **are clients** are screened following the recommendations for client screening (Page 4).

If a treatment center admits a **client with** small children or adolescents, these “non-client” children or adolescents can be admitted and then screened following client screening recommendations.

Note: For children < **5 years of age**, there is an increased risk of acquiring more severe forms of TB disease (e.g. meningitis) if infected with latent tuberculosis. However, the risk assessment form (Page 5) can identify those children who are at risk for TB who should be tested. Children in this age group with a TB risk, who have a positive tuberculin skin test or blood test, may show no outward symptoms, and are strongly encouraged to have a medical evaluation.

CLIENTS WHO LEAVE BEFORE TESTING COMPLETION

Clients should be counseled about the importance of completing the TB evaluation process and be given the telephone number of a TB clinic to contact for an appointment upon discharge. (A list of the current TB Clinics can be found on the TB Division website <http://www.mass.gov/dph/cdc/tb/>) The client will need to be provided with the results of testing to date (date of skin test planting, etc.).

REPEAT CLIENT SCREENING

On-going: Educate clients, with a TB history or TB risk, about **changing** signs and symptoms (such as weight loss, new cough or change in chronic cough, etc.), which may reflect TB disease and the need for medical follow up **immediately**, should such symptoms develop.

Annual evaluation: For clients who reside in a facility more than a year:

- For clients with a documented **positive** tuberculin skin test or TB blood test: **NO FURTHER TESTING** is indicated. These clients need to have an annual TB risk assessment done and, if a new risk has developed (e.g. Diabetes and/or symptoms) the client needs to be referred for a medical evaluation.
- For clients with no documented TB history or risk or a documented **negative** tuberculin skin test or TB blood test: Conduct an annual TB risk assessment and, if a new risk has developed (e.g. Diabetes and/or symptoms) the client needs to be referred for a tuberculin skin test or TB blood test.

STAFF

Staff must show freedom from active TB disease after hire and before working with clients or other staff. Proof of freedom from TB disease can be obtained by:

A. TB medical clearance documentation from their primary care provider.

OR

B. An on-site TB history and TB risk assessment completed (with appropriate follow up as needed)

For staff who have an on-site TB history and TB risk assessment completed:

- All staff with **NO** identified TB history or TB risk may have client contact. **No further evaluation is necessary** (Flowchart 1).
- Staff with an identified TB history or TB risk **must have a TB symptom screen documented** (Flowchart 2).

SYMPTOMATIC STAFF: Follow Flowchart 2 [Screen for symptoms]

Early identification of persons with **active, potentially infectious TB** is critical to preventing TB transmission. Educate all staff to recognize the signs and symptoms of active TB disease, (e.g. prolonged unexplained cough lasting more than 3 weeks or recent change in chronic cough, night sweats, recent unexplained weight loss ≥ 10 lbs, fever of more than 100⁰F for more than 2 weeks, recent unexplained fatigue) and if symptoms are present to obtain medical clearance.

If this medical evaluation results in active TB disease being ruled out then staff may have client and staff contact.

If a medical evaluation results in a diagnosis of suspected active TB disease, the following will occur:

- TB case management for the staff member will begin in conjunction with the local board of health/health department public health nurse (PHN) case manager.
- The PHN will assure that the staff member is on TB therapy, not infectious, and is medically cleared to have client contact.

- The supervision of TB therapy for the staff member and follow-up examinations will be the responsibility of the health care provider and the PHN in collaboration with the TB Division.

NON- SYMPTOMATIC STAFF: Follow Flowchart 3 [Symptoms Absent]

For non-symptomatic staff with an identified TB history or TB risk and:

- *No documented history of a having a TST or TB blood test done, or the history is unknown:*
 - Must have a TST or TB blood test completed on site or by a private provider and the results documented before having client contact.
 - Any staff who is newly TST or TB blood test positive, should be referred to a TB clinic (or to their health care provider) for a medical evaluation.
 - Report any positive TST or TB blood test identified through on-site testing to the Department of Public Health's Office of Integrated Surveillance and Informatics Services (ISIS), on the LTBI reporting form.
- *Documentation of a negative past TST or TB blood test:*
 - May have client contact if they have documentation of a **negative TST or TB blood test that was done less than 3 months before hire**. No further testing is needed at this time.
 - May have client contact if the testing was done **more than 3 months before hire** however, the individual should make arrangements for a TST or TB blood test as soon as possible and follow up as needed.
- *Documentation of a history of a past positive TST:*
 - May have client contact if they have **documentation** of the past positive TST or TB blood test with a follow up normal chest x-ray (CXR).

REPEAT STAFF SCREENING

On-going: Educate staff, with a TB history or TB risk, about **changing** signs and symptoms (such as weight loss, new cough or change in chronic cough, etc.), which may reflect TB disease and the need for medical follow up **immediately**, should such symptoms develop.

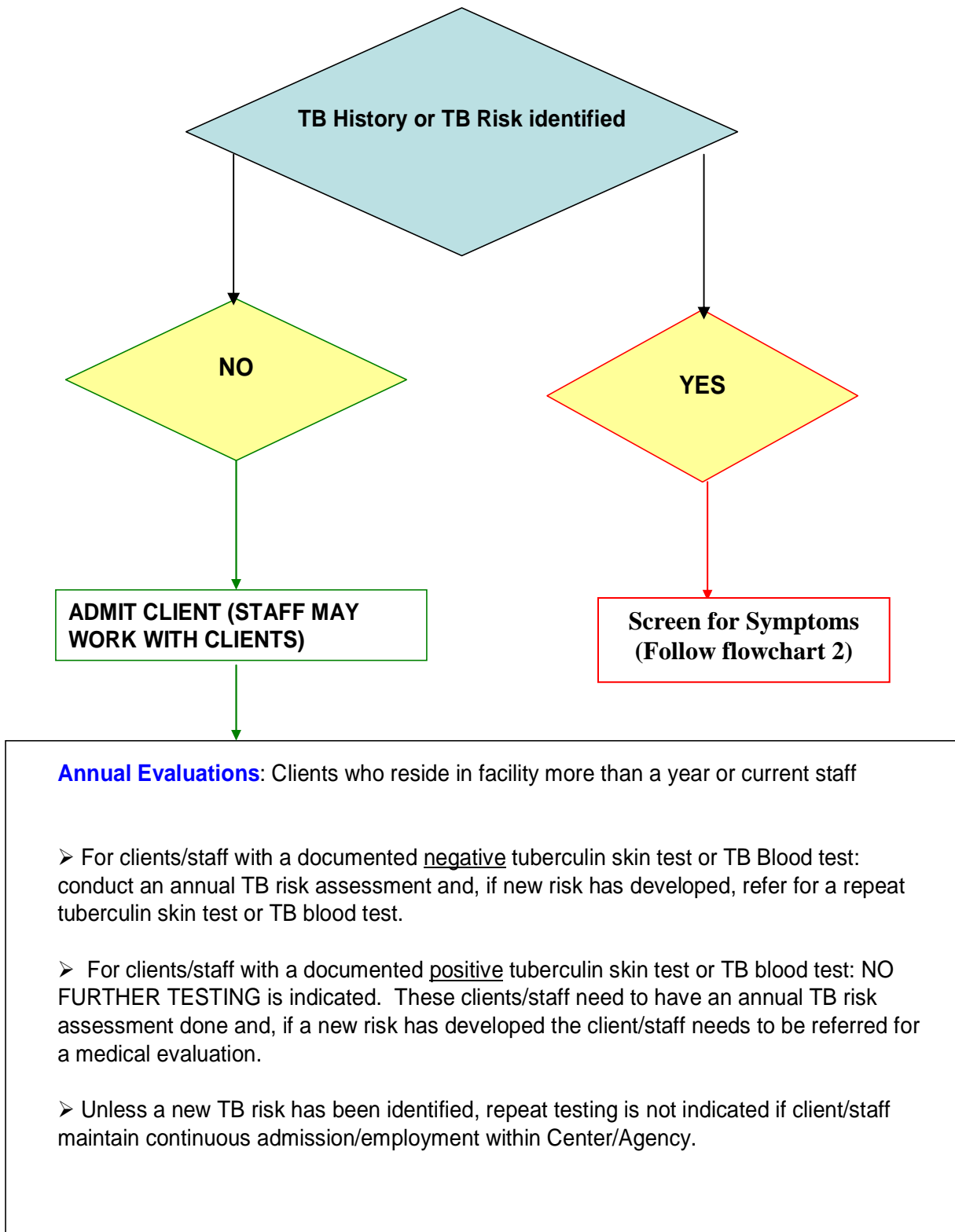
Annual evaluation:

- For staff with a documented **positive** TST or TB blood test: **NO FURTHER TESTING** is indicated. These individuals need to have an annual TB risk assessment done and, if a new risk has developed (e.g. Diabetes and/or symptoms), the staff member should be encouraged to have a medical evaluation from a TB clinic or medical provider.
 - For staff with a documented **negative** TST or TB blood test: These individuals need to have an annual TB risk assessment done (on-site or by a medical provider, and, if a new risk has been identified (e.g. Diabetes and/or symptoms), the staff member should be encouraged to have a repeat TST or TB blood test.
 - **Unless a new TB risk is identified, repeat testing is not indicated if staff maintains continuous employment within the Agency.**
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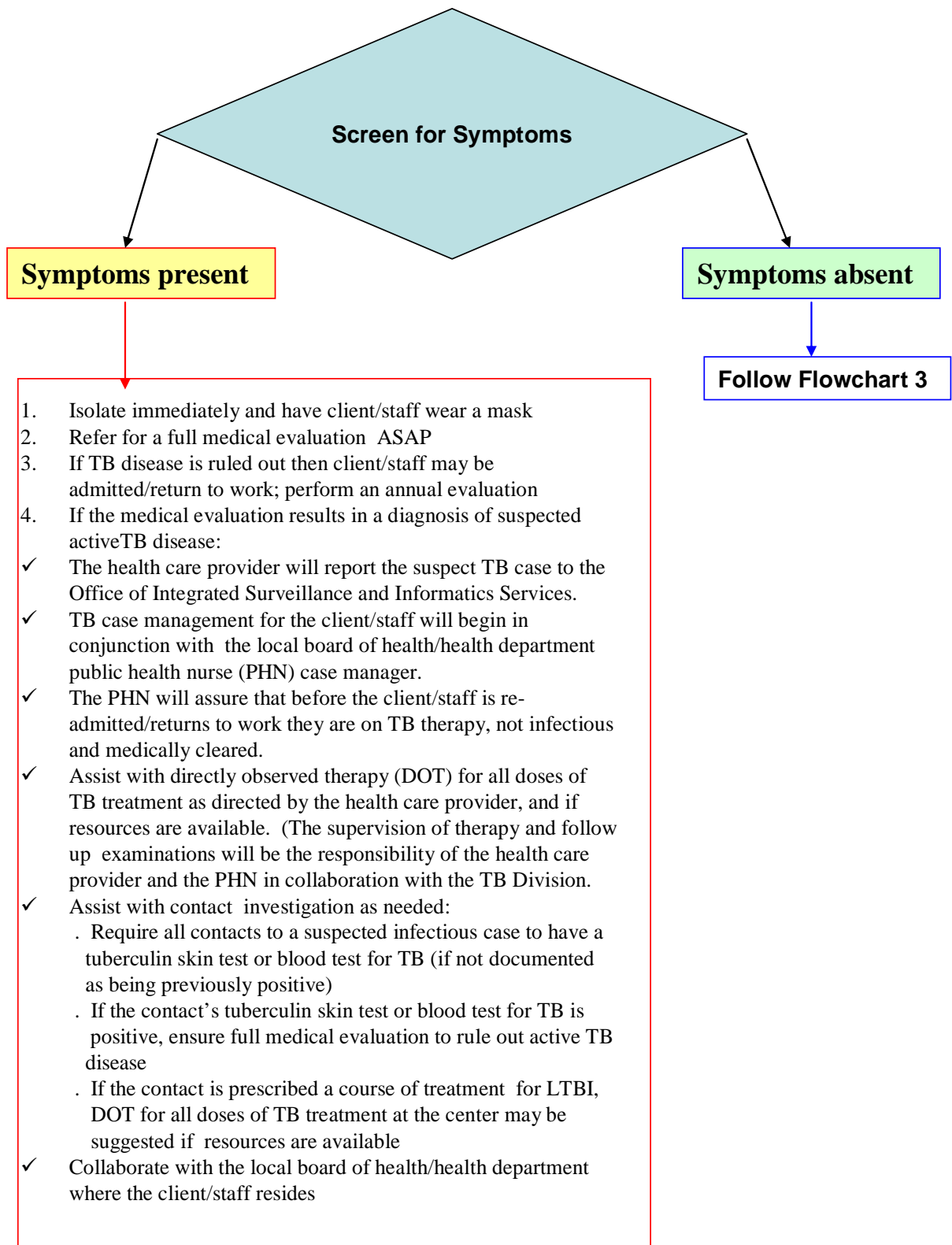
TUBERCULIN SKIN TEST CONVERSIONS

NOTE: On an annual basis, the facility should refer any client or staff member who, after annual risk assessment are found to need repeat TB testing and who then subsequently “convert” their tuberculin skin test from negative to positive (an increase of >10 mm in skin test reaction size within a 2 year interval), to a TB clinic or medical provider. A conversion reflects recent exposure and may indicate the need for a source case investigation at the facility. Consult the TB Division for additional guidance.

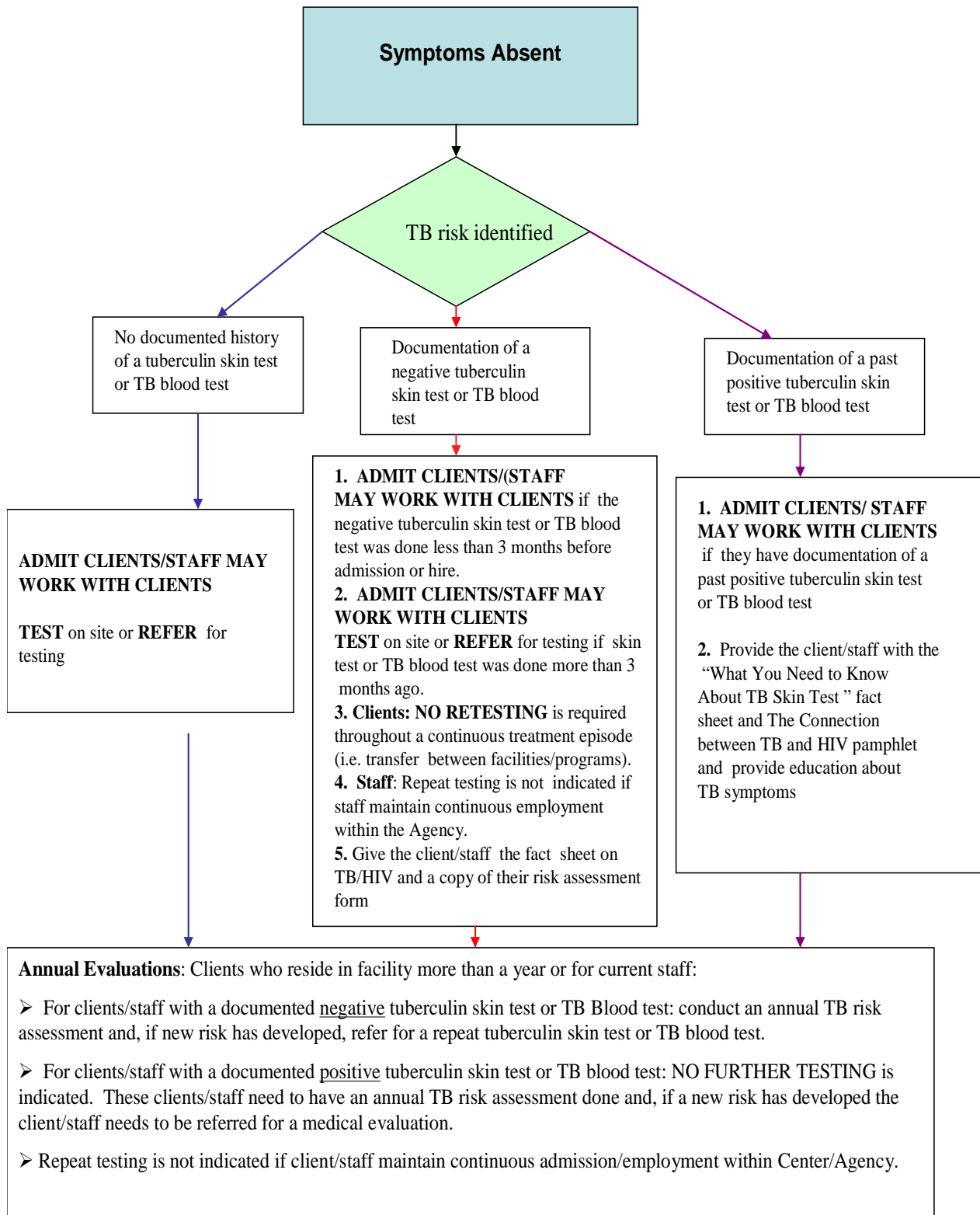
Flowchart 1



Flowchart 2



Flowchart 3



Appendices

Tuberculin Skin Testing

What is it?

The **Mantoux tuberculin skin test (TST)** is the standard method of determining whether a person is infected with *Mycobacterium tuberculosis*. Reliable administration and reading of the TST requires standardization of procedures, training, supervision, and practice.

How is the TST Administered?

The TST is performed by injecting 0.1 ml of tuberculin purified protein derivative (PPD) into the inner surface of the forearm. The injection should be made with a tuberculin syringe, with the needle bevel facing upward. The TST is an intradermal injection. When placed correctly, the injection should produce a pale elevation of the skin (a wheal) 6 to 10 mm in diameter.

How is the TST Read?

The skin test reaction should be read between 48 and 72 hours after administration. A patient who does not return within 72 hours will need to be rescheduled for another skin test.

The reaction should be measured in millimeters of the induration (palpable, raised, hardened area or swelling). The reader should not measure erythema (redness). The diameter of the indurated area should be measured across the forearm (perpendicular to the long axis).

How Are TST Reactions Interpreted?

Skin test interpretation depends on two factors:

- Measurement in millimeters of the induration
- Person's risk of being infected with TB and of progression to disease if infected

Classification of the Tuberculin Skin Test Reaction

<p>An induration of 5 or more millimeters is considered positive in</p> <ul style="list-style-type: none">-HIV-infected persons-A recent contact of a person with TB disease-Persons with fibrotic changes on chest radiograph consistent with prior TB-Patients with organ transplants-Persons who are immunosuppressed for other reasons (e.g., taking the	<p>An induration of 10 or more millimeters is considered positive in</p> <ul style="list-style-type: none">-Recent immigrants (< 5 years) from high-prevalence countries-Injection drug users-Residents and employees of high-risk congregate settings-Mycobacteriology laboratory personnel	<p>An induration of 15 or more millimeters is considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.</p>
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equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF- α antagonists)	-Persons with clinical conditions that place them at high risk -Children < 4 years of age - Infants, children, and adolescents exposed to adults in high-risk categories	
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What Are False-Positive Reactions?

Some persons may react to the TST even though they are not infected with *M. tuberculosis*. The causes of these false-positive reactions may include, but are not limited to, the following:

- Infection with nontuberculosis mycobacteria
- Previous BCG vaccination
- Incorrect method of TST administration
- Incorrect interpretation of reaction
- Incorrect bottle of antigen used

What Are False-Negative Reactions?

Some persons may not react to the TST even though they are infected with *M. tuberculosis*. The reasons for these false-negative reactions may include, but are not limited to, the following:

- Cutaneous anergy (anergy is the inability to react to skin tests because of a weakened immune system)
- Recent TB infection (within 8-10 weeks of exposure)
- Very old TB infection (many years)
- Very young age (less than 6 months old)
- Recent live-virus vaccination (e.g., measles and smallpox)
- Overwhelming TB disease
- Some viral illnesses (e.g., measles and chicken pox)
- Incorrect method of TST administration
- Incorrect interpretation of reaction

Who Can Receive a TST?

Most persons can receive a TST. TST is contraindicated only for persons who have had a severe reaction (e.g., necrosis, blistering, anaphylactic shock, or ulcerations) to a previous TST. It is not contraindicated for any other persons, including infants, children, pregnant women, persons who are HIV-infected, or persons who have been vaccinated with BCG.

How Often Can TSTs Be Repeated?

In general, there is no risk associated with repeated tuberculin skin test placements. If a person does not return within 48-72 hours for a tuberculin skin test reading, a second test can be placed as soon as possible. There is no contraindication to repeating the TST, unless a previous TST was associated with a severe reaction.

What is a Boosted Reaction?

In some persons who are infected with *M. tuberculosis*, the ability to react to tuberculin may wane over time. When given a TST years after infection, these persons may have a false-negative reaction. However, the TST may stimulate the immune system, causing a positive, or boosted reaction to subsequent tests. Giving a second TST after an initial negative TST reaction is called two-step testing.

Why is Two-Step Testing Conducted?


Two-step testing is useful for the initial skin testing of adults who are going to be retested periodically, such as health care workers or nursing home residents. This two-step approach can reduce the likelihood that a boosted reaction to a subsequent TST will be misinterpreted as a recent infection.

Can TSTs Be Given To Persons Receiving Vaccinations?

Vaccination with live viruses may interfere with TST reactions. For persons scheduled to receive a TST, testing should be done as follows:

- Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine
- At least one month after smallpox vaccination

Additional Information

- [American Thoracic Society and CDC. Diagnostic standards and classification of tuberculosis in adults and children](#)⁵. (PDF) *Am J Respir Crit Care Med* 2000; 161.
- [CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005](#). *MMWR* 2005; 54 (No. RR-17).
- CDC. Mantoux Tuberculin Skin Test: Training Materials Kit (2003).
- [CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection](#) . *MMWR* 2000; 49 (No. RR-6).

Interferon-Gamma Release Assays (IGRAs) - Blood Tests for TB Infection

What are they?

Interferon-Gamma Release Assays (IGRAs) are whole-blood tests that can aid in diagnosing *Mycobacterium tuberculosis* infection, including both latent tuberculosis infection (LTBI) and tuberculosis (TB) disease. Three IGRAs that have been approved by the U.S. Food and Drug Administration (FDA) are commercially available in the U.S.:

- QuantiFERON®-TB Gold test (QFT-G);
- QuantiFERON®-TB Gold In-Tube test (QFT-GIT);
- T-SPOT®.TB test (T-Spot)

How do they work?

IGRAs measure a person's immune reactivity to *M. tuberculosis*. White blood cells from most persons that have been infected with *M. tuberculosis* will release interferon-gamma (IFN-g) when mixed with antigens (substances that can produce an immune response) derived from *M. tuberculosis*.

To conduct the tests, fresh blood samples are mixed with antigens and controls. The antigens, testing methods, and interpretation criteria for IGRAs differ (see Table 1).

Table1: Differences in Currently Available IGRAs

	QFT-G	QFT-GIT	T-Spot
Format	Process whole blood within 12 hours.	Process whole blood within 16 hours	Process peripheral blood mononuclear cells (PBMCs) within 8 hours.
<i>M. tuberculosis</i> Antigen	Separate mixtures of synthetic peptides representing ESAT-6 & CFP-10	Single mixture of synthetic peptides representing ESAT-6, CFP-10 & TB7.7.	Separate mixtures of synthetic peptides representing ESAT-6 & CFP-10
Measurement	IFN-g concentration	IFN-g concentration	Number of IFN-g producing cells (spots)
Possible Results	Positive, negative, indeterminate	Positive, negative, indeterminate	Positive, negative, indeterminate, borderline

What are the advantages of IGRAs?

- Requires a single patient visit to conduct the test.
- Results can be available within 24 hours.
- Does not boost responses measured by subsequent tests.
- Prior BCG (bacille Calmette-Guérin) vaccination does not cause a false-positive IGRA test result.

What are the disadvantages and limitations of IGRAs?

- Blood samples must be processed within 8-16 hours after collection while white blood cells are still viable.
- Errors in collecting or transporting blood specimens or in running and interpreting the assay can decrease the accuracy of IGRAs.
- Limited data on the use of IGRAs to predict who will progress to TB disease in the future.
- Limited data on the use of IGRAs for:
 - Children younger than 5 years of age;
 - Persons recently exposed to *M. tuberculosis*;
 - Immunocompromised persons; and
 - Serial testing.
- Tests may be expensive.

What are the steps in administering an IGRA test?

Confirm arrangements for testing in a qualified laboratory, and arrange for delivery of the blood sample to the laboratory in the time the laboratory specifies to ensure testing of samples with viable blood cells.

- Draw a blood sample from the patient according to the test manufacturer's instructions.
- Schedule a follow-up appointment for the patient to receive test results, and to arrange for further medical evaluation and possible treatment for LTBI or TB disease if needed.

How do you interpret IGRA test results?

IGRA interpretations are based on the amount of IFN-g that is released or on the number of cells that release IFN-g. Both the standard qualitative test interpretation (positive, negative, or indeterminate) and the quantitative assay measurements should be reported.

IGRAS [like tuberculin skin tests (TSTs)] should be used as an aid in diagnosing infection with *M. tuberculosis*. A positive test result suggests that *M. tuberculosis* infection is likely; a negative result suggests that infection is unlikely. An indeterminate result indicates an uncertain likelihood of *M. tuberculosis* infection. A borderline test result (T-Spot only) also indicates an uncertain likelihood of *M. tuberculosis* infection.

A diagnosis of LTBI requires that TB disease be excluded by medical evaluation. This should include checking for signs and symptoms suggestive of TB disease, a chest radiograph, and, when indicated, examination of sputum or other clinical samples for the presence of *M. tuberculosis*. Decisions about a diagnosis of *M. tuberculosis* infection should also include epidemiological and historical information.

Recommendations on when to use IGRA tests

- IGRAs can be used in place of (but not in addition to) TST in all situations in which CDC recommends TST as an aid in diagnosing *M. tuberculosis* infection with preferences and special considerations noted below. This includes contact investigations, testing during pregnancy, and screening of health care workers and others undergoing serial evaluation for *M. tuberculosis* infection. Despite the indication of a preference, use of the alternative test (FDA-approved IGRA or TST) is acceptable medical and public health

practice. Caution in interpretation should be used when testing certain populations because of limited data on the use of IGRAs ([see Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection, United States](#)).

- Populations in which IGRAs are preferred for testing:
 - Persons who have received BCG (either as a vaccine or for cancer therapy); and
 - Persons from groups that historically have poor rates of return for TST reading.
- TST is preferred over IGRAs for testing children less than 5 years of age.
- As with TST, IGRAs generally should not be used for testing persons who have a low risk of infection and a low risk of disease due to *M. tuberculosis*.
- Each institution and TB control program should evaluate the availability and benefits of IGRAs in prioritizing their use.
- Routine testing with both TST and IGRA is **not** recommended. However, results from both tests might be useful in the following situations:
 - When the initial test is **negative** and:
 - The risk for infection, the risk for progression to disease, and the risk for a poor outcome are high (e.g., HIV infected persons or children under 5 years of age who are exposed to a person with infectious TB).
 - There is clinical suspicion for TB disease (e.g., signs, symptoms, and/or radiographic evidence suggestive of TB disease) and confirmation of *M. tuberculosis* infection is desired.
 - Taking a positive result from a second test as evidence of infection increases detection sensitivity.
 - When the initial test is **positive** and:
 - Additional evidence of infection is required to encourage acceptance and adherence (e.g., foreign-born healthcare workers who believe their positive TST is due to BCG). A positive IGRA might prompt greater acceptance of treatment for LTBI as compared with a positive TST alone.
 - The person has a low risk of both infection and progression from infection to TB disease. Requiring a positive result from the second test as evidence of infection increases the likelihood that the test reflects infection. An alternative is to assume, without additional testing, that the initial result is a false positive or that the risk for disease does not warrant additional evaluation or treatment, regardless of test results.
- In addition, repeating an IGRA or performing a TST might be useful when the initial IGRA result is indeterminate, borderline, or invalid and a reason for testing persists.

Multiple negative results from any combination of these tests cannot exclude *M. tuberculosis* infection. Steps should be taken to minimize unnecessary and misleading testing of persons at low risk.

Selection of the most suitable test or combination of tests for detection of *M. tuberculosis* infection should be based on the reasons and the context for testing, test availability, and overall cost of testing.

Can IGRAs Be Given To Persons Receiving Vaccinations?

As with TST, live virus vaccines might affect IGRA test results. However, the effect of live virus vaccination on IGRAs has not been studied. Until additional information is available, IGRA testing in the context of live virus vaccine administration should be done as follows:

- Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine
- At least one month after smallpox vaccination

Additional Information

- Centers for Disease Control and Prevention. [Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection, United States](#). *MMWR* 2010; 59 (No.RR-5)

TB SKIN TESTING PROTOCOLS FOR SITES WITH NURSING CAPACITY

NURSING CAPACITY is defined as the ability to perform a tuberculin skin test or a TB blood test on clients with an identified risk factor

Tuberculin skin testing (TST) (Mantoux method only)

1. Administer the Mantoux TST by intracutaneous (intradermal) injection of one tenth of a milliliter (0.1mL) of standardized purified protein derivative (PPD-S) antigen, which contains 5 tuberculin units (TU), into inner aspect of the forearm, two to four inches below the elbow, unless precluded for medical reasons. Record the site of TST administration (e.g. left forearm).
2. Measure the TST transverse to the long axis of the forearm 48-72 hours after administration. Record results in millimeters (mm) of induration (swelling), not redness. For most clients, a positive TST measures ≥ 10 mm of induration. However there are some individuals for whom ≥ 5 mm would be considered positive. These persons include:
 - those clients who are known to be HIV infected or HIV status is unknown, but have a risk for HIV
 - persons who have had recent close contact to someone with active, infectious TB
 - persons with fibrotic changes on CXR consistent with prior TB
 - persons with organ transplants and other immunosuppressed persons (receiving the equivalent of ≥ 15 mg/d of prednisone for 1 month or more)

NOTE: Skin Test Conversions: “Recent converters” are determined by both the size of the induration and the length of time since the last negative skin test. A >10 mm increase within a two year period is considered a “recent conversion”.

3. State regulation requires reporting persons with LTBI (positive TST) directly to the Massachusetts Department of Public Health (MDPH), Integrated Surveillance and Informatics Services (ISIS) via fax (617.983.6220) or mail.
4. Counsel all individuals with a positive TST about the significance of the positive result. Refer them to the local TB clinic, or to a provider experienced in TB for a medical evaluation and possible treatment.
5. Evaluate clients with a negative (<5 mm) TST result who are HIV-infected or at risk for HIV infection for possible exposure to TB and refer for further evaluation, when indicated.
6. Record the client’s TST result in the client’s medical record in such a place that allows easy reference when, and if, the client returns to that facility. This system will help to avoid re-testing clients who have already tested positive in a previous encounter. Give the client a copy of his/her risk assessment form and TST result.
7. A history of vaccination with BCG should be ignored per CDC recommendations (Appendix 8)

What You Need to Know About the TB Tuberculosis Skin Test

“I was told I needed a TB skin test, so I went to the health clinic. It was quick and didn’t hurt. In two days, I went back to the clinic so the nurse could see the results. It’s important to go back in 2 or 3 days to get your results or you will have to get the test again.”

A TB skin test will tell you if you have ever had TB germs in your body. • A harmless fluid is placed under your skin on the inside of your arm. A very small needle is used, so you will only feel a light pinch. • Make sure you don’t put a bandage or lotion on the test spot. Also—don’t scratch the spot. If the area itches, put an ice cube or cold cloth on it. It is okay for the test spot to get wet, but do not wipe or scrub the area. • Return to the clinic or doctor’s office in 2 to 3 days so your healthcare provider can look at the test spot on your arm. He or she will look at the test spot and measure any bump that appears there. Your healthcare provider will let you know if your test is negative or positive. Write the time and date you will need to return here: _____

When your skin test is positive: • You have TB germs in your body. • You may need to get an x-ray of your chest or give a phlegm sample. These extra tests will help show if you have TB disease or TB infection. • Your doctor or healthcare provider may ask if you have HIV. TB infection and HIV together can make you very sick very quickly. If you don’t know if you have HIV, your doctor or healthcare provider may suggest you take an HIV test.

The good news: TB can be CURED if you follow the medicine plan you and your doctor set up. Remember—only a healthcare provider can read your TB skin test results the right way

Did you know?

Once you have a positive TB skin test you will always have a positive TB skin test, even if you complete treatment. Ask your doctor for a written record of your positive skin test result. This will be helpful if you are asked to have another TB skin test in the future.

When your TB skin test is negative:

- You don’t have TB germs in your body. OR
- TB germs are not showing up in your body at this time. Sometimes the test may have been done too soon to show the TB germs.

If your TB skin test is negative, you still may need to have more tests if:

- You have been around someone with TB disease.
- Your TB skin test was within 8 weeks of your exposure to TB.
- You have signs of TB disease, like coughing, chest pain, fever, weight loss, or tiredness.
- You have HIV infection, since the TB skin test may not react the way it should.

The facts on the BCG vaccine and TB:

“I always thought that because I got a BCG vaccine, my TB skin test would be positive. My doctor said that some people who get BCG vaccines have positive skin tests and some have negative skin tests. I learned that a positive TB skin test result often means a person has TB infection, even if they had the BCG vaccine.”

Get a TB skin test if your healthcare provider says you need one. For more information on TB, call your local health department at or visit the CDC Division of Tuberculosis Elimination website at

<http://www.cdc.gov/tb> Produced 2005

Tuberculosis: The Connection between TB and HIV (the AIDS virus)

People infected with HIV (the virus that causes AIDS) are more likely than uninfected people to get sick with other infections and diseases. Tuberculosis (TB) is one of these diseases.

What is TB?

TB is a disease that usually affects the lungs. It sometimes affects other parts of the body, such as the brain, the kidneys, or the spine. TB disease can cause serious health problems, including death, if untreated.

How is TB spread?

TB germs are spread from person to person through the air. TB germs are put into the air when a person with TB disease of the lungs or throat coughs, sneezes, laughs, or sings. TB is NOT spread by sharing silverware or cups, or sharing saliva when kissing someone.

What are the symptoms of TB?

People with TB disease often feel weak or sick, lose weight, have fever, and have night sweats. If their TB disease is in the lungs, they may also cough and have chest pain, and they may cough up blood. Other symptoms depend on what part of the body is affected.

What is the difference between TB disease and TB infection?

People with TB disease are **sick** from the large number of TB germs that are active in their body. They usually have one or more of the symptoms of TB disease. These people may pass the TB germs to others. TB disease can cause permanent body damage and death. Medicines which can cure TB disease are given to these people.

People with TB infection also have the germs that cause TB in their body. But they are **not sick** because there are not as many of the germs, and the germs lie dormant (sleeping) in their body. They cannot spread the germs to others. However, these people could develop TB disease in the future, especially if they have HIV infection. People with TB infection can take medicine to prevent them from developing TB disease.

Why is it important to know if I have TB and HIV infections?

HIV infection weakens the immune system. If a person's immune system gets weak, TB infection can activate and become TB disease. Someone with TB infection and HIV infection has a **very high risk** of developing TB disease. Without treatment, these two infections can work together to shorten the life of the person infected with both.

Good News!

The good news is that TB infection can be prevented from developing into TB disease and TB disease can be cured. The first step is to find out if you are infected with the TB germ. You can do this by getting a TB skin test.

What is a TB skin test?

For a TB skin test, a health worker uses a small needle to put some testing material, called tuberculin, just under your skin. This is usually done on the lower inside part of your arm. After you get the test, you must return in 2 to 3 days to see if there is a reaction to the test. If there is a reaction, the size of the reaction is measured.

Some people who are infected with both HIV and TB will not react to the TB skin test. This is because the immune system, which causes the reaction, is not working properly. Anyone who is HIV infected and has a negative skin test should also have other medical tests, especially if they have symptoms of TB disease.

What must I do if I have TB infection?

Get the required follow-up tests. Follow your doctor's advice and take the medicine as prescribed. Today, both TB infection and TB disease can be treated and cured with medication.

It is especially important for people with both TB and HIV infections to take their TB medication. The HIV-weakened immune system makes it **much** more likely for them to develop TB disease than people who are not HIV infected. TB is one of the few diseases related to HIV infection that is easily prevented and cured with medication.

For more information on TB or to get a TB skin test, call your doctor or local health department.

For further information on TB visit:

CDC Division of Tuberculosis Elimination Website at
www.cdc.gov/tb

Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection (LTBI) During Pregnancy Rationale and Recommendations

Pregnancy is not associated with an increased incidence of TB infection or disease. However, pregnant women have been targeted for TB testing for several reasons:

- A pregnant woman with untreated, active pulmonary TB can endanger her newborn baby at delivery.
- Active TB and treatment for active TB during pregnancy could, in unusual cases, endanger the pregnancy, or complicate the pregnancy because of adverse drug reactions.
- Pregnancy may be the first encounter for many women with the health care system, and it provides an opportunity for targeted testing and for treatment of latent TB infection for high-risk women.

Testing for TB infection - The tuberculin skin test (TST) and *QuantiFERON*[®] (QFT):

- The tuberculin skin test is the only test currently approved (2003) for testing for TB infection during pregnancy; the new *QuantiFERON*[®] blood test for TB infection has not been studied adequately in pregnant women.
- *Testing of all pregnant women is not indicated.* Testing should be limited to women at high risk for TB infection and/or progression to active TB. The most common indications for testing include:
 - Birth of the woman in a high-risk country for TB and arrival within 5 years of the time of presentation.
 - Immunocompromised state.
 - Exposure to an active, potentially infectious, pulmonary TB case.
 - Known to have an abnormal chest radiograph (x-ray; CXR) consistent with “old TB”.
 - Residence in a high-risk, congregate living setting.
- Under low-prevalence conditions, over-testing for TB is likely to produce a large proportion of false-positive reactions due to technical problems with the test and cross-reactivity of tuberculin in persons with hypersensitivity to environmental mycobacteria.
- Tuberculin Skin Testing is *not* contraindicated during any stage of pregnancy. Testing early in pregnancy, when indicated, provides greater opportunity for the medical evaluation if the test is positive.
- Pregnancy has no effect on the performance of the TST; its effect on QFT is not known.
- History of BCG vaccination for TB (common in many non-US born persons) is *not* a reason not to test for or treat latent TB infection.
 - BCG rarely produces a positive PPD that persists into adulthood.

- Large PPD reactions in adults (≥ 15 mm) are highly unlikely to be due to BCG given early in life.
- 5 TU of PPD by the Mantoux, intradermal technique is the only acceptable type of skin test for TB infection during pregnancy. Results are read as *mm induration (not redness)* at 48 to 72 hrs, measured with a ruler or a caliper across the arm (not in the long dimension of the arm). In referring patients for evaluation of a positive TST, please indicate the size of the reaction. *“Positive” is not sufficient information for clinical decision making.*
 - Three thresholds are used to interpret a TST reaction as “positive”:
 - 5 mm – for the highest risk persons (HIV-infected or otherwise immunocompromised, close contacts to active cases, and persons known to have abnormal CXRs suggestive of “old TB”)
 - 10 mm – for most people who are tested and have some risk factor for TB infection.
 - 15 mm – for persons who were tested but who have no TB risk factors (*and otherwise should not have been tested*).
- Reasons *not* to test include:
 - Documented positive TST in the past, with or without previous treatment.
 - No known TB risk factors.
 - Allergic reaction to a TST in the past (very rare)

Persons testing positive by TST: (refer to CDC Guidelines for *Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection*¹)

- Should be evaluated for signs and symptoms of TB disease.
 - Pregnant women with chronic cough, hemoptysis, longstanding fever, night sweats, or other symptoms of active TB should be evaluated *promptly*; this should include a medical history, a physical examination, and a shielded chest radiograph (PA projection only is sufficient).
- With or without symptoms, a PA chest radiograph should be done (1) to rule out active TB disease, and (2) to provide clinical data needed to evaluate patients for treatment for latent infection.
- Shielded chest x-rays can be done at any time during pregnancy, but may be deferred in asymptomatic and in lower risk women until at least the 2nd trimester because:
 - It is closer to the time of delivery when the threat of TB to the newborn is greatest.
 - The radiation risk to the fetus, however small, is least.

Reporting of LTBI:

- **Report all pregnant women with LTBI to the MDPH Division of TB Prevention and Control by mail or by fax (617-983-6960), using the required reporting form.**

Treatment:

- Isoniazid (INH) 300mg daily for 6 - 9 months is the only approved treatment for latent TB infection during pregnancy; 9 months therapy confers the greatest protection. Pyridoxine (50 mg/d) usually is administered with the INH. Treatment of latent TB infection in high-risk women may be initiated during pregnancy, although in many cases it can be delayed until soon after the birth of the child.
 - Latent TB infection should be treated during pregnancy (even during the 1st trimester) in the following situations:
 - Close contact to an active case (where recent infection is presumed). Note that this may not be the case for persons from some high-risk countries where infection earlier in life may be more likely.
 - Recent TST converter
 - When the woman is HIV-infected.
 - INH is known to be safe for the fetus during pregnancy and although small amounts are excreted in breast milk it has no effect on newborn babies (and is not considered sufficient treatment for newborns who have been exposed to, or are infected with TB)

Monitoring:

Studies have suggested that during pregnancy and in the early postpartum period, women are at increased risk of INH hepatotoxicity. Therefore, careful clinical and/or laboratory monitoring for hepatitis should accompany INH treatment during pregnancy and for at least 3 months postpartum. Isoniazid should be discontinued if serum transaminases increase to more than 5 times the upper limit of normal without symptoms, or if the patient develops signs or symptoms of hepatitis. Patients must be educated about signs and symptoms of hepatotoxicity, and instructed to stop treatment immediately and notify their providers if they suspect they are experiencing an adverse effect from their medications.

Infection Control:

- Latent TB infection in asymptomatic persons is not contagious – no precautions are needed to protect the newborn or staff.
- Asymptomatic persons with abnormal chest x-rays demonstrating old TB are generally not infectious, and no precautions are needed.
- TST positive persons symptomatic with a cough should have a CXR as soon as possible and, if suggestive of active TB, should be isolated from their newborn (and from others) until fully evaluated for active TB and started on appropriate therapy.
 - In general, 2 weeks of effective treatment (cough responding, and other clinical and laboratory signs of improvement) is considered adequate to allow contact with the newborn and other vulnerable persons.
 - Newborn babies and young children exposed to a mother with potentially infectious TB should be tuberculin skin tested and treated with INH, *regardless of the child's TST reaction*, pending a definite diagnosis and effective treatment of the mother. Treatment may be stopped subsequently if ongoing transmission is no longer a concern and a repeat TST 8 – 12 weeks following the last possible exposure is negative (<5mm).
 - **Report the mother as a TB Suspect or Case to the MDPH Division of TB Prevention and Control (1-888-MASS MTB; 1-888-627-7682).**

BCG Vaccine

Introduction

BCG, or bacille Calmette-Guerin, is a vaccine for tuberculosis (TB) disease. Many foreign-born persons have been BCG-vaccinated. BCG is used in many countries with a high prevalence of TB to prevent childhood tuberculous meningitis and miliary disease. However, BCG is not generally recommended for use in the United States because of the low risk of infection with *Mycobacterium tuberculosis*, the variable effectiveness of the vaccine against adult pulmonary TB, and the vaccine's potential interference with tuberculin skin test reactivity. The BCG vaccine should be considered only for very select persons who meet specific criteria and in consultation with a TB expert.

Recommendations

Children. BCG vaccination should only be considered for children who have a negative tuberculin skin test and who are continually exposed, and cannot be separated from, adults who

- Are untreated or ineffectively treated for TB disease (if the child cannot be given long-term treatment for infection); or
- Have TB caused by strains resistant to isoniazid and rifampin.

Health Care Workers. BCG vaccination of health care workers should be considered on an individual basis in settings in which

- A high percentage of TB patients are infected with *M. tuberculosis* strains resistant to both isoniazid and rifampin;
- There is ongoing transmission of such drug-resistant *M. tuberculosis* strains to health care workers and subsequent infection is likely; or
- Comprehensive TB infection-control precautions have been implemented, but have not been successful.

Health care workers considered for BCG vaccination should be counseled regarding the risks and benefits associated with both BCG vaccination and treatment of latent TB infection (LTBI).

Contraindications

Immunosuppression. BCG vaccination should not be given to persons who are immunosuppressed (e.g., persons who are HIV infected) or who are likely to become immunocompromised (e.g., persons who are candidates for organ transplant).

Pregnancy. BCG vaccination should not be given during pregnancy. Even though no harmful effects of BCG vaccination on the fetus have been observed, further studies are needed to prove its safety.

Testing for TB in BCG-Vaccinated Persons

The tuberculin skin test (TST) and blood tests to detect TB infection are not contraindicated for persons who have been vaccinated with BCG.

Tuberculin Skin Test (TST). BCG vaccination may cause a false-positive reaction to the TST, which may complicate decisions about prescribing treatment. The presence or size of a TST reaction in persons who have been vaccinated with BCG does not predict whether BCG will provide any protection against TB disease. Furthermore, the size of a TST reaction in a BCG-vaccinated person is not a factor in determining whether the reaction is caused by LTBI or the prior BCG vaccination. (See below for specific guidance on skin test results.)

TB Blood Tests. Blood tests to detect TB infection, unlike the TST, are not affected by prior BCG vaccination and are less likely to give a false-positive result.

Treatment for LTBI in BCG-Vaccinated Persons

Treatment of LTBI substantially reduces the risk that TB infection will progress to disease. Careful assessment to rule out the possibility of TB disease is necessary before treatment for LTBI is started. Evaluation of TST reactions in persons vaccinated with BCG should be interpreted using the same criteria for those not BCG-vaccinated. Persons in the following high-risk groups should be given treatment for LTBI if their reaction to the TST is at least 5 mm of induration or they have a positive result using a TB blood test:

- HIV-infected persons
- Recent contacts to a TB case
- Persons with fibrotic changes on chest radiograph consistent with old TB
- Patients with organ transplants
- Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF- α antagonists)

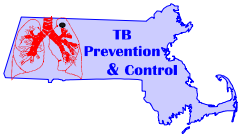
In addition, persons in the following high-risk groups should be considered for treatment of LTBI if their reaction to the TST is at least 10 mm of induration or they have a positive result using a TB blood test:

- Recent arrivals (less than 5 years) from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities)
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that place them at high-risk for developing TB disease (e.g., diabetes)
- Children less than 4 years of age, or children and adolescents exposed to adults in high-risk categories

Persons with no known risk factors for TB may be considered for treatment of LTBI if their reaction to the tuberculin test is at least 15 mm of induration or they have a positive result using a TB blood test. Targeted skin testing programs should only be conducted among high-risk groups. All testing activities should be accompanied by a plan for follow-up care for persons with TB infection or disease.

Additional Information

- CDC. [Development of new vaccines for tuberculosis: recommendations of the Advisory Council for the Elimination of Tuberculosis \(ACET\)](#). *MMWR* 1998; 47 (No. RR-13).
- CDC. [The role of BCG vaccine in the prevention and control of tuberculosis in the United States: a joint statement by ACET and the Advisory Committee on Immunization Practices](#). *MMWR* 1996; 45 (No. RR-4).
- [World Health Organization. Issues Relating to the Use of BCG in Immunization Programmes-A Discussion Document](#) (1999).



Massachusetts Department of Public Health
Division of Tuberculosis Prevention and Control
305 South Street, Jamaica Plain, MA - (617) 983-6970

Websites

Massachusetts Division of TB Prevention and Control

<http://www.mass.gov/dph/cdc/tb>

Bureau of Communicable Disease Control

<http://www.mass.gov/dph/cdc/bcdc.htm>

Massachusetts Reportable Diseases, Surveillance and Isolation and Quarantine

<http://www.mass.gov/?pageID=eohhs2subtopic&L=5&L0=Home&L1=Provider&L2=Reporting+to+the+State&L3=Diseases+%26+Conditions&L4=Reportable+Diseases%2c+Surveillance+and+Isolation+%26+Quarantine+Requirements&sid=Eeohhs2>

CDC Division of TB Elimination

<http://www.cdc.gov/tb/>

Regional Tuberculosis Training and Medical Consultation Centers

- **Northeastern National Tuberculosis Center**
<http://www.umdnj.edu/globaltb/home.htm>
- **Southeastern National Tuberculosis Center**
<http://sntc.medicine.ufl.edu/Default.aspx>
- **Francis J. Curry National Tuberculosis Center**
<http://www.nationaltbcenter.edu/>
- **Heartland National Tuberculosis Center**
<http://www.heartlandntbc.org/>