Tuberculin skin tests and interferon- γ release assays in the diagnosis of tuberculosis infection

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- Tuberculin skin tests (TSTs) and interferon- γ release assays (IGRAs) are intended for the diagnosis of tuberculosis (TB) infection, not active disease

Tuberculin skin tests and IGRAs detect evidence of immunity to TB antigens but cannot distinguish TB infection from disease. Negative results do not exclude TB disease, as false negatives may occur for several reasons, including illness-induced anergy.¹ Therefore, TSTs and IGRAs should be avoided in adults in whom TB disease is suspected.

2 The primary goal of testing for TB infection is to identify people who would benefit from preventive treatment

Testing should be considered among people with an increased risk of progression to TB disease (e.g., people living with HIV, before starting immunosuppressive therapy). A positive test result should prompt additional investigations (e.g., chest imaging) to exclude TB disease before offering preventive treatment.

The positive predictive values for progression to TB disease for TSTs and IGRAs are similar, and the tests can be used interchangeably, with some exceptions

Tuberculin skin tests require a second visit for reading 48–72 hours after placement and may be falsely positive due to previous bacille Calmette–Guérin (BCG) vaccination. Interferon- γ release assays are not affected by BCG vaccination and require only 1 visit, but their cost and availability vary by province. Interferon- γ release assays are preferred (but TSTs are still acceptable) for people who may not return for TST reading or may have false-positive TST results (i.e., the patient is 2–9 yr of age and previously received a BCG vaccine; the patient is at least 10 yr of age and previously received a BCG vaccine after age 1 yr; the age of BCG vaccination is unknown; multiple BCG vaccinations were received).¹

- To enhance diagnostic certainty, TSTs and IGRAs may be performed sequentially

 If the initial test result is negative, but the suspicion for infection remains high, the other type of test may be performed to improve sensitivity. If a TST result is suspected to be falsely positive, then an IGRA may be performed to improve specificity.¹
- **5** Web-based tools can be used to quantify the risk-benefit profile of TB preventive treatment

Evidence-based tools include the Online TST/IGRA Interpreter³ (https://www.tstin3d.com/) and PERISKOPE•TB⁴ (http://periskope.org/).

References

- 1. Campbell JR, Pease C, Daley P, et al. Chapter 4: Diagnosis of tuberculosis infection. Can J Respir Crit Care Sleep Med 2022;6(Suppl 1):49-65.
- 2. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice guidelines: diagnosis of tuberculosis in adults and children. Clin Infect Dis 2017;64:e1-33.
- 3. Menzies D, Gardiner G, Farhat M, et al. Thinking in three dimensions: a web-based algorithm to aid the interpretation of tuberculin skin test results. *Int J Tuberc Lung Dis* 2008;12:498-505.
- 4. Gupta RK, Calderwood CJ, Yavlinsky A, et al. Discovery and validation of a personalized risk predictor for incident tuberculosis in low transmission settings. *Nat Med* 2020;26:1941-9.

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