**Testing for Tuberculosis Infection:**

**Guidelines on the Use of Interferon-Gamma Release Assays and**

**the Tuberculin Skin Test in Massachusetts**

Massachusetts Department of Public Health

Division of Global Populations and Infectious Disease Prevention



**INTRODUCTION**

The interferon-gamma release assays (IGRAs) and tuberculin skin test (TST) are diagnostic tests for *Mycobacterium tuberculosis* infection. This document is intended to assist medical care providers in determining when to test for tuberculosis (TB) infection and which diagnostic TB test to use.

The American Thoracic Society/Infectious Disease Society of America/Centers for Disease Control and Prevention (ATS/IDSA/CDC) 2016 [guidelines on the treatment of drug-susceptible tuberculosis](https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf) were published in Clinical Infectious Diseases. These guidelines include information on testing for latent TB infection (LTBI).

**TESTING FOR TUBERCULOSIS INFECTION**

TB testing of low-risk persons is discouraged. As with many other diagnostic tests, the TST and IGRA are neither 100% sensitive nor 100% specific. A positive TB test in persons at low risk for TB infection is unlikely to represent true TB infection. Targeted TB testing of persons at high risk will increase the predictive value of the TB tests.

Medical care providers are encouraged to utilize the Massachusetts TB Risk Assessment and User Guide to help identify patients with increased risk for TB. Testing is recommended for persons with TB risk.

**The interpretation of IGRA and TST results should always be considered in the context of epidemiology, and the physical examination and other diagnostic tests. A IGRA or TST should never be used to establish or rule out a diagnosis of active tuberculosis disease.**

**CHOOSING A DIAGNOSTIC TUBERCULOSIS TEST**

A provider’s choice of TB test is based on several factors, including reason for testing, patient demographics (including age), other medical conditions, test availability and cost. Two IGRA tests are FDA-approved for use in the United States: QuantiFERON®-TB Gold In-Tube (QFT-G) and T-SPOT®.TB. Two formulations of PPD are available for skin testing: Tubersol (Aventis Pasteur Limited) and Aplisol (Squibb).

* An IGRA can be used in most situations in which the TST is indicated, and is preferred for those persons who have received bacille Calmette-Guerin (BCG) vaccine.
* Use TST for children <2 years of age.
* Unlike the TST, IGRAs do not require a return visit and results are less likely to be affected by cross-reactivity with BCG or infection due to most non-tuberculous mycobacteria.

In general, it is **not** recommended to test a person with both a TST and an IGRA. However, there are situations where using both tests may be useful.

In situations where TB testing is required, but one of the diagnostic tests (TST or IGRA) is unavailable, medical providers may need to use the test that is available. If the initial IGRA result is indeterminate, borderline, or invalid, and a reason for testing persists, consider repeating an IGRA or performing a TST.

Production of gamma interferon (which is what is detected by an IGRA) may be influenced by many factors. If test results are questioned following a negative or borderline result, the IGRA may be repeated at a later time. Similarly, a negative TST may occur in a patient with existing TB infection whose response to PPD has waned over time and two-step testing may reveal evidence of existing TB infection through boosting. For additional details on two-step testing, see: <https://www.mass.gov/service-details/booster-or-recall-effect-and-two-stage-tuberculin-skin-testing>

**Summary of TB diagnostic tests (IGRA and TST usage)**

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| **One Test Preferred** | **Either IGRA or TST** **can be used** | **Testing with both IGRA and TST is justified** |
| **IGRA is preferred for:*** Persons born outside the U.S. who have received BCG vaccination
* Persons unlikely to return for TST reading
 | * Contact Investigations:

The same test (IGRA or TST) should be used for initial and repeat (8-10 weeks post-exposure) testing of contacts. * Immunocompromised persons: If performance of IGRA or TST is thought to be compromised by immunosuppression, consider repeat testing using the alternative-format test if risk for TB is identified and an initial false-negative test result is suspected.
* Only one test is available to the provider
 | * The result of a positive TST is not believed: If a patient refuses to believe the positive result of a given test (e.g., a positive TST), follow-up testing with an IGRA may be helpful.
* Initial test (TST or IGRA) is negative, but the risk for progression to TB disease is high and the increased sensitivity associated with two tests will contribute to a diagnosis.
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| **TST is preferred for:*** Children < 2 years of age

 * Serial testing (e.g., healthcare workers)
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**WHAT SHOULD BE DONE AFTER A POSITIVE IGRA TEST OR TST**

All persons with a positive IGRA or TST result should be evaluated for the possibility of active TB disease. This can be done in a primary care or other clinical setting or at a Massachusetts TB Clinic. A list of TB clinics can be found at <https://www.mass.gov/lists/tuberculosis-information-for-health-care-providers-and-public-health#tb-clinics->

**Report TB**: Report newly diagnosed cases of latent TB infection, and suspected or confirmed TB disease to the Massachusetts Department of Public Health.

<https://www.mass.gov/how-to/report-a-case-of-tuberculosis-disease-or-latent-tb-infection>

**RESOURCE INFORMATION**

CDC Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection - United States, 2010 <http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf>

Menzies R Effect of bacillus Calmette-Guérin vaccination on tuberculin reactivity. Am Rev Respir Dis 1992;145:621-5.

MDPH and CDC information about TB evaluation, testing and treatment <http://www.cdc.gov/tb/> and <http://www.mass.gov/tuberculosis>

MDPH TB Risk Assessment and User Guide <https://www.mass.gov/lists/tuberculosis-information-for-health-care-providers-and-public-health#screening-and-testing-for-tb-infection->

For further information, contact the MDPH Tuberculosis Program at 617-983-6970.

**REGULATIONS**

**105 CMR 300**

Reportable diseases, surveillance, and isolation and quarantine requirements

<https://www.mass.gov/regulations/105-CMR-30000-reportable-diseases-surveillance-and-isolation-and-quarantine>