Tuberculosis Blood Test: Interferon Gamma Release Assay (IGRA)

The Wisconsin Tuberculosis Program recommends an interferon gamma release assay (IGRA) rather than a tuberculin skin test (TST) in individuals 2 years or older. An IGRA provides an equally sensitive, but much more specific, test of the body's immune response to tuberculosis (TB) than a TST. Local and Tribal health departments (LTHDs) can use this guide to interpret IGRA results and decide on next steps.

Next steps after a patient gets a positive IGRA result

Does my patient have any of the risk factors for TB?

- Lives, has traveled (for 1 month or more), or was born in a country with high TB prevalence
- Close contact with someone with infectious TB disease
- Recent TB symptoms—persistent cough lasting more than three weeks and one or more of the following symptoms: fever, night sweats, coughing up blood or sputum (thick mucus), weight loss, or fatigue
- Current or former employee or resident of a high-risk congregate setting (correctional facility, long-term residential care facility, or shelter for the homeless) in a state or district with an elevated TB rate (Alaska, California, Florida, Hawaii, New Jersey, New York, Texas, or Washington DC)

YES

Do they have two or more of the following symptoms?

Cough more than three weeks, fever, night sweats, coughing up blood or sputum (thick mucus), weight loss, or fatigue

YES

Patient should isolate (stay at home) until you perform a chest X-ray and **medical evaluation to assess for active TB disease.**

- If the chest x-ray is abnormal, collect three sputum specimens for acid-fast bacilli (AFB) smear and culture, eight to 24 hours apart, with at least one being an early morning specimen.
- If pulmonary and extra-pulmonary TB are ruled out, the patient has latent tuberculosis infection (LTBI) and should be offered preventive treatment.
- Report LTBI to the LTHD.

NO

Perform a chest X-ray and **medical evaluation to assess for active TB disease**.

- If active TB is ruled out, the patient has LTBI and should be offered preventive treatment.
- No restriction on movements or work (no quarantine or isolation) is needed.
- Report LTBI to the LTHD.

NO

Retest in 3–6 months with another IGRA (QuantiFERON® or T-SPOT®) as a second diagnostic confirmatory test.[1]

The person is considered infected only if both tests are positive.

- The bacille Calmette-Guerin (BCG) vaccination does not cause false-positive results on an IGRA.
- When people who are low risk have low-level positive results, it may suggest a false positive. Results are low-level positives when TB-Nil (TB antigen levels minus Nil results) is between 0.36 and 1.10 IU/mL. Retest in 3–6 months. See "Low-level positive QFT results" on page 2.
- Non-tuberculous mycobacteria (*M. kansasii*, *M. szulgai*, and *M. marinum*) may cause a false positive IGRA reaction.

Interpreting IGRA results

Two IGRAs are approved and commercially available in the U.S: QuantiFERON®-TB Gold In-Tube test (QFT-GIT) and T-SPOT®.TB test (T-Spot).

IGRA Test Result	QuantiFERON	T-Spot	Notes
Positive	TB-Nil is higher than or equal to 0.35 IU/mL	8 spots or more	Infection is likely in individuals with risk factors. Consider retesting in low- or no-risk individuals.
Negative	TB-Nil is lower than 0.35 IU/mL	4 spots or less	Infection is unlikely.
Indeterminate or invalid	High nil value or low mitogen value	High nil value or low mitogen value	Collect another specimen for retesting since these results cannot be interpreted. This occurs if controls do not perform as expected.
Borderline (not clear)	Not applicable	5, 6 or 7 spots	Uncertain likelihood of TB infection. Collect another specimen for retesting.

Low-level positive QFT results

Retest low-risk individuals in 3–6 months if their initial QFT-GIT has TB-Nil results between 0.36 and 1.10 IU/mL.[1–3] Studies show most low-level positive IGRA results for low-risk individuals become negative when retested 6 months later (a sign that they are false positives).[2, 3] This was most likely to happen if their initial QFT results were higher than 0.35 IU/mL and lower than 1.11 IU/ml.[2]

Prevent boosted results from TST

TSTs may cause an immune response which can later be detected by IGRA testing. If an IGRA (either a T-Spot or QFT-GIT®) is performed shortly after a TST, the numeric results might increase and may be misinterpreted as a new infection.[4] This is called boosting. If a TST was administered, the Wisconsin TB Program recommends IGRA testing at least 90 days after a TST to avoid potential boosting.

References

1. CDC. Tuberculosis screening, testing, and treatment of U.S. health care personnel: Recommendations from the National Tuberculosis Controllers Association and CDC, 2019. MMWR 2019: 68(No. 19).
2. Thanassi et al. Delineating a Retesting Zone Using Receiver Operating Characteristic Analysis on Serial QuantiFERON Tuberculosis Test Results in US Healthcare Workers. Pulm Med. 2012;2012:291294. doi: 10.1155/2012/291294. Epub 2012 Dec 30. PMID: 23326660; PMCID: PMC3544373.
3. Dorman et al. Tuberculosis Epidemiologic Studies Consortium. Interferon-γ release assays and tuberculin skin testing for diagnosis of latent tuberculosis infection in healthcare workers in the United States. Am J Respir Crit Care Med. 2014 Jan 1;189(1):77-87. doi: 10.1164/rccm.201302-0365OC. PMID: 24299555.
4. van Zyl-Smit et al. Within-subject variability and boosting of T-cell interferon-gamma responses after tuberculin skin testing. Am J Respir Crit Care Med. 2009 Jul 1;180(1):49-58. doi: 10.1164/rccm.200811-1704OC. Epub 2009 Apr 2. PMID: 19342414.