Indiana State
Department of Health

Guidelines and Recommendations on the Use of QuantiFERON®-TB Gold for the Diagnosis of Active and Latent Tuberculosis Infection

The QuantiFERON®-TB Gold test was approved by the Food and Drug Administration in May 2005, as an aid for diagnosing *Mycobacterium tuberculosis infection*, including both latent tuberculosis infection (LTBI) and tuberculosis (TB) disease. The QFT-G is manufactured by Cellestis, Ltd., Carnegie, Victoria, Australia. It is a laboratory-based assay that detects interferon ? (IFN- ?) in fresh heparized whole blood from sensitized persons. Recommendations for the use of the QFT-G were published in the MMWR December 16, 2005, V54, RR15; 49-55.

The QFT-G is more specific test than the original QuantiFERON -TB test, which it has replaced and is no longer available. Several studies have been published which report the specificity of the QFT-G as high as 98.1%[i] and sensitivity at between 64% to 89%[ii]. The QFT-G detects antigenic proteins that are specific to *M. tuberculosis*, pathogenic *M. bovis* and from commonly encountered nontuberculosis mycobateria including *M. kansasii*, *M. szulgai*, and *M. marinum*. These proteins are not found in other atypical mycobacteria, such as *M. Avium*, and are not found in the Bacille Calmette-Guerin BCG strain.

In Indiana, the tuberculin skin test (TST) is still the standard of care, however when used in accordance with Food and Drug Administration procedures and in approved circumstances outlined by the Centers for Disease Control, the results of the QFT-G will be accepted in the lieu of the TST. The Indiana State Health Department TB Program will accept the QFT-G in all circumstances in which the TST is currently used, including contact investigations, evaluation of recent arrivals from TB endemic countries who have had BCG vaccination, and TB screening of health care workers and others undergoing serial evaluation for *M. tuberculosis*. Caution should be used when testing persons known to be HIV positive and children <17 because of limited data and the need for future research.

In comparison with the TST, the QFT-G test:

- requires only one patient visit
- results can be available within 24 hours of lab receiving blood
- not affected by repeat TST "booster phenomenon"
- is not subject to reader bias that can occur with TST
- is influenced less by infection with atypical mycobacterial infection
- is less likely to be positive in patients with past exposure to BCG vaccine

Limitations of QFT-G include

- the need for phlebotomy
- processing of the whole blood within 12 hours of collection by a qualified laboratory
- limited data on the use of QFT-G in children younger than 17 years of age, among persons recently exposed to *M. tuberculosis*, and in immunocompromised persons (e.g., impaired immune function caused by HIV infection or acquired immunodeficiency syndrome [AIDS], current treatment with immunosuppressive drugs, selected hematological disorders, specific malignancies, diabetes, silicosis, and chronic renal failure)
- errors in collecting or transporting blood specimens or in running and interpreting the assay can decrease the accuracy of QFT-G

- limited data on the use of QFT-G to determine who is at risk for developing TB disease
- cost associated with QFT-G maybe more than administration of TST

Who should get tested with QFT-G?
Like the TST, the QFT-G is a useful but imperfect diagnosis aide. Patients with active TB can be either TST negative, QFT-G negative, or both. The QFT-G should not replace clinical judgment.

If a practitioner chooses to use the QFT-G for diagnostic purposes, the Indiana State Department of Health recommends testing with QFT-G for the following groups:

1. Persons who have an increased risk for LTBI
    - persons born in countries where TB is common
    - injection drug users
    - residents and employees of high-risk congregate settings, such as jails, prisons, and homeless shelters
    - residents and employees of long-term care facilities
    - health-care workers and others who serve high-risk clients
2. Groups who are historically at low risk for LTBI, but 1) whose occupation may place them at risk for exposure, or 2) who are part of mandatory LTBI surveillance programs. Such groups include but are not limited to:
    - most health care workers
    - military personnel
    - U.S.-born college students

Reading the results of QFT-G tests:
QFT-G results can include "positive", "negative" or "indeterminate".

Positive: A positive QFT-G result should prompt a chest x-ray and medical evaluation to exclude active TB disease and confirm LTBI. No reason exists to follow a positive QFT-G result with a TST.

Negative: Health adults who have negative QFT-G results are unlikely to have M. tuberculosis infection and do not require further evaluation. However, for persons with recent contact with persons who have infectious TB, negative QFT-G results should be confirmed with a repeat test performed 8-10 weeks after the end of exposure, as is recommended for a negative TST result. Until more information is available, the timing of QFT-G testing should be the same as that used for the TST.[iii iv]

Indeterminate: An indeterminate QFT-G result indicates test failure as a result of either low mitogen response or high levels of background level of interferon-gamma in the specimen. A TST should be administered as a diagnostic tool for LTBI or TB.

Regardless of the QFT-G or TST result a diagnosis of LTBI requires that TB disease be excluded by medical evaluation, which should include checking for signs and symptoms suggestive of TB disease, a chest radiograph, and, when indicated, examination of sputum or other clinical samples for the presence of *M. tuberculosis*. Anyone with TB symptoms or TB risk factors and a new abnormal chest radiograph may be a TB suspect.

Discordant results:
Persons with a previously positive TST, should not be retested with either TST or QFT-G. If QFT-G was done after TST status was known proceed based on the new results.

These guidelines were adopted by the Indiana State Department of Health after review and approval by the State TB Medical Advisory board in July 2007.

---

[i] Mori T, Sakatani M, Yamagishi F, et al. Specific detection of tuberculosis infection: an interferon-gamma-based assay using new antigens. *Am J Respir Crit Care Med.* 2004;170:59-64.
[ii] Puneet K. Dewan, Jennifer Grinsdale, and L. Masae Kawamura. Low sensitivity of a Whole-Blood Interferon- γRelease Assay for Detection of Active Tuberculosis. Clinical infectious Disease, volume 44 (2007), pages 69-73.
[iii] Menzies D. Interpretation of repeated tuberculin tests: boosting, conversion, and reversion. *Am J Respir Crit Care Med* 1999;159 15-21.
[iv] CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. MMWR 2005;54 (No. RR-17):1-47. http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf (PDF)