New Tests on the Horizon to Detect Latent TB

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KEYSTONE, COLO. — New tests that detect latent tuberculosis infection by quantifying interferon-γ released from sensitized lymphocytes in whole blood may be a big step toward the elimination of TB, Dr. Charles Daley said at a meeting on allergy/clinical immunology, asthma, and pulmonary medicine.

This class of tests, called in vitro T-cell–based interferon-γ release assays (IGRAs), is the first replacement for the flawed tuberculin skin test, which has been in use in one form or another for a century.

"We absolutely can and must replace the tuberculin skin test, and the reason we can is because of these specific mycobacterium tuberculosis antigens, ESAT-6 and CFP-10," Dr. Daley said at the meeting, sponsored by the National Jewish Medical and Research Center.

The first replacement for the tuberculin skin test in a century, Quantiferon-TB (Cellestis), was approved by the Food and Drug Administration in 2001.

A version called Quantiferon-TB Gold In-Tube, which should be available this summer, will allow the drawing of blood directly into tubes containing the antigens, said Dr. Daley, who is head of mycobacterial and respiratory infections at National Jewish, Denver.

Another impending test is T-Spot.TB (Oxford Immunotec Ltd.), which detects or spots individual T cells, and can be used for the diagnosis of latent disease simply by detecting the presence of an effector T-cell response.

A major advantage of these new tests is that they avoid false-positive results caused by previous inoculation with the BCG vaccine, which is widely used outside the United States and is a critical factor in the screening of foreign-born individuals.

"Over time, this cross reactivity has led to a distrust of the skin test in vaccinated people, many of whom can't remember when or even if they received BCG," Dr. Daley explained.

Dr. Daley, who consults for both companies, said that IGRAs are more sensitive and specific than the tuberculin skin test, and that the T.Spot-TB is more sensitive than Quantiferon-TB while Quantiferon-TB is more specific.

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DR. DALEY

Both IGRAs correlate with exposure better than does the tuberculin skin test, and may be more cost effective as well, he explained.

In addition, IRGAs require only one patient visit, assess responses to multiple antigens simultaneously, do not boost anamnestic immune responses, provide results within a day, and greatly reduce interreader variability.

A prospective study of 393 consecutively enrolled patients with latent tuberculosis infection or suspected TB looked at agreement between the tuberculin skin test and both interferon-γ release assays, and found that indeterminate results were more common with Quantiferon-TB than with T-Spot.TB, particularly in young children and those who were immunocompromised (Lancet 2006;367:1328-34).

"We still need to study more populations to optimize sensitivity and specificity in these IRGA tests. I'm not convinced that the cut-points currently recommended by the companies are appropriate, and we need to know how these are going to work in the immunocompromised and in young children.

"There aren't enough data to guide us in these areas, so most people are kind of holding off on using these new assays," Dr. Daley said.

In addition, more needs to be learned about using IRGAs for serial testing. To that end, Dr. Daley and others are launching a four-center U.S. study of 3,000 health care workers who will be tested every 6 months with skin tests and both IRGAs.

Meanwhile, Dr. Daley and his colleagues at National Jewish are using Quantiferon-TB Gold and will begin using T-Spot.TB this summer. ■