

QuantiFERON®-TB Gold In-Tube Method

FOR USE IN THE DIAGNOSIS OF LATENT MYCOBACTERIUM TUBERCULOSIS INFECTION

Test Highlights

- Whole-blood assay measures IFN- γ production in patients who are sensitized to TB antigens.
- May be used in *all* circumstances in which the tuberculin skin test (TST) is currently used.
- May be used in contact investigations, evaluation of recent immigrants who have had BCG vaccinations, and TB screening of health care workers.
- Only requires a single patient visit to draw a blood sample.
- Collection-to-specimen processing time extended to 16 hours.
- Specimen stability, after incubation and centrifugation, is two weeks refrigerated.

Clinical Background

- TB is a communicable disease caused by *Mycobacterium tuberculosis* (*Mtb*). It is spread primarily by airborne particles (droplet nuclei) expelled by an individual with infectious TB.
- Persons who have latent tuberculosis infection (LTBI) are infected but do not have TB disease. They are asymptomatic and not infectious.
- About 10 percent of persons with LTBI will develop TB disease at some time in life, but the risk is considerably higher for individuals who are immunosuppressed, especially those with HIV infection.

Disease Overview

- TB disease most commonly affects the lungs; 73 percent of TB cases are exclusively pulmonary.
- Patients with active pulmonary TB usually have a cough and an abnormal chest radiograph, and are likely to be infectious.
- TB may also occur as a pleural effusion, or as an infection of the central nervous system, lymphatic system, genitourinary tract, bones and joints, or as disseminated disease (military TB).
- Extrapulmonary TB is more common in immunosuppressed persons and in young children.

Epidemiology

- TB is the number one microbial killer in the world, causing nearly two million deaths per year.
- Over one-third of the world's population has been exposed to TB.
- Seventy-five percent of all *Mtb* infection occurs in developing countries.
- Foreign-born persons and racial/ethnic minority populations continue to be affected disproportionately by TB in the United States at a rate of 9.5 times that of U.S.-born persons.

Pathophysiology and Immunology

- The immune response to a TB infection is primarily cell-mediated.

- Part of the immune response results from the sensitization of T-cells to TB antigens.
- The T-cells retain "memory" to the TB antigens and, when stimulated (i.e., by the PPD skin test or recombinant TB antigens in the *in vitro* test), produce the TH1 type cytokine interferon gamma (IFN- γ).
- The humoral immune response (antibodies to TB antigens) will be activated when the mycobacterial load reaches a critical mass. Production of antibodies to TB antibodies occurs very rarely, but the presence of these antibodies can predict which exposed patients are likely to have or to advance to active disease.

Indications for Ordering

- Order QuantiFERON®-TB Gold In-Tube (QFT-In Tube) if latent TB infection is suspected. A diagnosis of LTBI requires that active TB disease be excluded by medical evaluation, which should include a thorough history and physical exam, a chest X-ray, and, when indicated, TB antibody testing and/or the examination of specimens for *M. tuberculosis*.
- QFT-In Tube may be used in *all* circumstances in which the tuberculin skin test (TST) is currently used.
- QFT-In Tube may be used in contact investigations, evaluation of recent immigrants who have had BCG vaccinations, and TB screening of health care workers.

Interpretation

- Interpretation of the QFT-In Tube results is based on IFN- γ concentrations in test samples.
- Each QFT-In Tube result and its interpretation should be considered, in addition to other epidemiological, historical, physical, and diagnostic findings.
- A positive result suggests that exposure to *Mtb* is likely; a negative result suggests that exposure is unlikely.
- An indeterminate result indicates that the QFT-In Tube test cannot be interpreted as a consequence of low mitogen response (due to improper handling of specimen, low T-cell numbers, or immunosuppression) or high background (IFN- γ) response (due to recent viral infection or vaccination).

Limitations

- There is limited data on the use of QFT-In Tube to determine who is at risk for developing active disease. TB antibody testing, in addition to AFB culture, may be helpful for determining which exposed patients are likely to have or develop active disease.
- Errors in collecting, processing, or transporting blood specimens can decrease the accuracy of QFT-In Tube.

Additional Ordering Notes

Handling of the blood specimen by the client site

- Please note: Accuracy of the test relies on proper collection and incubation of the blood specimen. The test relies on maintaining the viability of the T-cells and measuring their response to the TB antigens.
- STAGE 1: COLLECTION BY PHLEBOTOMY AT CLIENT SITE
 - Collect 1 mL of patient blood into each of three specialized blood-collection tubes (nil control tube [grey cap], mitogen control tube [red cap], and TB antigen tube [purple cap]). (ARUP Supply # 45112)
 - Immediately following collection, each specimen tube must be mixed vigorously by shaking the tubes vigorously up and down 10 times to ensure that the entire inner surface of the tube has been coated with blood. (Proper mixing is needed to allow T-cells to contact antigen.)
- STAGE 2: SPECIMEN PROCESSING AT CLIENT SITE
 - After mixing and within 16 hours of collection, incubate tubes upright in a 37°C incubator for 16 to 24 hours. (Incubation is needed to allow memory T-cells to respond to the TB antigen.)

- After incubation, centrifuge tubes for 15 minutes at 2,000 to 3,000 RCF (g) to separate the plasma and the red cells.
- Transport original collection tubes, after incubation and centrifugation, at 2°C to 8°C.

Methodology

- Patient blood is collected into three specialized blood-collection tubes.
- The amount of INF- γ produced by each tube (nil, mitogen, antigen) is measured using a standard ELISA format.
- QFT-In Tube results are based on the amount of INF- γ that is released in response to the antigen and are reported as positive, negative, or indeterminate.

Related Tests

- AFB Culture (Includes AFB Stain [0060151](#)), ([0060152](#))
- *Mycobacterium tuberculosis* Antibody, IgG by ELISA ([0051698](#))

References

1. Carvalho AC, et al. QuantiFERON®-TB Gold test in the identification of latent tuberculosis infection in immigrants. *J Infect* 2007;55(2):164–8.
2. Mazurek GH, et al. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR Recomm Rep* 2005;54:49–55.
3. Gennaro ML, et al. Antibody markers of incident tuberculosis among HIV-infected adults in the USA: a historical prospective study. *Int J Tuberc Lung Dis* 2007;11(6):624–31
4. Kanaujia GV, et al. Integration of microscopy and serodiagnostic tests to screen for active tuberculosis. *Int J Tuberc Lung Dis* 2005;9:1120–6.

Test Information

0051729

QuantiFERON®-TB Gold In Tube

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.