

Testing for Tuberculosis Infection: Guidelines on the Use of Interferon-Gamma Release Assays and Tuberculin Skin Test in Massachusetts

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

1. Testing for TB 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 providers are encouraged to utilize the Massachusetts [TB Risk Assessment and Screening Form](http://www.mass.gov/eohhs/gov/departments/dph/programs/id/tb/testing-screening/) to help identify patients with increased risk for TB who may require TB testing and evaluation <http://www.mass.gov/eohhs/gov/departments/dph/programs/id/tb/testing-screening/>. Screening should be used to determine whom to test; in general, low risk persons should not be tested.

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

2. Choosing a diagnostic TB 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 BCG vaccine and in whom it is believed that BCG might affect a TST result (such as those who received multiple BCG vaccinations after infancy).
- Use TST for children <5 years of age. **The accuracy of IGRAs has been more difficult to assess in children, thus the use of IGRAs in children aged <5 years is NOT recommended.**
- Unlike the TST, IGRA tests 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 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 to see if gamma interferon release was transient. 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: <http://www.mass.gov/eohhs/gov/departments/dph/programs/id/tb/testing-screening/public-health-cdc-tb-2-step-skin-testing.html>

Summary of TB diagnostic tests (IGRA and TST usage)

One Test Preferred	Either IGRA or TST can be used	Testing with both IGRA and TST is justified
<p>IGRA is preferred for:</p> <ul style="list-style-type: none"> • Non-U.S. born persons who have received BCG vaccination <i>and</i> the patient or provider may believe that this will affect TST result • Persons unlikely to return for TST reading <p>TST is preferred for:</p> <ul style="list-style-type: none"> • Children < 5 years of age • Serial testing (e.g., healthcare workers) 	<ul style="list-style-type: none"> • Contact Investigations: The same test (IGRA or TST) should be used for initial and repeat (8-10 week 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. 	<ul style="list-style-type: none"> • 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 clinician wishes additional supporting information.

3. What should be done after a positive IGRA test or TST?

All persons with a positive TST or IGRA 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 <http://www.mass.gov/eohhs/docs/dph/cdc/tb/regional-clinic-list.pdf>

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

<http://www.mass.gov/eohhs/gov/departments/dph/programs/id/isis/case-report-forms.html>

4. Resources

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/dph/cdc/tb>

MDPH Adult TB Risk Assessment and Screening Form <http://www.mass.gov/eohhs/docs/dph/cdc/tb/ma-tb-risk-assessment-form.pdf>

MDPH Recommendations on Screening Infants and Children for Tuberculosis <http://www.mass.gov/eohhs/docs/dph/cdc/tb/recommendations-screening-children-tb.pdf>

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