Marshfield Labs™
A division of Marshfield Clinic

Laboratory News

VOL. 35, NO. 8 - JUNE 6, 2012

Inside This Issue

QuantiFERON®-TB Gold In-Tube Assay Update: Now Reporting Numerical Results

Thomas Novicki, PhD, DABMM, Clinical Microbiologist, and Thomas Fritsche, MD, PhD, Section Head of Microbiology

QuantiFERON®-TB Gold In-Tube (test code QGOLD) is a blood-based test more generally referred to as an interferon gamma release assay (IGRA) that may be used as an alternative to the tuberculin skin test (TST) in most situations that present to the clinician. Since our last publication on this subject (see Laboratory News Vol. 31, No. 5 - June 27, 2008), the Centers for Disease Control and Prevention (CDC) have published additional recommendations for the use of IGRAs. Included in this is the recommendation to report the numerical values of an IGRA as well as the qualitative interpretation of those values (i.e., Positive, Negative or Indeterminate). Effective June 18, 2012, all Positive and Indeterminate QGOLD results will include the following numerical values that are associated with that interpretation:

- **Nil** The baseline interferon gamma level produced by the patient's lymphocytes.
- **Tb Antigen-Nil (TbAg-Nil)** The level of interferon-gamma production by the patient's lymphocytes due to stimulation by *M. tuberculosis* antigens minus the Nil (i.e., basal) level of interferon-gamma.
- **Mitogen-Nil** The maximum non-specific stimulated interferon-gamma level that may be produced by the patient's lymphocytes minus the Nil (i.e., basal) level of interferon-gamma.

(The reporting range for the Nil is 0 - >8.0. The reporting range for the Tb Antigen-Nil and Mitogen-Nil is 0 - ≥10 IU/mL.)

continued on page 2

BEYOND numbers

The use of these values will require careful consideration by the clinician. The most important of the three is the TbAg-Nil value; a level close to the cut point of ≥0.35 suggests a lower level of confidence that the patient has latent or active tuberculosis. Such cases will require close scrutiny of other factors such as risk level for exposure to TB, clinical signs, radiological evidence, and the potential risk to the patient of re-activated TB (e.g., in patients being considered for TNF alpha inhibitor therapy).

While Nil values ≤8.0 are considered valid for a Positive or Negative interpretation, an acute non-tuberculous infection may cause an elevated normal Nil level. The CDC therefore suggests a single repeat IGRA test in two to four weeks if the Nil value is ≥0.7 and the IGRA interpretation is not consistent with other findings.

A Nil value >8.0 and/or a Mitogen-Nil level of <0.5 will automatically result in an interpretation of Indeterminate regardless of the TbAg-Nil value. An extremely high Nil may indicate a problem with specimen handling, while an extremely low Mitogen-Nil level can be seen in immunosuppressed and severely lymphopenic patients. Consideration of these values may be of interpretive value in the event of an Indeterminate result.

It is important to remember that the Food and Drug Administration fundamentally considers this to be a qualitative test. The numerical values are therefore useful only as an additional guide in the interpretation of a single test result. Neither single nor serial values should be used to predict disease progression or to monitor therapeutic response.

Notes:

- In contrast to the tuberculin skin test, BCG vaccination will not cause a false positive QGOLD result.
- QGOLD is not a definitive test for *M. tuberculosis* infection.
- QGOLD cannot differentiate latent and active disease.
- Infection by *Mycobacterium kansasii, Mycobacterium marinum* or *Mycobacterium szulgai* may cause a false-positive QGOLD result.
- QGOLD has not been well-validated in pediatric patients, pregnant women, HIV-infected individuals, transplant recipients, individuals receiving long term immunosuppressive therapy, individuals with diabetes, hematological disorders and malignancies. QGOLD in these patients should be used with some caution. (Note that performance of the tuberculin skin test may also be affected in some of these populations.)
- Some evidence suggests that a negative QGOLD result may occur in individuals with longstanding latent Mtb infection and in those with active Mtb infection, the latter presumably due to the immunosuppressive effect of Mtb itself.

Regarding the use of an IGRA such as the QGOLD test vs. the TST, in general they may be considered interchangeable as part of the diagnostic process for TB, and results of one do not need to be confirmed with the other. However, there are some situations where one test may be preferable to the other, or where both tests may be warranted:

continued on page 3

- QGOLD is preferred but a TST is acceptable in persons who have received BCG vaccine, and in groups who may be lost to the follow-up TST reading.
- TST is preferred but QGOLD is acceptable in children aged <5yrs.
- Both QGOLD and TST may be warranted when:
  - The first test is negative, and the risk for infection, progression, and/or poor outcome is high (e.g., patients being considered for TNF-alpha inhibitor therapy), or the index of suspicion for TB is high, and a confirmatory test is required.
  - The first test is positive in order to encourage compliance (e.g., in a foreign-born person from a TB-endemic region who believes the initial result is due to a distant BCG inoculation).

Repeating the QGOLD or performing a TST may be useful if the initial QGOLD is Indeterminate or borderline-positive, and a reason for testing persists (e.g., in a healthy healthcare worker).

For additional information please contact Dr. Thomas Novicki or Dr. Thomas Fritsche (internal ext. 16300; external 715-221-6300).

Information on the QuantiFERON-TB Gold In Tube (QGOLD) test

- Specimen: Specialized collection tubes and processing are required. Collection is done by phlebotomy staff only, Monday – Thursday.
- Availability: Marshfield center and select regional centers. Contact the laboratory's Customer Service department for details. (Outreach clients should contact their account executive.)

Test is performed Monday, Wednesday and Friday.
The analytic time is 1-2 days for Negative results and for Positive results with a TbAg-Nil value ≥0.5 IU/mL. All Positive results with a TbAg-Nil value of <0.5 IU/mL will be repeated with the next regularly scheduled run before results are released.

- Method EIA
- CPT 86480

Reference

Centers for Disease Control and Prevention. "Updated guidelines for using interferon gamma release assays to detect Mycobacterium tuberculosis infection." United States, 2010. MMWR 2010; 59(RR-5).