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QuantiFERON®-TB Gold Assay

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Effective Date:
October 20, 2008
Mnemonic:
QFTB
Performed:
Monday-Friday (days)
Specimen:
Special QFT Blood Collection Tubes (Cellestis Product # 05900301) are required.

Each collection requires three tubes: Nil Control Tube (Grey Top)
TB Antigen Tube (Red Top)
Mitogen Control Tube (Purple Top).

See separate collection and processing instructions QFT BLOOD COLLECTION INSTRUCTION FLYER (Available at www.cpallab.com under the Technical Notes section or call to request glossy color copies).

Proper incubation and processing is required for accurate results!!

Summary:
QuantiFERON®-TB Gold IT is an indirect test for *M. tuberculosis* infections (including disease) and is intended for use in conjunction with risk assessment, radiography and other medical and diagnostic evaluations.

Tuberculosis is a communicable disease caused by infection with *M. tuberculosis* complex organisms, which typically spreads to new hosts via airborne droplet nuclei from patients with respiratory tuberculosis diseases. A newly infected individual can become ill from

tuberculosis within weeks to months, or can remain latently infected for years. Latent tuberculosis infection (LTBI), a non-communicable asymptomatic condition, persists in some, who might develop tuberculosis disease months or years later. The main purpose of diagnosing LTBI is to consider medical treatment for preventing tuberculosis disease. Until recently the tuberculin skin test (TST) was the only available method for diagnosing LTBI. Cutaneous sensitivity to tuberculin develops from 2 to 10 weeks after infection. However, some infected individuals, including those with a wide range of conditions hindering immune functions, but also others without these conditions, do not respond to tuberculin. Conversely, some individuals who are unlikely to have *M. tuberculosis* infection exhibit sensitivity to tuberculin and have positive TST results after vaccination with Bacilli-Calmette-Guerin (BCG), infection with mycobacteria other than *M. tuberculosis* complex, or undetermined factors.

The QuantiFERON®-TB Gold IT test is a test for Cell Mediated Immune (CMI) responses to peptide antigens that simulate mycobacterial proteins. These proteins, ESAT-6, CFP-10, and TB7.7, are absent from all BCG strains and from most non-tuberculous mycobacteria. Individuals infected with *M. tuberculosis* complex organisms usually have lymphocytes in their blood that recognize these and other mycobacterial antigens. This recognition process involves the generation and secretion of the cytokine, IFN-γ. The detection and subsequent quantification of IFN- γ forms the basis of this test.

The QuantiFERON®-TB Gold IT system uses specialized blood collection tubes, which are used to collect whole blood via venipuncture that contain antigens representing certain *M. tuberculosis* proteins or controls. Incubation of the blood occurs in the tubes for 16 to 24 hours, after which, plasma is harvested and tested for the presence of IFN- γ produced in response to the peptide antigens.

Notes:

1. A negative result does not preclude the possibility of *M. tuberculosis* infection or tuberculosis disease. False negative results can be due to stage of infection, co-morbid conditions which affect immune function, or other individual immunological factors.

2. A positive result should not be the sole or definitive basis for determining infection with *M. tuberculosis.* The result should be followed by further medical evaluation for active tuberculosis disease.

3. The effect of lymphocyte count on reliability of QuantiFERON®-TB Gold IT results is unknown. Lymphocyte counts may vary over time for any individual and from person to person. The minimum number of lymphocytes required for a reliable test result has not been established and may also be variable.

4. The predictive value of a negative result in immunosuppressed individuals has not been determined.

5. The rate of people not responding to the Mitogen Positive Control (i.e. indeterminate result) in the QuantiFERON®-TB Gold IT assay depends on the population group being tested. In population groups where varying levels of immunosuppression may be expected, indeterminate results are encountered at a commensurate rate. Examples of people who may be unresponsive are as follows:

    - For healthy, apparently immunocompetent people (low TB risk, healthcare workers, etc.) the rate of Indeterminate results in the QuantiFERON®-TB Gold IT assay is very low (0 to 0.3%), and possibly reflects the very low number of technical errors encountered with this assay.
    - QuantiFERON®-TB Gold IT provides valid results in HIV positive patients, but in those with a CD4 count less than 100, Indeterminate results are more likely.
    - In renal dialysis patients, who are commonly suffering from immunosuppression, valid results are obtained in more than 93% of cases.
    - Indeterminate results are uncommon in patients with rheumatological disorders, and QuantiFERON®-TB Gold IT performs well in patients undergoing therapy with corticosteroids and other anti-rheumatic drugs.
    - Patients undergoing treatment with anti-TNF-α therapies are more likely to be QuantiFERON®-TB Gold IT Indeterminate. However, the test works well in these patients prior to the use of the anti-TNF-α therapies, when a test for tuberculosis infection is most needed.
    - Severe immunosuppressive therapies, such as chemotherapy for cancer result in a high rate of indeterminate results – as should be expected.
    - Indeterminate results are significantly associated with 0mm TST responses – strongly confirming the fact that the TST does not work well in people with immunosuppression, but unlike QuantiFERON®-TB Gold IT, the TST does not control for immune status.

6. The Mitogen Positive Control provides a major benefit over the TST in the screening of people with possible immunosuppression for *M. tuberculosis* infection. A negative TST in a person who is immunosuppressed is of no value as it is uninformative as to the true infection status of the individual. In contrast, an Indeterminate QuantiFERON®-TB Gold IT response informs the healthcare provider that there may be an underlying reason for immunosuppression in their patient and that the true status of *M. tuberculosis* infection cannot be ascertained by the test (and is also unlikely to be obtained with the TST).