

These cases also included patients that did not have previous exposure to tuberculin. It is imperative that health care providers should have Epinephrine Hypochloride solution (1:1000) and other appropriate agents available for immediate use in the case of a hypersensitivity reaction. As per NACI, recommendations all patients must be monitored for 15 minutes after inoculation.

## Interferon Gamma Release Assay (IGRA)

Interferon gamma release assay (IGRA) is a blood test that has recently been introduced as another method to diagnose LTBI. Therefore, it can complement the TST in certain situations. In general, IGRAs are more specific than the TST in populations vaccinated with BCG, especially if BCG is given after infancy or multiple times.

When a person is exposed to MTB it produces many immune cells, which produce various proteins. Among these proteins are interferon gamma or IFN- $\gamma$ . The interferon gamma release assay (IGRA) is a blood test that measures IFN- $\gamma$ . Therefore, if a person has been exposed and infected with TB, IFN- $\gamma$  can be detected with this test.

There are two IGRA tests used in Canada, the T-SPOT.TB test and the QuantiFERON<sup>®</sup>-TB Gold test. Provincial Laboratory (ProvLab) Alberta uses QuantiFERON<sup>®</sup>-TB Gold (QFT) test in the NWT. Specimens must be received by the regional laboratory and incubated for 16–24 hours. This limits availability of this test in the NWT. **IGRA can only be ordered through the Office of the Chief Public Health Officer and Stanton Regional Hospital Specialists who are involved in TB management and treatment.**

IGRAs require laboratories with adequate equipment and trained personnel to perform the assays. In addition, IGRAs require fresh blood samples: pre-analytical steps and transportation delays can affect test performance.

Table 4.2: QuantiFERON<sup>®</sup>-TB Gold (QFT) Assay

QuantiFERON <sup>®</sup> -TB Gold (QFT) assay
<ul style="list-style-type: none"> <li>• Uses whole blood</li> <li>• Mixes blood + MTB antigen components</li> <li>• Measures amount of IFN-<math>\gamma</math> (concentration: IU/ml)</li> <li>• Possible Results: positive, negative or indeterminate</li> </ul>

(Adapted from CDC fact sheet: <http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.pdf>)

There can be difficulty in how to interpret disagreement between TST and IGRA tests results (positive TST and negative IGRA and vice versa). It makes interpretation and appropriate management difficult. More studies are required to understand these contradictions.

Advantages and important limitations of IGRA tests are listed in the table on the following page.

Table 4:3: Advantages and Disadvantages of IGRA Tests

Advantages	Disadvantages
<ul style="list-style-type: none"> <li>• Requires one visit to screen for TB (rather than 2 visits for TST)</li> <li>• Does not cause a booster phenomenon</li> <li>• Prior BCG vaccination does not cause a false positive result</li> </ul>	<ul style="list-style-type: none"> <li>• Blood samples are required</li> <li>• Technical errors in collecting, transporting or interpreting results decreases the accuracy of the test</li> <li>• Limited evidence on the use of IGRA to predict those who will progress to having TB disease</li> </ul>

(Adapted from **CDC fact sheet** <http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.pdf>)

While both the TST and IGRA are acceptable alternatives for LTBI diagnosis, **TST is the preferable choice in NWT** due to transport constraints in the smaller communities for IGRA specimens. Indications and exceptions for the use of these screening tests are outlined below.

1. Situations in which **neither TST nor IGRAs** should be used for testing

- Neither the TST nor the IGRA should be used for testing people who have a low risk of infection and a low risk that there will be progression to active TB disease if they are infected. However, low-risk individuals are commonly tested before exposure, when repeat testing is likely. In this situation TST is recommended (see 3 below); if the TST is positive then an IGRA may be useful to confirm a positive TST result to enhance specificity.
- Neither TST nor IGRA should be used for active TB diagnosis in adults (for children, see 4).
- Neither TST nor IGRA should be used for routine or mass screening for LTBI of all immigrants (adults and children).
- Neither TST nor IGRAs are useful tools for monitoring anti-TB treatment response.

2. Situations in which **IGRAs are preferred** for testing but a TST is acceptable

- People who have received BCG as a vaccine after infancy (1 year of age) and/or have received BCG vaccination more than once.
- People from groups that historically have poor rates of return for TST reading.

3. Situations in which **TST is recommended** for testing but an **IGRA is NOT acceptable**

- The TST is recommended whenever it is planned to repeat the test later to assess risk of new infection (i.e. conversions), such as repeat testing in a contact investigation, or serial testing of health care or other populations (e.g. corrections staff or prison inmates) with potential for ongoing exposure.

4. Situations in which **both tests** can be used (sequentially, in any order) to enhance sensitivity
- Although routine dual testing with both TST and IGRA is not recommended, there are situations in which the results from both tests may be helpful to enhance the overall sensitivity:
    - When the risk of infection, of progression to disease and of a poor outcome are high.
    - In children (under age 18 years) with suspected TB disease, IGRAs may be used as a supplementary diagnostic aid in combination with the TST and other investigations to help support a diagnosis of TB. However, IGRA should not be a substitute, or obviate the need, for appropriate specimen collection. A negative IGRA (or TST) does NOT rule out active TB at any age and especially not in young children.
    - 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.
    - IGRA testing can be used as a supplementary test to increase the specificity of the TST for those determined to have borderline positive TSTs.

## Importance of Considering the Clinical Context

The results of both TST and IGRA should be interpreted with other relevant clinical information, such as age, BCG status, history of contact with active TB and factors that increase the risk of progression to active disease.

An **online TST/IGRA algorithm** ([www.tstin3d.com](http://www.tstin3d.com)) has been developed to facilitate the three-dimensional interpretation of these tests. All individuals with positive TST or IGRA results should undergo evaluation to determine whether they have LTBI or active TB disease and be managed accordingly.