QuantiFERON In-Tube®: Use of Quantitative Information
Provider Information and Guidance

New CDC IGRA Guidelines

Updated CDC guidelines on the use of interferon gamma release assays (IGRA) were published this year (MMWR, June 25, 2010/vol.59/RR-5) and call for the reporting of quantitative information in addition to the qualitative result “to permit a more refined assessment of results and promote understanding of the tests.”

Background

QuantiFERON In-Tube® (QFT-IT) is a blood based TB assay that uses quantitative cut points to determine positive, negative and indeterminate results. These results are based on gamma interferon (IFN-γ) produced by T-cells from whole blood in response to specific M. tuberculosis proteins. When antigens are recognized, T-cells release IFN-γ, a chemical messenger or cytokine that is critical for the innate and adaptive immune response against intracellular bacteria.

Quantitative values from the TB antigen containing tubes are compared to negative and positive controls, necessary to determine the validity of the test. If the negative control has levels of IFN-γ that are inappropriately high, the test is considered a “high nil” indeterminate. Likewise, a “low mitogen” indeterminate result can occur due to an inappropriately low IFN-γ mitogen response in the positive control.

IFN-γ responses that are close to the positive cut point of .35 IU/L may represent weak responses to circulating TB antigen. Unlike Tspot-TB, QFT-IT does not have a borderline range or gray zone that can be used when a conservative approach is needed (eg. in particular for immunocompromised patients, contacts with significant exposure to active TB or patients strongly suspected of having active disease).

What is currently known

Multiple studies of serial pre- and post-treatment IGRA testing for active and latent infection have shown that treatment reduces IFN-γ levels. However, many patients on treatment will not lower quantitative values sufficiently to revert their result to negative. Experts conclude that qualitative and quantitative reversion commonly occur with treatment but are not consistent enough to determine treatment efficacy.

Individual variability of quantitative results on different days has been documented by researchers (Detjen 2009, Perry 2008). This may have implications for persons receiving serial testing and the need for review of the quantitative change between tests if no TB exposure has occurred.

In serial testing, higher QFT-IT conversion rates compared to concurrent skin testing have been reported. However, exploratory thresholds using twice the manufacturer’s cut-off point (.70 IU/L) improved concordance rates among TST and QFT-IT converters in 2 studies (Pai 2006, Lee 2008).

IFN-γ production may be reduced in immunocompromised persons as documented in a several HIV studies and Japanese rheumatoid arthritis patients with a history of active TB (Maeda 2009).

A risk of progression study observed that very high levels of IFN-γ (≥10IU/L limit) in patients with LTBI preceded disease development (Diel 2008).

QFT-IT Result interpretation

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
<th>Gray Zone</th>
<th>Indeterminate</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥0.35*</td>
<td>&lt;0.35 *</td>
<td>None</td>
<td>Low mitogen Mitogen - Nil &lt; 0.50 IU/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High Nil Nil &gt; 8.0 IU/mL</td>
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</tbody>
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* (TB Ag - Nil) and assumes appropriate control responses
Limitations

No diagnostic test can replace clinical judgment.

Normal variation may occur in quantitative results of a single individual but the range of normal, nor its clinical implications has been determined.

Quantitative results cannot determine cure and should be NOT be used to stop treatment for active TB or latent TB infection.

Cautious interpretation of quantitative results is advised until more information is known.

Resources

San Francisco TB Control: 415-206-8524
www.sftbc.org
Francis J. Curry National Tuberculosis Center Warmline: 415-512-4700
Updated Guidelines for Using Interferon gamma Release Assays to Detect Mycobacterium tuberculosis Infection – United States, 2010
MMWR, Vol. 59/RR-5

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