A Clinician’s Perspective: Using the T-SPOT®.TB Test to Screen Rheumatology Patients for TB

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INTRODUCTION
Biologic-targeted suppression of key inflammatory pathways for the treatment of patients with rheumatoid arthritis (RA) has been beneficial to managing this condition. Management, however, must be balanced with the patient’s risk of infection from other diseases, such as tuberculosis (TB).

Reactivating TB continues to be a serious concern for RA patients. RA patients are at an increased risk of developing TB while on tumor necrosis factor (TNF) antagonist therapy because TNF plays a key role in keeping *Mycobacterium tuberculosis* (MTB) in granulomas and sufficiently suppressing the MTB to maintain the latent tuberculosis infection (LTBI) state. Thus, identifying patients with LTBI and prophylactically treating them before starting anti-TNF-α treatment is critical to reducing the patient’s risk for active TB while being immunosuppressed.

For more than 100 years, the tuberculin skin test (TST) has been used to detect LTBI; however, emerging data indicate that false-negative results are higher for patients who are on immunosuppressive therapies or who have defective cutaneous cell-mediated immunity. In addition, false positives may result from previous administration of the bacille Calmette-Guérin (BCG) vaccine and common non-tuberculosis mycobacteria such as *M. avium*. New tests known as interferon gamma release assays have been developed which address the issues associated with the TST.
WHAT IS AN IGRA?

Interferon gamma release assays (IGRAs) are in vitro blood tests for TB infection. These tests detect cell-mediated immune responses to *Mycobacterium tuberculosis* (MTB) antigens. IGRAs provide an objective measurement of the patient’s T cell response, as compared to the subjectivity of the TST.

While two commercially available IGRAs are currently FDA-approved, only the T-SPOT.TB test addresses the different immune statuses of patients. The T-SPOT.TB test isolates peripheral blood mononuclear cells (PBMC) from the patient’s blood sample and uses a standard number of PBMCs in the assay to directly measure the secretion of interferon-γ (IFN-γ), the immune response to infection with MTB. The T-SPOT.TB test uses two antigens that are specific to MTB: ESAT-6 and CFP10. Importantly, these antigens do not cross react with BCG or most common environmental mycobacteria; therefore, BCG vaccination status of the patient and exposure to nontuberculosis mycobacteria do not affect the T-SPOT.TB test results.

IGRAs eliminate the multiple visits required by the TST as they require only one patient visit for the blood draw. According to the Centers for Disease Control\(^5\) (CDC), “As laboratory-based assays, IGRAs are not subject to the biases and errors associated with TST placement and reading.” In addition, unlike the TST, IGRAs cannot boost subsequent IGRA tests.

In 2010 the CDC issued updated guidelines for IGRAs that recommend the T-SPOT.TB test in all situations that require TB testing. The guidelines state that the T-SPOT.TB test is preferred over the TST for those individuals who had received a BCG vaccine.

HOW DOES THE TEST WORK?

A standard number of PBMCs in combination with ESAT-6 and CFP10 are added to the wells of microtiter plates that are coated with high-affinity antibodies to IFN-γ. Activated effector T cells secrete IFN-γ in response to the specific antigens. The IFN-γ is captured by the IFN-γ antibodies coated within the well. After removal of the T cells and antigens, conjugated second antibody followed by a substrate are added to produce spots where IFN-γ was secreted by the T cells. Thus, the number of spots provides a measure of the abundance of MTB–sensitive effector T cells.\(^6\)
THE BENEFITS OF USING THE T-SPOT.TB TEST IN OUR RHEUMATOLOGY PRACTICE

Dr. Robert Jenkins is a board-certified rheumatologist and one of 11 physicians in practice at Rheumatology Associates, located in Dallas, Texas. Of the 120 patients he generally sees in a week, 10 are typically referred for tuberculosis screening. A year ago, he started using the T-SPOT.TB test to screen his patients before starting them on TNF blockers. He describes his experience using the T-SPOT.TB test:

"I started looking into an alternative to the TST because after reading TST results for over 30 years, I know they are hard to interpret. I think the diameter of the induration is not nearly as definitive as we all pretend. So, I was happy to have a different technology. As I learned about the T-SPOT.TB test, I was impressed by how convenient it was, and that convenience, in my mind, has improved patient care in my practice.

"Collecting the testing sample is very straightforward. We draw blood right in our office, ship it overnight to the Oxford Diagnostic Laboratory in packaging they provide, and then receive the results in 36 to 48 hours via fax. With the TST, many patients would not return to have their results read, so my staff was spending a lot of time reminding patients and trying to track them down to read their results. If patients did return to have their results read, many times they were coming without an appointment, so the nurses were being interrupted throughout the day to read the results, and the doctors had to make time to talk with patients who returned with a positive TST. The system was just a pain. Now the staff really appreciates that it only takes one visit for patients to get tested—it’s just like every other blood test.

"I like that the T-SPOT.TB test results are objective, rather than the subjective results we got with the TST. I get a numerical result, as well as a positive, borderline, or negative reading from the T-SPOT.TB test. With the TST, studies have shown that the results vary based on who reads the results, so I never had much confidence in the results, especially if I wasn’t there to see the reaction myself. Knowing the results with the T-SPOT.TB test are objective gives me a confidence boost—I just think it’s a better test.

"And because the test is so much more convenient, we are testing patients more frequently, so we’re going to find more of these people who have latent tuberculosis or have acquired it, and hopefully catch them before anything happens. On average, I test patients on biologics therapy every 2 to 3 years, and test more frequently if they travel to areas where
tuberculosis is more common. We didn’t do this frequency of testing with the TST because it was too inconvenient. We typically tested them at the start of therapy and often didn’t do it again, which concerned me.

“Overall, I am really happy with my experience using the T-SPOT.TB test over the past year. My staff appreciates the convenience, I have more confidence in the results, and it has enhanced our overall patient care.”

REFERENCES


