What is the Optimal Test for Diagnosis of Latent Tuberculosis?

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This is an Editorial for an article entitled "Diagnosis of latent TB infection in candidates for kidney transplantation (1)."

On May 2, 2005, a new in vitro test, Quanti-FERON®-TB Gold (QFT-G, Cellestis Limited, Carnegie, Victoria, Australia), received final approval from the U.S. Food and Drug Administration as an aid for diagnosing Mycobacterium tuberculosis infection (2).

As interferon gamma (IFN-γ) plays a critical role in regulating cell-mediated immune responses to M. tuberculosis infection led to development of interferon gamma release assays (IGRAs) for the detection of M. tuberculosis infection (3), and This test detects the release of interferon-gamma (IFN-g) in fresh heparinized whole blood from sensitized persons (4).

Tuberculin skin testing (TST) has been used for years as an aid in diagnosing latent tuberculosis infection and includes measurement of the delayed type hypersensitivity response 48-72 hours after intradermal injection of PPD.

Clinical evaluation and additional tests (chest radiograph, sputum smear, and culture) are needed to differentiate between a diagnosis of latent tuberculosis (TB) or active TB.

Advantages of the QuantiFERON®-TB Gold test are:

- Requires a single patient visit to draw a blood sample.
- Results can be available within 24 hours.
- Does not boost responses measured by subsequent tests, which can happen with tuberculin skin tests.
- Is not subject to reader bias that can occur with TST.
- Is not affected by prior BCG (bacille Calmette-Guérin) vaccination.

Disadvantages and limitations of the Quanti-FERON®-TB Gold test are:

- Blood samples must be processed within 12 hours after collection while white blood cells are still viable.
- There are 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 /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.
- False positive results can occur with Mycobacterium szulgai, Mycobacterium kansasii, and Mycobacterium marinum (4).
- Finally its price that is, relatively high.
- Assessments of accuracy of tests for M. tuberculosis infection are difficult because there is no “gold standard” to confirm a diagnosis of LTBI (5).
- Both tests TSTs and IGRAs are indirect tests that measure immunologic responses and are not direct tests that detect the causative organism or components of the organism
- Agreement in these tests has been affected by test interpretation criteria, prevalence of infection and the proportion of infections that are confirmed microbiologically, estimates of recent and remote exposure, age, race, prior BCG vaccination, recent TST, and coexisting diseases, and conditions with immunosupression (6).
- Additional studies examining the effect of PPD injection on IFN-γ responses are needed to define the frequency, magnitude, induction time, and longevity of IGRA boosting following a TST (6,7).
- The cost for an IGRA is greater than TST, cost-effectiveness studies are limited by the lack of critical data on the relative ability of these tests to predict subsequent disease (8).

Both tests show us latent tuberculosis but in persons with discordant test results (one positive and the other negative), As we can see the this article overall agreement between QFT and TST was 75%, the others (25%) have discordant test. As we haven’t any gold standard for latent TB, the best decisions is clinical judgment.

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The most important Questions are:

- Are QuantiFERON®-TB Gold better at predicting subsequent active tuberculosis than TST?
- Are persons with discordant TST and Quanti FERON®-TB Gold results at increased risk for active tuberculosis compared with persons with concordant negative results?
- For the tuberculin skin test, conversion is defined as an increase in induration of 10 mm or more,what is no definition of conversion for QuantiFERON®-TB Gold?

The best assessment for these question is to have a gold standard test for tuberculosis infection.

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