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# Tuberculosis

Tuberculosis (TB) is a disease caused by *Mycobacterium tuberculosis*. It occurs most often in people with compromised immune systems and in people who weren't born in the United States or their close family contacts. It most commonly affects the lungs, but it can also occur in other sites. Extrapulmonary TB is usually not infectious, but pulmonary TB usually is. TB occurs as a latent infection or an active disease.

## Latent Tuberculosis Infection

In the first weeks or months after exposure, most (>90%) people mount a granulomatous immune response. This controls bacterial replication and results in latent TB infection (LTBI). People with LTBI:

- Are asymptomatic
- Aren't contagious
- Usually test positive with a TB skin test or interferon-gamma release assay (IGRA) blood test
- Usually have a normal chest x-ray and negative sputum smear or culture
- Can be treated to substantially reduce the risk of developing active disease

## Tuberculosis Disease

When bacteria overwhelm the immune system, active disease develops. Anyone with LTBI can develop active disease. But people who were recently infected (in the previous 2 years) are at increased risk. People with weakened immune systems are at especially high risk. Other factors that increase risk include<sup>1</sup>:

- Age <5 years
- HIV infection (CD4 count <200)
- Some immunosuppressive medicines including biologics or antibodies used to treat autoimmune conditions
- Certain conditions, eg, silicosis, diabetes, chronic renal failure, leukemia, lymphoma, and cancer of the head, neck, or lung
- Gastrectomy or jejunioileal bypass
- Being underweight (less than 90% of ideal body weight)
- Smoking
- Drug and/or alcohol abuse



## Symptoms of Tuberculosis Disease

Most people with TB disease have 1 or more of these general symptoms:

- Weakness or fatigue
- Weight loss
- Loss of appetite
- Chills
- Fever
- Night sweats

Symptoms of pulmonary TB include:

- Coughing for 3 weeks or longer
- Chest pain
- Coughing up blood

Symptoms of extrapulmonary TB depend on the part of the body that is affected. For example:

- TB of the spine may cause back pain.
- TB of the kidney may cause blood in the urine.
- TB meningitis may cause headache or change in mental status.

# Tuberculosis

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### People Who Should Be Screened

Testing is appropriate for people who are at increased risk of infection or progression to TB disease if they are infected. In addition to those who have a risk factor listed above, this includes people who<sup>1,2</sup>:

- Have had close contact with someone who has TB disease
- Are from a country or have visited areas where TB disease is very common<sup>a</sup>
- Live or work where TB disease is more common (homeless shelters, jails, nursing homes)
- Are hospital healthcare workers
- Are other healthcare workers who work closely with those at increased risk of TB disease
- Are infants, children, or adolescents exposed to adults who are at increased risk of TB

<sup>a</sup> Includes most countries in Latin America, the Caribbean, Africa, Asia, Eastern Europe, and Russia.

People with symptoms of TB disease should also be tested.

### Diagnosis of Latent Tuberculosis Infection

TB skin tests and IGRA blood tests are indirect indicators of infection. So diagnosis should not be based on these screening tests alone. People with a positive screen should be evaluated for:

- Risk of TB infection (ie, epidemiologic and medical history)
- Risk for progression to active TB if infected
- Symptoms and signs of active disease

When the TB screen is positive and the person is asymptomatic, additional testing should be done to rule out active disease. This should include a chest x-ray and may also include sputum culture or DNA-based (PCR) testing.<sup>3</sup>

A negative chest x-ray in an asymptomatic person most likely rules out TB disease.<sup>1</sup> If the follow-up tests are negative and the person has a low likelihood of TB, the screening test may be a false-positive.<sup>1</sup> A false-positive result is much more likely with a skin test than an IGRA (see sidebar).<sup>1</sup> On the other hand, if the person has negative follow-up tests and a high risk for TB, he/she may have LTBI.<sup>1</sup>

### Tuberculosis and BCG Vaccination

Bacille Calmette-Guerin (BCG) is a TB vaccine that is used in many countries. It isn't used in the United States, and it doesn't completely prevent people from getting TB. It may cause a false-positive TB skin test. This is because the skin test and the BCG vaccine may contain some of the same *M tuberculosis* proteins. People who have had the BCG vaccine may already have antibodies against the proteins. So they may react to the skin test even though they don't have latent or active TB.

IGRA blood tests aren't affected by BCG vaccination and won't give a false-positive result in people who have received BCG.

### Diagnosis of Tuberculosis Disease

A positive TB skin test or IGRA blood test in a symptomatic person is likely to be diagnostic.<sup>1</sup> Confirmation with sputum culture and/or DNA-based testing, however, is recommended.

### Tuberculosis Testing

There is no perfect test for TB infection. Two tests in common use are:

- TB skin test
- IGRA blood test

IGRAs have a significantly higher specificity than does the skin test.<sup>4</sup> False-positive results in the skin test may be caused by prior vaccination with bacille Calmette-Guerin (BCG) (see sidebar).<sup>2</sup> They may also be caused by a reaction to mycobacteria in the environment.<sup>1</sup>

Both tests have limitations. Neither can differentiate between LTBI and active disease. And a negative result with either test doesn't exclude the possibility of LTBI or active disease. This is particularly true in patients with symptoms or other evidence of active disease and in patients at high risk of a poor outcome if disease develops.

IGRAs are preferred for people who<sup>2</sup>:

- Have received the BCG vaccination (see sidebar)
- Can't or aren't likely to return 2 to 3 days later to have a skin test read by a trained healthcare worker

Guidelines state that the skin test is preferred in children younger than 5 years of age.<sup>1</sup> However, data in this age group is limited and expert opinion varies.<sup>5</sup> Some pediatric infectious disease specialists do use IGRAs for their patients 2 years of age or older.

### How the Lab Can Help

Quest Diagnostics offers QuantiFERON®-TB Gold, an IGRA. Quest also offers acid fast bacilli smears, mycobacterial culture and sensitivity tests, and DNA (PCR-based) tests. For more information about these, visit the Quest Diagnostics' [Test Center](#).

### References

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5. Starke JR; Committee On Infectious Diseases. Interferon-γ release assays for diagnosis of tuberculosis infection and disease in children. *Pediatrics*. 2014;134:e1763-e1773.