## Clinical



# Clinical Review of Current Best Practices for Tuberculosis Screening, Testing, and Treatment in the Urgent Care Setting

**Urgent Message:** Patients may present with needs surrounding tuberculosis (TB) screening, testing, and treatment to urgent care centers. There is considerable nuance in the approach to these scenarios with consequences for both patient and public health. Urgent care centers should develop clear guidelines for ensuring clinicians select the appropriate TB test for each patient and interpret the results accurately.

Erin Loo, PA-C; Lindsey E. Fish, MD

**Citation**: Loo E., Fish LE. Clinical Review of Current Best Practices for Tuberculosis Screening, Testing, and Treatment in the Urgent Care Setting. *J Urgent Care Med.* 2025; 19(5): 17-25

### Introduction

uberculosis (TB) is caused by infection by the bacteria *Mycobacterium tuberculosis*. Clinically, TB can present in 2 patterns: TB disease and latent TB infection (LTBI).

- 1. TB disease is defined as a symptomatic infection with characteristic and suggestive findings based on the anatomic site of infection. For example, pulmonary TB disease often presents with a combination of cough, fever, night sweats, and changes on chest radiography (CXR).
- 2. Latent TB Infection, in contrast, is defined as an asymptomatic infection with *M. tuberculosis*. However, these patients harbor viable organisms and are at risk for developing symptomatic infections (ie, *TB disease*) in the future. These patients are not contagious and cannot spread TB to other people.<sup>1</sup> Understanding these definitions is a critical first step



Author affiliations: Lindsey E. Fish, MD, Denver Health, Department of General Internal Medicine, Denver, Colorado; University of Colorado School of Medicine, Department of Medicine, Division of General Internal Medicine, Aurora, Colorado. Erin Loo, PA-C, Integrity Urgent Care, College Station, Texas. Authors have no relevant financial relationships with any ineligible companies.

Table 1. Tuberculin Skin Testing Interpretation			
Induration Greater Than or Equal to 5mm	Induration Greater Than or Equal to 10mm	Induration Greater Than or Equal to 15mm	
Measured induration of 5mm or more considered positive for the following populations: • HIV+ • Recent contacts of people with infectious TB disease • Fibrotic changes on CXR • History of organ transplant • Immunocompromised, including patients on prolonged corticosteroids equivalent to or greater than 15mg of prednisone per day, and those on anti- TNF agents	<ul> <li>Measured induration of 10mm or more considered positive for the following populations:</li> <li>Born in a country with high prevalence of TB (eg, Latin America, the Caribbean, Africa, Asia, Eastern Europe, and Russia)<sup>3</sup></li> <li>Drug or alcohol misuse</li> <li>Handling mycobacteria in a lab</li> <li>Residence in a congregate living setting (eg, nursing home, correctional facility, or shelter)</li> <li>Medical conditions that increase risk for TB (eg, diabetes mellitus; severe kidney disease; silicosis; cancer of the head, neck, or lung; and patients with history of gastrectomy or jejunoileal bypass surgery)</li> </ul>	Measured induration of 15mm or more is always considered positive	

when TB testing is considered or ordered. Importantly, the terminology around tuberculosis has been updated, and therefore, older publications may use the historic terminology. These terminology changes occurred in 1999 when the American Thoracic Society updated its guidelines.<sup>2</sup> TB disease was previously referred to as "active TB" and LTBI was called "latent TB" or "TB infection." Likewise, the terms for LTBI treatment were updated from "preventive treatment" to "treatment of LTBI."<sup>2</sup>

#### **Tuberculosis Burden**

Tuberculosis remains a leading cause of morbidity and mortality worldwide with an estimated 13 million individuals in the United States currently infected with *M. tuberculosis.*<sup>3</sup> The Centers for Disease Control and Prevention (CDC) monitors TB in the United States, and more than 9,000 cases of TB disease were reported in 2023.<sup>4</sup> Approximately 5-10% of immunocompetent patients with LTBI will develop TB disease at some point in their lifetime, however, appropriate screening and treatment of LTBI is approximately 90% effective at preventing progression to TB disease.<sup>5</sup> The United States Preventive Services Task Force's (USPSTF) recommendations focus on the value of screening specific populations of asymptomatic adults to capture cases of LTBI and prevent progression to TB disease.<sup>3</sup>

#### **Epidemiology of Tuberculosis**

The prevalence and incidence of TB cases vary geographically within the United States with the highest levels occurring in New York, Florida, Texas, and California.<sup>6</sup> Nearly three-fourths of cases of TB disease in the United States occur in individuals born in another country, and most of these cases of TB disease result from progression of LTBI to symptomatic disease.<sup>7</sup> There are also significant ethnic disparities in the prevalence of TB with higher rates among Native Hawaiian, Pacific Islander, Asian, Native Americans, Alaskan Natives, Hispanic or Latino, and Black or African American patients.<sup>4</sup> Social determinants of health (SDoH) also play a strong role in the risk of LTBI and TB disease.<sup>3</sup>

Since 2020, after nearly 3 decades of decline, there has been a slight increase in cases and incidence rates.<sup>4</sup> This increase has been attributed to disruptions in TB surveillance and treatment during the COVID-19 pandemic as public health resources were reallocated to mitigate the spread of COVID-19.<sup>4</sup> Furthermore, the United States has also seen a dramatic increase in levels of immigration since pandemic lock-downs, which may be related to rising rates of TB.<sup>4</sup> In fact, 2023 saw the highest number of new TB disease cases the United States in over a decade (9,633 cases).<sup>4</sup> These trends underscore the importance of investing in robust TB surveillance programs. Given that urgent care (UC) is the first (and often only) contact with the healthcare system for many patients, we play a critical role in supporting these efforts.

Improving surveillance begins with an understanding of patients at increased risk for TB. Risk factors for LTBI and TB disease include:

- Those with known close contact with someone with TB disease
- Children <5 years of age (with confirmed exposure</p>

to TB disease; this population is also at higher risk of converting from LTBI to TB disease)

- Immigrants from areas of high prevalence
- People experiencing homelessness
- Intravenous drug users
- Patients with HIV infection
- Healthcare workers
- Residents in congregate living situations
- Those who work with high-risk populations
- Those with impaired immune systems due to conditions such as substance misuse, silicosis, diabetes mellitus, severe kidney disease, low body weight, organ transplant, malignancy and those using immunosuppressant medications (eg, high-dose chronic steroid use, tumor necrosis factor alpha inhibitors, biologic agents)<sup>8</sup>

#### Tuberculosis Signs and Symptoms: Distinguishing LTBI From TB disease

By definition, LTBI is asymptomatic. Importantly, those with LTBI also cannot spread the infection to others.<sup>5</sup> In contrast, patients with TB disease are symptomatic and contagious.<sup>1</sup> TB disease most commonly affects the lungs, and patients with pulmonary TB commonly experience prolonged cough (ie, >3 weeks in duration), chest pain, and/or hemoptysis.<sup>9</sup> Extrapulmonary TB disease symptoms may occur from infection of the pleura, lymph nodes, meninges, central nervous system (CNS), pericardium, and bone.<sup>10</sup> Other systemic symptoms include "B symptom" type complaints such as weakness, fatigue, weight loss, decreased appetite, fever, chills, and night sweats.<sup>9</sup>

#### Who Should Be Tested or Screened for TB?

The terms "screening" and "testing" are often used interchangeably, and the terms are not specifically defined in the literature. For purposes of this review, screening indicates evaluation and testing of asymptomatic patients for employment or other purposes. This is the type of patient visit most likely to occur in UC settings. Testing will be used to describe diagnostics used to evaluate patients who are either at-risk for LTBI, at risk for progression from LTBI to TB disease, or who are symptomatic with concern for TB disease.

The USPSTF and CDC recommend screening asymptomatic patients at higher risk *M. tuberculosis* infection or those at high risk of progression to TB disease (from LTBI) if infected with *M. tuberculosis*.<sup>3</sup> This involves risk assessment, symptom evaluation, and either tuberculin skin test (TST) or interferon-gamma release assay (IGRA).<sup>3</sup>

According to the CDC, patients with signs and symp-

toms suggestive of possible TB disease should be tested.<sup>9</sup> Conversely, screening for the general population is not recommended because of the risk and consequences of false positive test results.<sup>11</sup> The USPSTF has specific guidelines for populations at risk.<sup>3</sup> In the United States, a large proportion of TB screening encounters in UC are among healthcare workers or others with occupational health requirements for testing.

"By definition, LTBI is asymptomatic. Importantly, those with LTBI also cannot spread the infection to others."

## Screening Test Options for LTBI: 'The Skin Test or the Blood Test?'

Two screening test options for LTBI are available in the United States: the TST and the IGRA.<sup>1</sup> The TST, Mantoux test, and purified protein derivative (PPD) test all refer to TB skin testing, and the terms are often used interchangeably. The Mantoux test is an eponym for the physician who developed the skin testing technique used in TST; PPD refers to solution which is injected intradermally for a TST.<sup>12</sup> Both TST and IGRA tests are equivalent in assessing the future risk of TB disease, and selection should be determined by factors such as test availability, convenience, and cost.<sup>1</sup>

The TST involves injecting 0.1mL of tuberculin—a purified protein derivative of the bacteria that causes TB—intradermally (usually on the forearm) and measuring the length of induration (not erythema) after 48-72 hours.<sup>12</sup> Any reaction over 15mm is considered positive, however, reactions less than 15mm may also be positive based on individual risk factors.<sup>1</sup> Based on these accepted criteria/definitions, a 2023 systematic review found that the pooled sensitivity and specificity of the TST were between 60-80% and 90-95% respectively.<sup>7</sup>

While interpretation of the TST seems straightforward, there are common pitfalls to be aware of. To interpret a TST, the clinician must consider both the size of induration and the patient's risk of LTBI. When reading a TST, the response should be recorded in millimeters of induration rather than simply "positive" or "negative."<sup>1</sup> A response under 5mm is negative, and a result greater than or equal to 15mm is always positive, regardless of risk factors.<sup>1</sup> Patients with positive TSTs should be referred to the local public health department

TST Advantages	TST Disadvantages	
<ul> <li>No special equipment required</li> <li>Inexpensive (\$20)</li> <li>Long history of use in diagnosis of LTBI</li> <li>Well established criteria for skin test conversions</li> <li>Useful in serial testing</li> </ul>	<ul> <li>Requires trained staff</li> <li>Variability in administration and interpretation of results</li> <li>Requires 2 visits</li> <li>High rate of false positives</li> <li>Cross reactivity with BCG vaccine</li> <li>Low sensitivity if immunocompromised</li> </ul>	
IGRA Advantages	IGRA Disadvantages	
<ul> <li>More specific to <i>M. tuberculosis</i></li> <li>Only requires 1 visit</li> <li>Can be used in patients with history of BCG vaccination</li> <li>Results in 24 hours</li> <li>Not subject to bias in interpretation</li> <li>No booster phenomenon</li> </ul>	<ul> <li>Requires phlebotomy</li> <li>Specialized laboratory equipment needed</li> <li>No consensus on conversions for interpretation</li> <li>More costly (approximately \$85)</li> </ul>	

Table adapted from references 1,12,13

Cost data sourced from 2022 article regarding cost-utility in screening high risk populations, however, cost to patient may vary depending on clinic/lab location.<sup>14</sup> Booster phenomenon: When an initial TST is negative due to remote LTBI but follow up TST done within a year is positive. Initial TST "boosts" immune system to respond to the follow up TST and thus is considered a positive TST.<sup>1</sup>

for further assessment.<sup>1</sup> Any induration from 5-15mm in size requires more information about the patient's medical and social history to allow for appropriate interpretation. The risk factors to be considered when interpreting the TST are described in **Table 1**.

The IGRA is a blood test that measures antigens that are largely specific to the M. tuberculosis bacteria.13 The QuantiFERON-TB Gold In Tube and T-SPOT.TB test are the 2 most widely available FDA-approved IGRA blood tests for TB testing/screening used in the United States.<sup>13</sup> Because these tests measure an antibody-related immune response to M. tuberculosis, they are preferred for patients who have received the Bacillus Calmette-Guérin (BCG) vaccine, which is commonly used in countries outside of the United States.<sup>13</sup> Patients will typically have a positive IGRA test within 6-8 weeks of TB infection, however, IGRAs do not distinguish between LTBI and TB disease.<sup>13</sup> The 2023 systematic review of TB screening test characteristics found that IGRA had a pooled sensitivity and specificity of 80% and 95%, respectively-similar to that of TST.7 Additional advantages and disadvantages to this test are identified in Table 2.

#### Special Screening and Testing Considerations BCG Vaccination

While the BCG vaccine is not available in the United States, it is often administered in countries where TB infection is common.<sup>3, 12</sup> Individuals who have received the BCG vaccine are more likely to have false positive TSTs due to cross-reactivity.<sup>12</sup> Therefore, the CDC recommends to screen and test for TB using the IGRA in

such patients, however, TST is not strictly contraindicated in this population.<sup>5, 12</sup>

#### Healthcare Workers

According to the CDC, healthcare workers should be screened upon hire, but annual screening is only recommended if ongoing TB exposure is expected. Instead, individual risk assessments and TB questionnaires evaluating for signs and symptoms of TB should be used in lieu of an annual TB screening test.<sup>15</sup>

#### Immunocompromised Patients

Immunocompromised patients are at higher risk of progression to TB disease. This includes patients living with HIV, organ transplant, end stage renal failure on dialysis, cancer, and silicosis.<sup>16</sup> In addition, drugs that suppress the immune system are a risk factor for progression to TB disease, including tumor necrosis factor alpha (TNF) antagonists, biologics, steroids with daily dose of greater than or equal 15mg equivalent of prednisone, chemotherapy, and antirejection prophylaxis.<sup>16</sup> In addition to higher risk of progression to TB disease, immunocompromised individuals often will not mount enough immune response to TST or IGRA testing, leading to false negatives.<sup>16</sup> A taskforce with members from the CDC, the American Thoracic Society (ATS), and the Infectious Disease Society of America (IDSA) recommend repeat testing in this population because of high risk of progression from LTBI to TB disease.<sup>17</sup> This involves performing either TST or IGRA and doing a second test if the first test is negative.<sup>17</sup> Routine screening with both

modalities is typically not recommended outside of immunocompromised populations because of decreased specificity that results from this type of testing and risk of false positive.<sup>17</sup> Consider using both tests when the risk of a poor outcome is high if LTBI is missed, or if TB disease is suspected and first screening test is negative.<sup>1,17</sup>

#### **Common Causes for False Negative TST Results**

Given the variability in placement techniques, false negatives may occur with TST, even in appropriately selected patients. Errors in administration can lead to false negative results, such as a wheal not being formed.<sup>1</sup> Other scenarios where the TST may result in a false negative include exposure to TB <8 weeks prior, history of live virus vaccination in the previous month, concurrent viral or bacterial illness (specifically HIV, measles, mumps, typhus, and pertussis), and use of immunosuppressive drugs. IGRA testing would be more reliable for use with patients with these circumstances.<sup>1</sup>

#### **History of Prior Positive Screening TB Test**

Once a person has had a positive TB test—regardless of TST or IGRA use—neither TB screening test should be used for future assessments.<sup>15,17</sup> Patients should be reminded to maintain documentation of prior positive TB screening and any history of LTBI treatment to present if TB testing is required later.<sup>18</sup> In addition, serial CXR is not recommended in patients treated for LTBI. Instead, patients should monitor for symptoms of TB disease.<sup>18</sup> Healthcare workers with previous positive TB testing but no LTBI treatment should have annual TB disease symptom screening and consider risks/benefits of treatment.<sup>17</sup>

#### **Clinical Scenarios and Discussion**

Editor's Note: All clinical case scenarios in this article are hypothetical.

**Case 1:** A 46-year-old man who works as a laboratory technician presented for a mandatory pre-employment TB screening test. He had a past medical history of LTBI, which was treated appropriately with isoniazid (INH). He was tested with IGRA for the employment screening, and the result was positive. Subsequently, the patient was referred to the health department for further evaluation.

- Case Analysis: In this case, this patient has had a previous positive test. Patients with a history of a positive TST or IGRA should not have either test used for subsequent TB screening.<sup>15</sup>
- Discussion: Unfortunately, there is little consensus or guidance in the existing literature for monitoring patients with a history of a previous positive TB test

and/or those who have been treated for LTBI or TB disease. The use of TB screening tests and/or annual CXR are specifically not recommended.<sup>15</sup> Instead, risk assessments and symptom checklists are pre-ferred.<sup>15</sup> If the patient is a healthcare worker, a baseline assessment tool should be completed upon hire. The Texas Department of Health and Human Services has a baseline assessment tool for healthcare personnel that can be used in this setting.<sup>19</sup>

"The diagnosis of TB disease is based on clinical judgment and expertise, as there are no diagnostic criteria to diagnose this condition definitively."

**Case 2:** A 4-year-old girl presented for TB screening as part of a physical examination for her visa application. She was born in a country with a high prevalence of TB disease and her parent reported that she received the BCG vaccination. The clinician performed a TST. On follow-up, 20mm of induration was noted, and the patient was referred for a CXR, which was normal.

- Case Analysis: While the TST is the preferred test in children <5 years old, the IGRA test would have been more appropriate in this situation because the TST is not recommended in patients who have received the BCG vaccination.<sup>13</sup>
- Discussion: TST is not contraindicated in patients with a history of BCG vaccine, but clinicians should be aware of increased risk of false positives. Because of this, the CDC recommends IGRA in this population.<sup>12,13</sup>

**Case 3:** A 19-year-old man presented for TB screening prior to incarceration in the county jail. A TST was placed, but the patient failed to return in 72 hours for evaluation. The patient had to pay a fine for failure to present for TB screening results, and booking into county jail was delayed until another TST could be performed.

- Case Analysis: IGRA testing is a much more practical option for patients with logistical issues complicating 48-72 hour follow-up, as was the case with this patient.
- Discussion: As both the TST and IGRA tests have similar test characteristics, other patient factors, like cost and the ability to return for a second visit,

Table 3. High Risk Factors for Tuberculosis Exposure and Progression of Disease		
High Risk of TB Exposure	High Risk of Progression to TB Disease	
<ul> <li>Contacts of patients with TB disease</li> <li>People born in or living in countries where TB is common<sup>23</sup></li> <li>People living in congregate settings where TB is more common, such as correctional facilities or homeless shelters</li> <li>Employees of congregate living settings</li> <li>Healthcare workers caring for TB patients</li> </ul>	<ul> <li>People living with HIV/AIDS</li> <li>Children &lt;5 years of age</li> <li>People with TB infection less than 2 years prior</li> <li>Patients who are Immunosuppressed, such as those on TNF antagonists, chronic steroids, or following organ transplant</li> <li>Intravenous drug users</li> </ul>	
Table adapted from reference 11	L	

should be considered when selecting the best test. Given the frequency of TB screening related visits in UC, centers should develop guidelines for clinicians with clear inclusion and exclusion criteria for each test to ensure uniformity of practice.

#### **Diagnosis of LTBI and TB Disease**

The diagnosis of TB disease is based on clinical judgment and expertise, as there are no diagnostic criteria to diagnose this condition definitively. All patients with a positive TST (depending on underlying patient characteristics) or positive IGRA test should be evaluated to determine what the positive test represents (ie, LTBI, TB disease, previously treated LTBI, previously treated TB disease, or history of BCG vaccine).

When clinical symptoms prompt clinicians to rule out TB disease, a detailed history and physical evaluation must be performed. Additional confirmatory testing is typically indicated. For pulmonary TB disease, this may include sputum acid fast bacilli (AFB) smears, sputum nucleic acid amplification testing (NAAT), and sputum TB culture (the gold standard microbiologic test for TB disease).<sup>11</sup> Of note, a CXR should be performed on patients with suspected TB disease.<sup>20</sup> CXR is most commonly normal, yet additional CXR findings may include hilar/mediastinal lymphadenopathy (15%), pleural effusion (3%), and segmental or lobar pulmonary consolidation (frequently in the upper lobes) (20%-40%).<sup>4,21</sup> For extrapulmonary TB disease with a fluid source (ie, pleural, cerebrospinal fluid, peritoneal, pericardial), suggested testing includes cell count, chemistries, adenosine deaminase levels, Interferon-gamma, AFB smears, NAAT, and TB culture. For extrapulmonary TB disease with a solid source (bone, lymph node), suggested testing includes histological exam (ie, biopsy) and TB culture.<sup>10,22</sup>

The risk of progression to TB disease is greatest in the first 2 years after infection and among those with underlying immunosuppression.<sup>11</sup> LTBI screening should be done for before patients are started on immunosup-

pressive therapies such as TNF antagonists, systemic corticosteroids (equivalent to/greater than 15 mg of prednisone per day), or immunosuppressive drug therapy following organ transplantation.<sup>11</sup>

#### **Treatment for LTBI and TB Disease**

The CDC advises against screening or testing patients for TB if adequate follow-up cannot be assured.<sup>11</sup> As such, it is critical that UC clinicians have a relationship with local public health departments that can facilitate further evaluation and treatment. If a patient presents with clinical signs or symptoms of TB disease, the patient should be placed in a surgical mask and transferred to the local emergency department (ED) for further medical evaluation.<sup>11</sup> If a patient is not clinically ill but there is suspicion for TB disease or LTBI, they should be placed in a mask and referred to the local public health department, following local guidelines.<sup>11</sup>

When considering LTBI and TB disease, patients can be divided into 2 related categories: those with a high risk of exposure to TB; and those at high risk of progression to TB disease once infected. Testing and treatment should be tailored based on the patient's risk for exposure and/or disease progression. If a patient is in neither category, and therefore low-risk for having LTBI or TB disease, screening is discouraged.<sup>11</sup>

#### **Treatment of LTBI**

Treatment of LTBI has evolved considerably over recent years. Months long daily regimens have been replaced with more simplified treatments that are both effective and shorter in duration. While daily medication is an option, one of the preferred regimens recommended by the CDC now consists of only 12 total doses over the course of 12 weeks. These changes have improved medication adherence and reduced adverse drug reactions.<sup>24</sup>

If the decision is made to proceed with LTBI treatment, collaboration with local public health is important. Additionally, the patient should be informed of drug-drug interactions and possible side effects. Patients

Advantages	Disadvantages
<ul> <li>High Adherence</li> <li>Short treatment course</li> <li>Low rate of hepatotoxic events</li> </ul>	<ul> <li>Discoloration of urine and other bodily fluids</li> <li>Drug interactions including hormonal contraceptives, HIV antiretrovirals, and warfarin</li> </ul>
<ul> <li>High adherence</li> <li>Low rate of adverse events</li> <li>Can be used in children older than 2 years</li> </ul>	<ul> <li>Potential for drug interactions, but fewe than with rifampin</li> <li>Risk of hepatotoxicity</li> <li>Some public health departments require directly observed treatment (DOT) for weekly regimen</li> </ul>
<ul> <li>Can self-administer</li> <li>Similar efficacy to monotherapy with isoniazid for 6-12 months</li> </ul>	<ul> <li>Drug interactions</li> <li>Risk of hepatotoxicity</li> </ul>
<ul> <li>Can be administered with HIV antiretrovirals</li> <li>Can be administered twice a week; some public health departments require DOT for this regimen</li> <li>Less costly than regimens containing rifampin</li> </ul>	<ul> <li>Requires close follow-up in those with underlying liver disease or alternative regimen</li> <li>Risk of hepatotoxicity</li> <li>Risk of peripheral neuropathy</li> <li>Lower adherence due to extended length of treatment</li> </ul>
	<ul> <li>Short treatment course</li> <li>Low rate of hepatotoxic events</li> <li>High adherence</li> <li>Low rate of adverse events</li> <li>Can be used in children older than 2 years</li> <li>Can self-administer</li> <li>Similar efficacy to monotherapy with isoniazid for 6-12 months</li> <li>Can be administered with HIV antiretrovirals</li> <li>Can be administered twice a week; some public health departments require DOT for this regimen</li> <li>Less costly than regimens containing</li> </ul>

should have monthly follow-up visits to monitor for adverse drug reactions, hepatotoxicity, and adherence to the prescribed treatment regime.<sup>25</sup> While routine liver function testing is no longer recommended, testing should be obtained if the patient has underlying liver disease, risk factors for liver disease, or if the patient is exhibiting potential liver complications.<sup>25</sup> Common adverse reactions related to the typical LTBI treatment regimens include vomiting, jaundice, fever, weakness, fatigue, change in stool color, change in urine color, decreased appetite, and paresthesias.<sup>25</sup> TST and IGRA testing cannot be used to monitor response to treatment as both tests evaluate the host immune response to infection and will remain positive despite treatment.<sup>11</sup>

#### **Special Populations**

#### **HIV-Positive Patients**

HIV-positive patients should be prescribed monotherapy with isoniazid because of drug interactions with rifampin and antiretroviral drugs. If monotherapy cannot be used, consider rifapentine, as there are fewer interactions than with rifampin.<sup>8</sup> Given the complexity of possible drug-drug interactions with antiretrovirals, these cases are best managed in conjunction with the patient's HIV specialist or referred to an appropriate infectious disease specialist.

#### Pregnancy

Pregnant patients who are at low risk of progression to TB disease should wait to initiate therapy until 2-3 months postpartum because there is concern for fetal exposure to the recommended antibiotics used in LTBI treatment regimens.<sup>8</sup>

#### Immunosuppression

Increasingly, disease modifying anti-rheumatic drugs (DMARDs) (including methotrexate, sulfasalazine, hydroxychloroquine, corticosteroids, leflunomide, tofacitinib, and TNF inhibitors—adalimumab, etanercept, and infliximab) are being used to manage many autoimmune conditions. Screening for LTBI is indicated prior to initiating these agents, and if a patient is found to have LTBI, they should complete at least 1 month of an LTBI regimen before initiating the DMARD.<sup>8</sup>

#### Healthcare Workers

The CDC highly recommends treatment of all healthcare workers diagnosed with LTBI due to concern for spread of TB among vulnerable patients they encounter.<sup>15</sup> An individual risk assessment of healthcare workers with a positive TB screening test should be performed to determine a diagnosis of LTBI. If the healthcare worker is low risk, consider a second screening test before initiating treatment. Following positive TST or IGRA, a CXR should be obtained. The CDC does not recommend follow-up CXRs unless symptoms develop.<sup>24,26</sup>

#### BCG Vaccinated

While the BCG vaccine does offer some degree of pro-

tection against severe TB disease in young children, it does not prevent all TB infections.<sup>27</sup> Patients with a history of receiving BCG vaccination who have risk factors for TB infection should be treated for LTBI if they have a positive IGRA screening.<sup>28</sup>

"Selection of appropriate testing in each patient scenario is critical to minimize unnecessary anxieties and to optimize recognition of patients who require treatment."

#### **Social Determinants of Health**

Many SDoH factors increase the risk of LTBI and TB disease. Patients with increased community exposure to TB, those living in congregate housing, non-White racial/ethnic groups, those with medical conditions including diabetes or HIV infection, those with limited access to healthcare, and those with low health literacy should all be considered at higher risk for TB infection.<sup>29</sup> The CDC recommends partnering with community resources, public health departments and organizations such as the TB Elimination Alliance to ensure access to materials that are culturally and linguistically appropriate to mitigate risks conferred by SDoH.<sup>29</sup>

#### **Clinical Scenarios and Discussion**

**Case 4:** A 23-year-old female student physician assistant (PA) presented with a TST of 17mm, which was 0mm in the previous year. She had no significant past medical history, and her only medication was an oral contraceptive. Her CXR was normal at this visit. She had no signs or symptoms of TB disease. Should this patient have been treated for LTBI?

Discussion: Because the risk of conversion to TB disease is most likely within 2 years of infection, and to minimize risk to vulnerable populations with whom the PA student is working, the treating physician appropriately recommended proceeding with treatment for LTBI.

**Case 5:** A 33-year-old man presented with 10 days of cough, diffuse myalgias, subjective fever, and sore throat. His vital signs were normal except for a fever of 38.5°C. He had no past medical history. He immigrated

to the United States 1 year prior from Venezuela. A CXR performed in UC demonstrated a cavitary lesion in the left upper lobe of the lung. How should the UC clinician have managed this patient?

Discussion: This patient has high risk for TB disease, however, the patient was not clinically ill at UC presentation enough to require hospitalization. As such, appropriate care begins with placing the patient in a surgical mask while in UC and performing further evaluation. TB testing with either a TST or IGRA is appropriate. As cavitary lung lesions have a broad differential diagnosis, ED referral for consideration of chest computed tomography (CT) is generally recommended as many of these lesions can have associated pneumothorax, and patients may benefit from therapeutic and/or diagnostic aspiration.<sup>30</sup> While TB is one possible etiology for a cavitary lung lesion, it is important to consider other infections, including pneumocystis and bacterial pneumonia as well.<sup>30</sup> Among patients with risk factors for TB exposure and signs and symptoms of TB disease who are not clinically ill, referral to the local public health department is critical once a positive TB test result returns.

#### Conclusion

It is vital for UC clinicians to be familiar with TB screening, testing, and treatment guidelines as well as the known risk factors for TB, including SDoH. Selection of appropriate testing in each patient scenario is critical to minimize unnecessary anxieties and to optimize recognition of patients who require treatment. While neither TST nor IGRA are perfect tests, they both have been extensively validated and are simple to administer in the UC setting. When LTBI is suspected, initiating treatment from UC is appropriate. With appropriate testing and treatment protocols in place, UC is an ideal setting to screen and treat TB (LTBI and TB disease) to minimize ongoing risks to our patients and communities.

*Manuscript submitted October 11, 2024; accepted December 26, 2024.* 

#### References

1. Centers for Disease Control and Prevention. Core Curriculum On Tuberculosis: What The Clinician Should Know. Seventh Edition (2021). Accessed August 15, 2024, at: https://www.cdc.gov/tb/media/Core\_Curriculum\_TB\_eBook.pdf

2. Behr MA, Kaufmann E, Duffin J, Edelstein PH, Ramakrishnan L. Latent tuberculosis: two centuries of confusion. *Am J Respir Crit Care Med*. 2021;204(2):142-148. doi:10.1164/rccm.202011-4239PP

3. United States Preventive Services Taskforce. Latent Tuberculosis Infection In Adults: Screening. Recommendation. May 2, 2023. Accessed August 15, 2024, at: https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/latenttuberculosis-infection-screening

4. Centers for Disease Control and Prevention. TB Incidence and Mortality: 1953–2023. Published October 31, 2024. Accessed August 15, 2024, at: https://www.cdc.gov/tbsurveillance-report-2023/tables/table-1.html

5. Centers for Disease Control and Prevention. Clinical Overview Of Latent Tuberculosis Infection. Accessed August 15, 2024, at: https://www.cdc.gov/tb/hcp/clinicaloverview/latent-tuberculosis-infection.html

6. Williams PM, Pratt RH, Walker WL, Price SF, Stewart RJ, Feng PI. Tuberculosis—United States, 2023. *MMWR Morb Mortal Wkly Rep.* 2024;73:265–270.

7. Jonas DE, Riley SR, Lee LC, et al. Screening for Latent Tuberculosis Infection in Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2023;329(17):1495–1509. doi:10.1001/jama.2023.3954

8. Huaman MA, Sterling TR. Treatment of latent tuberculosis infection—an update. *Clin Chest Med.* 2019;40(4):839-848. doi:10.1016/j.ccm.2019.07.008

9. Centers for Disease Control and Prevention. Clinical Overview Of Tuberculosis Disease: People With TB Disease. Accessed August 15, 2024, at: https://www.cdc.gov/tb/hcp/clinical-overview/tuberculosis-disease.html#:-: text=People%20with%20TB%20disease%3A,test%20result%20indicating%20TB%20 infection

10. Ketata W, Rekik WK, Ayadi H, Kammoun S. Les tuberculoses extrapulmonaires [Extrapulmonary tuberculosis]. *Rev Pneumol Clin.* 2015 Apr-Jun;71(2-3):83-92. French. doi: 10.1016/j.pneumo.2014.04.001. Epub 2014 Aug 15. PMID: 25131362.

11. Centers for Disease Control and Prevention. Clinical Testing And Diagnosis For Tuberculosis. Accessed August 15, 2024, at: https://www.cdc.gov/tb/hcp/testing-diagnosis/index.html.

12. Kestler B, Tyler SK. Latent tuberculosis testing through the ages: the search for a sleeping killer. *Am J Physiol Lung Cell Mol Physiol*. 2022;322(3):L412-L419.

 Centers for Disease Control and Prevention. Clinical Testing Guidance For Tuberculosis: Interferon Gamma Release Assay. Accessed August 15, 2024, at: https://www.cdc.gov/tb/hcp/testing-diagnosis/interferon-gamma-release-assay.html.
 Mahon J, Beale S, Holmes H, et al. A systematic review of cost-utility analyses of screening methods in latent tuberculosis infection in high-risk populations. *BMC Pulm Med*. 2022;22(1):375.

15. Centers for Disease Control and Prevention. Baseline Tuberculosis Screening and Testing For Health Care Personnel. Accessed August 15, 2024, at: https://www.cdc.gov/tb-healthcare-settings/hcp/screening-testing/baseline-testing.html.

16. Prakash, Lohith Kumar Bittugondanahalli, et al. Pulmonary Tuberculosis in Immunocompromised Patients: A Review. *Indographics* 3.02 (2024): 054-071

17. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/ Infectious Diseases Society of America/ Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis Of Tuberculosis In Adults And Children. *Clin Infect Dis.* 2017;64(2):e1-e33.3.

18. Centers for Disease Control and Prevention. Latent Tuberculosis Infection: A Guide For Primary Health Care. Accessed August 15, 2024, at: https://www.cdc.gov/ tb/media/pdfs/Latent-TB-Infection-A-Guide-for-Primary-Health-Care-Providers.pdf 19. Texas Department of State Health Services. Baseline Tuberculosis (TB) Assessment for Health Care Personnel. Accessed August 15, 2024, at: https://www.dshs.texas. gov/sites/default/files/LIDS-TB/forms/TB-600.pdf.

20. Centers for Disease Control and Prevention. Clinical and laboratory diagnosis of tuberculosis. Published May 4, 2016. Updated September 1, 2022. Accessed August 15, 2024, at: https://www.cdc.gov/tb/hcp/testing-diagnosis/clinical-and-laboratory-diagnosis.html

21. Lyon SM, Rossman MD. Pulmonary Tuberculosis. *Microbiol Spectr.* 2017; 5(1). 22. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis Of Tuberculosis In Adults And Children.

*Clin Infect Dis.* 2017;64(2):e1-e33. doi:10.1093/cid/ciw694 23. World Health Organization Website. Health Topics: Tuberculosis. Accessed August 15, 2024, at: https://www.who.int/health-topics/tuberculosis#tab=tab\_1

24. Sterling TR, Njie G, Zenner D, et al. Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. MMWR Recomm Rep. 2020;69(No. RR-1):1–11.

25. Kim S, Thal R, Szkwarko D. Management of Latent Tuberculosis Infection. JAMA. 2023;329(5):421–422. doi:10.1001/jama.2022.24362

26. Sosa LE, Njie GJ, Lobato MN, et al. Tuberculosis Screening, Testing, and Treatment of UNITED STATES Health Care Personnel: Recommendations from the National Tuberculosis Controllers Association and CDC, 2019. *MMWR Morb Mortal Wkly Rep.* 2019;68:439–443. DOI: http://dx.doi.org/10.15585/mmwr.mm6819a3

27. Centers for Disease Control and Prevention. Bacille Calmette-Guérin (BCG) Vaccine for Tuberculosis. Accessed August 15, 2024, at: https://www.cdc.gov/tb/hcp/vaccines/index.html.

28. Centers for Disease Control and Prevention. Targeted Tuberculin Testing and Treatment Of Latent Tuberculosis Infection. Accessed August 15, 2024, at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm

29. Centers for Disease Control and Prevention. Health Disparities in Tuberculosis. Accessed August 18, 2024, at: https://www.cdc.gov/tb/health-equity/index. html#:--text=Racial%20and%20ethnic%20disparities,Black%20or%20African%20Am erican%20persons

30. Naggar A., Laasri K., Berrada K., at al. Differential Diagnoses Of Cavitary Lung Lesions On Computed Tomography: A Pictorial Essay. *Egypt J Radiol Nucl Med*. 54, 149 (2023). https://doi.org/10.1186/s43055-023-01098-7