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New York City Department of Health and Mental Hygiene

TESTING FOR AND TREATING LATENT TUBERCULOSIS INFECTION

- Tuberculosis (TB) remains an important public health concern in New York City.
- Identification and treatment of people with latent TB infection (LTBI) is essential to TB prevention efforts.
- Screen all patients for TB risk factors.
- Test patients at high risk for TB infection using a blood-based interferon gamma release assay (IGRA) as indicated.
- Rule out active TB disease in patients with a positive test for TB infection.
- Treat patients with LTBI using short-course regimens and ensure treatment completion.
- Report TB infection test results and LTBI treatment as required by the Health Code.

INSIDE THIS ISSUE (click to access)

Tuberculosis (TB) is a contagious airborne disease caused by *Mycobacterium tuberculosis*. It usually affects the lungs but can less commonly affect other sites, including the brain, lymph nodes, or spine. Symptoms may include fever, cough lasting more than 3 weeks, night sweats, chills, weight loss, fatigue, and anorexia. Left untreated, TB can cause significant morbidity and mortality.

Worldwide, TB has surpassed HIV as the leading infectious disease cause of death.[1] In 2019, approximately 1.4 million people died of

TB, including 230,000 children aged 14 years or younger.[1] Ten million people became sick with TB, including 465,000 with rifampin-/multidrug-resistant TB.[1]

In 2019, 566 people in New York City (NYC) were confirmed to have active TB, for a case rate of 6.9 per 100,000[2]—more than double the national rate of 2.7 per 100,000.[3] Every neighborhood in NYC reported at least one case of TB.[2] Most TB diagnoses were among persons born outside of the United States, but a majority had lived in the United States for more than 5 years at the time of diagnosis, implying reactivation of latent infection (**Box 1**[2]).

Latent TB infection (LTBI) is defined as infection with *M tuberculosis* in persons who do not yet exhibit signs, symptoms, or radiological or bacteriologic evidence of TB disease; people with LTBI are not infectious but are at risk of progressing to active TB disease.[4,5] Nearly a quarter (1.7 billion) of the world's population has LTBI, including approximately 13 million people in the United States.[1,6]

Early detection and treatment of LTBI can greatly decrease the risk of progression to active infectious TB disease.[7,8] Over the last decade, the decline of TB cases in NYC has plateaued.[2] To prevent TB transmission and accelerate the decline of TB rates in NYC, a citywide effort is needed to increase LTBI testing and treatment of people at high risk (**Box 2**[9,10]).[11-13]

TEST PERSONS AT HIGH RISK

Assess TB risk in all patients (**Box 3**[1,5,14-16]) and test those at risk (**Boxes 4**[5,15] and **5**[1,5,16-22]), regardless of how long they have lived in the

BOX 1. TUBERCULOSIS DISEASE IN NEW YORK CITY, 2019[2]

- West Queens, Sunset Park, and Hunts Point-Mott Haven were among the neighborhoods with the highest TB rates (19.9, 15.0, and 9.2 per 100,000, respectively)
- 566 people had TB disease, for a case rate of 6.9 per 100,000 persons
  - The most common countries of birth were China, United States, Ecuador, Dominican Republic, and Bangladesh, with 65 other countries represented
    - 84% were born outside of the United States; of these, 68% lived in the United States for >5 years at diagnosis
  - 19 were children and 174 were aged ≥65 years
  - 23% had diabetes, 6% had HIV infection, and 7% had non-HIV-related immunosuppression

BOX 2. PROVIDING CARE DURING THE COVID-19 PANDEMIC[9,10]

The COVID-19 pandemic has resulted in unprecedented disruptions in medical care. Use telehealth visits to provide continuity of care, while minimizing the health care-associated risk of COVID-19 exposure (**Resources**).

- Consider telehealth visits for patients who
  - are medically stable, without need for in-person supervision for clinical improvement
  - do not require an immediate follow-up visit for clinic-based tests (laboratory, chest x-ray, or sputum)
  - have demonstrated ability to use a video-enabled device
- Use telehealth to
  - conduct visual examination of the patient
  - provide electronic directly observed therapy
  - review treatment progress
  - inquire about side effects
  - provide counseling and education on side effects and treatment adherence
- Reserve in-person clinic visits for the highest priority patients (ie, newly identified contacts of people with infectious tuberculosis, those with confirmed or probable tuberculosis)
  - Use in-person clinic visits to
    - draw blood for analysis
    - obtain sputum
    - deliver medication that cannot be sent by mail
    - see patients who lack access to or facility with telehealth technology

BOX 3. RISK ASSESSMENT FOR TUBERCULOSIS[a,1,5,14-16]

The NYC Health Department strongly recommends testing people who meet any of the following criteria, as they are at high risk of TB infection or progression to TB disease if infected:

- Close contact with someone with infectious TB disease
- Immunosuppression[b,c]
- Born outside of the United States in a high TB incidence area[d]

OR

- Traveled or resided outside of the United States for ≥1 month consecutively in a high TB incidence area[d]

NYC, New York City; TB, tuberculosis

[a]This risk assessment is intended to focus screening efforts on the highest TB risk factors and is not an exhaustive list

[b]Testing results may be indeterminate or falsely negative depending on immune status, and the test may need to be repeated

[c]Includes HIV infection, cancer (eg, leukemias, lymphomas, or head, neck, or lung cancers), prolonged corticosteroid use (≥15 mg/d of prednisone for ≥1 month), and other immunosuppressive treatments (eg, tumor necrosis factor alpha inhibitors, Janus kinase inhibitors, interleukin receptor antagonists, chemotherapy, organ transplant medications)

[d]Any country other than the United States, Canada, Australia, New Zealand, or those in western or northern Europe is considered a high TB incidence area

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United States[23] or previous receipt of bacille Calmette-Guérin (BCG) vaccination.[21,24] Testing may also be considered for people who live or work in settings where TB exposure is possible (eg, health care facilities, correctional facilities, homeless shelters, and mycobacteriology laboratories), based on institutional and regulatory requirements,[22] epidemiological risk, and clinical judgment. Patients with a prior diagnosis of LTBI or TB disease do not require retesting.

For patients with symptoms that are consistent with active TB, rule out TB disease, regardless of whether the patient has known TB risk factors. Once active TB is ruled out, evaluate the patient for LTBI.

Educate patients about LTBI and testing for TB (**Box 6**[20,25,26]).

BOX 4. RISK FACTORS FOR PROGRESSION TO ACTIVE TUBERCULOSIS DISEASE[5,15]

- Close contact with someone with infectious TB disease
- Conversion of test for TB infection[a]
- Immunosuppression
  - HIV infection
  - immunosuppressive therapy
    - prolonged corticosteroid use (≥15 mg/d of prednisone for ≥1 month)
    - other immunosuppressive medications (eg, TNF-alpha inhibitors, JAK inhibitors, interleukin receptor antagonists, chemotherapy)
    - use of organ transplantation medication
  - some cancers (eg, leukemias, lymphomas, or head, neck, or lung cancers)
- Previous TB disease
  - evidence of old, healed TB lesions on chest x-ray
  - history of untreated or inadequately treated TB disease
- Any of the following clinical conditions or procedures
  - silicosis
  - diabetes mellitus
  - end-stage renal disease
  - body weight ≥10% below ideal body weight, or body mass index <18.5 kg/m^2
  - organ transplantation
  - gastrectomy or jejunoileal bypass
  - chronic malabsorption syndromes
- Injection drug or tobacco product use
- Aged <5 years and having a positive test for TB infection

JAK, Janus kinase; TB, tuberculosis; TNF, tumor necrosis factor

[a]Either by history or evidence of conversion of TB test result (change from negative to positive interferon gamma release assay result or an increase in size of tuberculin skin test reaction of ≥10 mm) within a 2-year period

USE IGRA OR TST

Two types of tests for TB infection are approved by the FDA: blood-based interferon gamma release assays (IGRAs) and the Mantoux tuberculin skin test (TST). IGRAs have numerous benefits over the TST and should be used preferentially for people aged 2 years and older (**Box 7**[5,15,27-33]), particularly those who have previously received the BCG vaccine[20,34] or who may have difficulty returning for the TST reading.[20] The TST is recommended for children aged younger than 2 years[35]; some experts recommend using IGRAs for children of all ages.[36]

BOX 5. TESTING INTERVALS FOR SELECT GROUPS AT RISK OF TUBERCULOSIS INFECTION[1,5,16-22]

Close contacts of people with active tuberculosis (TB) disease

- Test as soon as exposure is identified, in consultation with the NYC Health Department.[a] Call the TB Hotline at 844-713-0559
- If a baseline test for TB infection was obtained within 8 weeks of exposure (window period) and is negative, retest after 8 weeks following exposure to rule out a false-negative result
- If the exposed person is aged <5 years or is immunocompromised, evaluate with chest x-ray and physical examination to rule out active TB, regardless of the TB test result

People with immunosuppression

- Test at time of diagnosis of immunosuppressive condition or if other risk factors for TB develop
- Test annually if at risk for repeated or ongoing TB exposure
- Test prior to starting immunosuppressive medication

People born in OR who traveled/resided in (≥1 month consecutively) a high TB incidence area[b]

- Test at initial entry to the US health care system or if other risk factors for TB develop
- Test after 8 weeks following return from travel/residence in a country with high TB incidence

People who live or work in settings where TB exposure may be possible[c]

- Test based on institutional guidelines and state and local regulations
- Follow CDC guidelines for health care personnel

[a]All persons with potential or confirmed active TB and children aged <5 years diagnosed with LTBI must be reported to the NYC Health Department per Health Code Article 11. For more information, visit www.nyc.gov/health/tb

[b]Any country other than the United States, Canada, Australia, New Zealand, or those in western or northern Europe is considered a high TB incidence area

[c]As defined by local epidemiological risk and/or regulations; includes health care facilities, correctional facilities, homeless shelters, and mycobacteriology laboratories

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Neither IGRAs nor the TST can distinguish between LTBI and active TB disease. Patients who have a positive test for TB infection or are symptomatic should be evaluated to rule out active TB (**Box 8**[15,24,29,30]). LTBI is diagnosed when a person has a positive IGRA or TST result but has no evidence of TB disease following clinical, radiological, and laboratory examination.

Either test may be falsely negative despite the presence of TB infection or disease; use clinical judgment to determine if additional evaluation is needed (**Box 8**).

Use of both IGRA and TST is not recommended for routine testing but may be helpful in diagnosing TB infection when[5,31,34,37]:

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BOX 6. WHAT TO TELL PATIENTS ABOUT TUBERCULOSIS[20,25,26]

What is tuberculosis (TB)?

- TB is a disease caused by bacteria (germs). It usually attacks the lungs but can affect any part of the body.
- People with latent TB infection (LTBI) can have TB germs in their body for years before getting sick with active TB disease and becoming contagious.
- Getting tested and treated for LTBI can prevent you from developing active TB disease in the future.

How is TB spread?

- TB is spread from one person to another through the air. When a person sick with TB coughs, speaks, or sings, people around them can breathe in the TB germs and get infected.

When should you get tested for TB?

- You have symptoms of TB (for example, coughing for 3 weeks or more or coughing up blood, heavy sweating at night, feeling very tired, fever or chills, loss of appetite, or unplanned weight loss).
- You have spent a lot of time around someone with TB.
- You take certain medications or have a medical condition, such as HIV or cancer, that can weaken the immune system.
- You were born in or have traveled to or lived in a country (for 1 month or longer) where many people have TB.

How do you get tested and treated for LTBI?

- You can get a blood test. Blood tests for LTBI are not affected by previous TB vaccination (bacille Calmette-Guérin [BCG]).
- If the test for TB infection is positive, we will check for active TB disease using a chest x-ray and other tests.
- If you have active TB disease, we will refer you for further evaluation and treatment. If you don't, we will treat you for LTBI for as short a time as possible, which would be 3 to 4 months (**Box 12**, page 10).

BOX 7. BENEFITS OF IGRA VERSUS TST[5,15,27-33]

Feature	IGRA	TST
Antigens	• More specific to *M tuberculosis* complex[a]	• Less specific to *M tuberculosis* complex
Boosting	• No; two-step testing not needed	• Yes; two-step testing is recommended at baseline in settings that require surveillance testing
False-positive results	• Not with BCG vaccination, but with a few environmental mycobacteria[b]	• With both BCG vaccination and some environmental mycobacteria
Interpretation	• Positive/negative result • Indeterminate or borderline result may require retesting • Minimal interreader variability	• Based on size of induration (not erythema) and patient's relative risk for TB exposure or development of disease (**Box 9**) • Subject to errors during implantation and interpretation
Timeframe	• Blood samples must be processed within a manufacturer-determined timeframe	• Test must be read between 48 and 72 hours after administration
Minimum number of patient visits	• One	• Two

BCG, bacille Calmette-Guérin; IGRA, interferon gamma release assay; *M tuberculosis, Mycobacterium tuberculosis*; TB, tuberculosis; TST, Mantoux tuberculin skin test

[a]TB antigens ESAT-6 and CFP-10

[b]See package inserts for QuantiFERON®-TB Gold Plus and T-SPOT®.*TB*

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BOX 8. CLINICAL EVALUATION BASED ON TUBERCULOSIS TEST RESULT[15,24,29,30]

Test/result	Follow-up evaluation
Negative IGRA or TST	• No further evaluation is needed unless indicated by clinical judgment (eg, clinical suspicion of active TB, immunosuppression, new TB risk factor, live or work in high-risk setting)
Positive IGRA or TST	• Rule out active TB disease with clinical evaluation, chest x-ray, and other diagnostics as clinically indicated (See Tuberculosis Clinical Policies and Protocols for detailed guidance)
Indeterminate[a] or invalid[b] IGRA	• Result could be due to error in specimen collection or laboratory processing, or to the patient's reduced immune response to TB antigens (ie, anergy) • Repeat the IGRA. If 2 separate specimens from a patient yield indeterminate or invalid results, do not repeat the IGRA; consider medical evaluation and chest x-ray to rule out active TB
Borderline IGRA[b]	• Equivocal result; indicates uncertainty of *M tuberculosis* infection • Repeat the IGRA. If 2 separate specimens from a patient yield borderline results, do not repeat the IGRA; consider medical evaluation and chest x-ray to rule out active TB

IGRA, interferon gamma release assay; TB, tuberculosis; TST, Mantoux tuberculin skin test

[a]QuantiFERON®-TB Gold Plus only

[b]T-SPOT®.*TB* only

BOX 9. CRITERIA FOR A POSITIVE TST RESULT[15,32,33]

Size of induration	Criteria for a positive result
≥5 mm	People who • have had recent contact with someone with infectious TB disease • have HIV or another immunosuppressive condition • have fibrotic changes on chest x-ray consistent with old TB disease • are currently taking, or planning to take, certain medications that can cause immunosuppression, such as ◦ anti-TNF-alpha inhibitor treatment (eg, infliximab, etanercept), JAK inhibitors, interleukin receptor antagonists ◦ chemotherapy ◦ medications after organ transplantation ◦ steroids (≥15 mg/d of prednisone for ≥1 month)
≥10 mm	People who • were born in OR traveled/resided ≥1 month consecutively in a country with high TB incidence[a] • live or work in institutional settings where exposure to TB may be possible[b] • have medical conditions associated with increased risk of progression to active TB disease, including ◦ silicosis ◦ diabetes mellitus ◦ end-stage kidney disease ◦ gastrectomy ◦ jejunoileal bypass ◦ certain hematologic disorders (eg, leukemias or lymphomas) ◦ specific malignancies (eg, carcinoma of the head, neck, or lung) • are aged <5 years • are injection drug users
≥15 mm	People • at low risk for TB disease • for whom testing is not generally indicated

JAK, Janus kinase; TB, tuberculosis; TNF, tumor necrosis factor; TST, Mantoux tuberculin skin test

[a]Any country other than the United States, Canada, Australia, New Zealand, or those in western or northern Europe is considered a high TB incidence area

[b]As defined by local epidemiological risk and/or regulations; includes health care facilities, correctional facilities, homeless shelters, and mycobacteriology laboratories

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- the first test is negative but clinical suspicion for TB is high; or
- risk of infection, progression to TB disease, or poor outcome is increased (eg, immunosuppression or age younger than 5 years).

A positive result on either test would indicate further evaluation for TB infection versus TB disease.

Two-step testing

Health care workers or others with occupational exposure to TB may be required to have baseline and annual screening for TB.[22] When the TST is used for baseline, a two-step testing process is recommended: if the initial TST is negative, administer a second TST 1 to 3 weeks after the initial test and record the second test result as the baseline.

Some persons with remotely acquired TB infection may have a diminished immune response to the initial test. If a two-step baseline TST is not performed, individuals testing positive at the next annual testing may be incorrectly identified as newly infected due to a "boosting" of their immune response by the initial test.

Two-step testing is not required when an IGRA is used as the initial test.

Interpret results

Two IGRAs are currently available in the United States: QuantiFERON®-TB Gold Plus (QFT; Qiagen, Australia) and T-SPOT®.*TB* (Oxford Immunotec, United Kingdom). Laboratories report IGRA results according to algorithms established by the manufacturer.[29,30] QFT results are reported as "positive," "negative," or "indeterminate." T-SPOT.*TB* results are reported as "positive," "negative," "borderline," or "invalid."

TST interpretation is based on size of induration, not erythema, and patient risk factors (**Box 9**[15,32,33]). For a valid result, proper implantation and reading procedures must be used.[32,33]

RULE OUT ACTIVE TUBERCULOSIS DISEASE

If a person has a positive test for TB infection, rule out active TB disease.[15]

- Use clinical history, physical examination, and radiological testing including chest x-ray to assess for pulmonary or extrapulmonary TB (**Box 10**[5]).
- If the patient has signs or symptoms of TB or an abnormal chest x-ray suggestive of TB disease, obtain sputum samples for acid-fast bacilli smear and *M tuberculosis* culture, and perform any other clinically indicated tests (eg, bronchoscopy with bronchoalveolar lavage). Call the TB Hotline at 844-713-0559 for assistance.
- Do not treat for LTBI while awaiting culture results.

If there are no symptoms of TB disease and chest x-ray and other diagnostic tests are negative for active TB, diagnose LTBI and evaluate for treatment.

For treatment questions, contact the NYC Health Department's TB Provider Hotline at 844-713-0559 or refer patients to the Health Department's TB clinics (Resources)

BOX 10. DIFFERENTIATING LATENT TUBERCULOSIS INFECTION (LTBI) FROM ACTIVE TUBERCULOSIS DISEASE[5]

Feature	LTBI	Active TB disease
Symptoms/ physical findings	None	May include one or more • Fever • Cough • Chest pain • Weight loss • Night sweats • Hemoptysis • Fatigue • Decreased appetite
IGRA or TST	Usually positive	Usually positive; negative test does not rule out active TB
Chest x-ray	Usually normal	Usually abnormal[a]
Respiratory specimens	Generally not obtained[b]	Usually smear- or culture-positive[c]
Infectious	No	Yes (pulmonary or laryngeal disease)

IGRA, interferon gamma release assay; TB, tuberculosis; TST, Mantoux tuberculin skin test

[a]May be normal in persons with advanced immunosuppression or extrapulmonary disease

[b]Respiratory specimens are obtained only if ruling out active TB based on clinical suspicion, symptoms, or abnormal chest x-ray. If respiratory specimens are obtained and they are smear- and culture-negative, then LTBI diagnosis is considered

[c]May be negative in persons with extrapulmonary disease or minimal or early pulmonary disease

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TREAT INDIVIDUALS WITH LTBI

Offer treatment to patients of all ages with LTBI. There are 3 treatment options for LTBI, including rifampin (RIF), isoniazid (INH)/rifapentine (RPT; a long-acting rifamycin), and INH alone. RIF and INH/RPT are preferred due to shorter duration of treatment (**Box 11**[5,15,33,38-41] and **Table 1**[5,15,33,35,39,41-43]). If INH monotherapy must be used, a 6-month regimen is recommended, including for children and persons living with HIV; a 9-month regimen may be used based on clinical judgment.[39] An additional LTBI regimen of daily INH and RIF for 3 months may be used by experts in specific circumstances but is not routinely used for LTBI treatment by the NYC Health Department.[39]

The NYC Health Department recommends shorter treatment regimens in order to minimize risk of adverse effects (**Table 2,**[5,15,33,39,44] page 9) and to facilitate completion of treatment.[43,45] A 4-month course of RIF or 12-week course of INH/RPT has been shown to be as effective as 9 months of treatment with INH alone, is generally well tolerated with less hepatotoxicity, and results in better rates of treatment completion.[43,45-48]

As with all medications, check drug-drug interactions before initiating treatment for LTBI. For example, in people living with HIV, RIF, RPT, and other rifamycins, such as rifabutin, can be used only in conjunction with selected antiretroviral therapy (ART)[38] (**Table 2**, page 9), but INH can be administered concurrently with any ART.[38,40] Use current recommendations to guide treatment decisions.[38,40]

Clinical monitoring

Perform baseline assessments of liver function tests (eg, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase) for people[15,33,44]:

- with HIV infection or other immunosuppressive conditions,
- with a history of hepatitis (eg, viral) or other liver disease,
- with a history of chronic alcohol or injection drug use,
- who are pregnant or postpartum (≤3 months after delivery), or
- being treated with other potentially hepatotoxic agents.

Monitor liver function if baseline labs are elevated, adverse effects occur, or if otherwise clinically indicated.[15] People receiving LTBI treatment with RIF or RPT should also have a baseline complete blood count with platelets and serial monitoring as clinically indicated.[15]

Schedule monthly clinical assessments to review for:

- signs and symptoms of active TB,
- adverse reactions to TB medications,
- adherence to treatment, and
- new medications with potential drug interactions.

BOX 11. TREATMENT OPTIONS FOR LTBI[5,15,33,38-41]

	Indications	Contraindications
Rifampin (RIF)	• Preferred regimen for people of all ages • May be used in healthy people with HIV who are not receiving ART or are taking ART with acceptable drug-drug interactions with RIF (eg, EFV- or DTG-containing regimens)	• People with HIV/AIDS who are taking certain ART (eg, most PIs, NNRTIs, INSTIs, and TAF-containing regimens)[a] • People who were exposed to RIF-resistant TB
Isoniazid (INH)/ rifapentine (RPT)	• Preferred regimen for people aged ≥2 years • May be used in healthy people with HIV who are not receiving ART or are taking ART with acceptable drug-drug interactions with RPT (eg, EFV- or RAL-containing regimens)	• RPT is not recommended for persons who are pregnant or breastfeeding • Children aged <2 years • People with HIV/AIDS who are taking certain ART (eg, most PIs, NNRTIs, INSTIs, and TAF-containing regimens)[a] • People who were exposed to INH- or RIF-resistant TB
INH	• No longer a preferred regimen • May be used for people of all ages if RIF or RPT is contraindicated	• People who were exposed to INH-resistant TB • People with history of severe INH-induced reaction (eg, hepatic, skin, or allergic) or neuropathy

ART, antiretroviral therapy; DTG, dolutegravir; EFV, efavirenz; INSTI, integrase strand transfer inhibitor; LTBI, latent tuberculosis infection; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RAL, raltegravir; TAF, tenofovir alafenamide

[a]Visit https://hivinfo.nih.gov for the latest guidelines and complete list of contraindicated medications

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Counsel patients about LTBI (**Box 6**, page 4), and emphasize the need for treatment adherence and completion (**Box 12**, page 10):

- Explain potential complications, adverse drug reactions (**Table 2**), and the importance of stopping treatment and notifying their clinical provider if adverse reactions occur.
- Provide appropriate educational materials at treatment initiation (**Resources**).
- Use appointment reminders to facilitate monthly clinical check-ups.

SPECIAL POPULATIONS

Persons with recent tuberculosis test conversions

The conversion of a test for TB infection from "negative" to "positive" indicates recent infection with *M tuberculosis* and thus high risk for progression to active TB disease. With TST, recent conversion is defined as a ≥10-mm increase in induration within the past 2 years. For IGRAs, a change in result from "negative" to "positive" is considered a conversion. Active TB disease must be ruled out. Once active disease is ruled out, treat for LTBI using a short-course regimen (**Tables 1** and **2**).

Contacts

Contacts (persons exposed to an individual with infectious TB disease) are at high risk of both being infected with TB[16,49] and, if infected, progressing to active TB disease.[7,50]

Test the patient exposed to TB with IGRA or TST and evaluate including symptom review and assessment for additional TB risk factors. If the exposed person is aged younger than 5 years, evaluate with physical examination and a posteroanterior and lateral chest x-ray as soon as possible, regardless of IGRA or TST result.[16,51] Any exposed person with an initial positive test for TB infection should have a chest x-ray and begin treatment for LTBI once active TB is ruled out. Short-course regimens with either RIF or INH/RPT are recommended unless the index patient has TB that is resistant to one of these drugs (**Tables 1** and **2**).

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TABLE 1. TREATMENT REGIMENS FOR LTBI[5,15,33,35,39,41-43]

Drug	Interval and duration	Dose		Administration	Completion criteria
		Adults	Children		
Rifampin (RIF)	Daily for 4 months	10 mg/kg (600 mg max)	15-20[a] mg/kg (600 mg max)	Self	120 doses within 6 months
Isoniazid (INH)/ rifapentine (RPT)	Weekly for 12 weeks	INH Patients aged ≥12 years: 15 mg/kg rounded up to the nearest 50 or 100 mg (900 mg max)	INH Patients aged 2-11 years: 25 mg/kg rounded up to the nearest 50 or 100 mg (900 mg max)	Directly observed therapy preferred Self-administration acceptable for persons aged ≥2 years	12 doses within a 16-week period
		RPT • 10.0-14.0 kg: 300 mg • 14.1-25.0 kg: 450 mg • 25.1-32.0 kg: 600 mg • 32.1-49.9 kg: 750 mg • ≥50.0 kg: 900 mg max			
INH[b]	Daily for 6 months	5 mg/kg (300 mg max)	10-20 mg/kg (300 mg max)	Self	180 doses within 9 months
	Daily for 9 months				270 doses within 12 months
	Twice weekly for 6 months	15 mg/kg (900 mg max)	20-40 mg/kg (900 mg max)	Directly observed therapy required	52 doses within 9 months
	Twice weekly for 9 months				76 doses within 12 months

LTBI, latent tuberculosis infection

[a]The American Academy of Pediatrics acknowledges that some experts use rifampin at 20-30 mg/kg for the daily regimen when prescribing for infants and toddlers

[b]Breastfeeding is not contraindicated in people taking INH; the amount of INH in breast milk is inadequate for treatment of infants with LTBI

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TABLE 2. ADVERSE EFFECTS AND OTHER CONSIDERATIONS FOR LTBI TREATMENTS[5,15,33,39,44]

	Major adverse effects	Potential laboratory abnormalities	Considerations
Rifampin (RIF)	• Anorexia • Nausea/vomiting • Icterus • Abdominal pain • Hepatitis • Rash • Fever or influenza-like symptoms • Easy bruising or bleeding	• Liver enzyme elevation • Neutropenia • Thrombocytopenia	• Body secretions and contact lenses may turn orange • Levels of methadone, warfarin, contraceptives, oral hypoglycemic agents, dapsone, and antifungals may be reduced with concomitant RIF use; consult with providers prescribing these agents ◦ May impair glucose control in patients with diabetes ◦ Advise patients who use hormonal contraceptives to add a barrier method or switch to a nonhormonal option ◦ Methadone dosage may need to be increased to avoid withdrawal; monitor for withdrawal and consult with methadone maintenance program as needed • Certain medications are contraindicated (**Box 11**, page 7)
Isoniazid (INH)/ rifapentine (RPT)	As with INH and RIF,[a] plus • Influenza-like symptoms[b] • Polyarthralgia • Hypersensitivity reaction (ranging from mild reactions such as dizziness to more severe reactions including hypotension and thrombocytopenia)	• Liver enzyme elevation • Neutropenia • Thrombocytopenia	As with INH and RIF plus • DOT provider should ask patients about adverse reactions at each DOT visit • Certain medications are contraindicated (**Box 11**, page 7)
INH	As with RIF, plus • Peripheral neuropathy • Arthalgia • CNS effects • Lupus-like syndrome	• Liver enzyme elevation[c]	• Vitamin B6 (pyridoxine), 25 mg/d, may decrease peripheral and CNS effects and should be used in patients who ◦ are using alcohol, pregnant, breastfeeding,[d] or malnourished; or ◦ have HIV, cancer, diabetes, chronic kidney or liver disease, or preexisting peripheral neuropathy • Aluminum-containing antacids reduce INH absorption • Levels of acetaminophen, cimetidine, phenytoin, disulfiram, carbamazepine, valproate, clopidogrel, and citalopram may be increased with concomitant INH use[e]; may need to adjust dose or drug levels, or prescribe a different medication • Avoid tyramine-containing foods (eg, cheese, red wine, certain types of fish)

CNS, central nervous system; DOT, directly observed therapy; LTBI, latent tuberculosis infection; TB, tuberculosis

[a]RPT is a long-acting rifamycin, and thus has similar adverse effects as RIF

[b]More common when a rifamycin is given intermittently (eg, weekly RPT)

[c]Risk is increased with age, alcohol use, and concurrent hepatotoxic drugs

[d]Breastfeeding is not contraindicated in people taking INH; the amount of INH in breast milk is inadequate for treatment of infants with LTBI

[e]For more information, check a drug interaction website

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A negative test result within the first 8 weeks after TB exposure (ie, the window period) does not rule out infection,[15] as the immune system may not yet have developed a response to the TB infection. Repeat testing after 8 weeks in these individuals with the same test used at baseline so as not to confound the results.

For all contacts who are children aged 5 years and younger or contacts who have HIV or other immunosuppressive conditions, regardless of the test result during the window period, initiate treatment for LTBI immediately after evaluation. For contacts aged between 5 and 15 years, treatment during the window period is at the physician's discretion. If the test for TB infection after the window period is negative, treatment should be discontinued unless the person is immunosuppressed. For contacts who are immunosuppressed, complete treatment regardless of age or history of previous LTBI treatment. The LTBI regimen will be determined, in part, by the drugs the person with immunosuppression is concomitantly taking.

Aside from the above-mentioned populations, if a contact has a positive test for TB infection at the end of the window period, evaluate for active TB. Once active TB is ruled out, treat for LTBI using a short-course regimen (**Tables 1** and **2**).

Pregnant and breastfeeding patients

Assess all pregnant patients for TB risk early in pregnancy (**Box 3**, page 2). If they are at risk for TB, test with IGRA (preferable) or TST.

If the test is positive, active TB disease must be ruled out using a chest x-ray, with an abdominal lead shield. The chest x-ray can be deferred until the second trimester, based on clinical judgment, in asymptomatic pregnant patients who are not immunocompromised; however, a chest x-ray should be done prior to delivery. Chest x-ray may be obtained in the first trimester based on epidemiological risk and clinical judgment (eg, pregnant patient with HIV infection or other immunosuppressive condition or recent close contact with a person with infectious TB).

For most pregnant patients, LTBI treatment may be deferred until 3 months' postpartum. Treatment may be considered in the first trimester for pregnant patients with HIV infection or other immunosuppression and those who are contacts of persons with infectious TB, based on epidemiological risk and clinical judgment. Pregnant patients with documented conversion of their TB test within the past 2 years may be considered for treatment in the second trimester.

Treat pregnant patients with either RIF for 4 months or INH for 6 to 9 months (**Tables 1** and **2**). Monitor patients closely during treatment for adverse effects, particularly among pregnant patients with HIV infection.[52] Pregnant patients taking INH should also receive 25 mg of vitamin B6 (pyridoxine). INH/RPT is contraindicated in people who are pregnant or breastfeeding.

Breastfeeding is not contraindicated during LTBI therapy with RIF or INH.[5] Infants whose mothers are receiving INH should receive vitamin B6 because they receive small amounts of the drug in breast milk[5]; infants who require INH therapy should receive their own therapeutic dose of INH and vitamin B6.

People with x-ray evidence of old, healed tuberculosis

Obtain sputum specimens for acid-fast bacilli smear and *M tuberculosis* culture from people with an abnormal chest x-ray consistent with previous TB and a positive test for TB infection. If clinical suspicion of TB disease is high, report the patient to the NYC Health Department and ask for

BOX 12. PROMOTING TREATMENT ADHERENCE AND COMPLETION

- At the start of treatment, provide written information about potential adverse effects of medications and whom to contact if adverse effects occur (**Resources**)
- Encourage the use of pillboxes, medication logs, and reminder apps
- Simplify the number of medications, dosing, and administration schedules
- Use video or in-person directly observed therapy when appropriate (eg, for the short-course isoniazid/rifapentine regimen)
  - Call the Tuberculosis Provider Hotline at 844-713-0559 for assistance with directly observed therapy and other questions
- Send reminder texts or call patients prior to appointments
- Follow up promptly on missed appointments
- Have patients bring in their medication bottle(s) and monitor pill counts
- At each visit, reinforce the importance of adherence and educate patients about potential adverse effects of medications

See** Improving Medication Adherence **for guidance

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consultation on how to proceed (**Resources**). Do not initiate treatment of LTBI until the cultures are confirmed negative.

REPORT TUBERCULOSIS

Report confirmed and presumptive active TB disease to the NYC Health Department, per Health Code regulations, within 24 hours[53] using NYCMED. LTBI must also be reported to the NYC Health Department for certain populations including children aged younger than 5 years.[53]

For children aged younger than 5 years, providers must[54]:

- report positive TB tests, including both qualitative and quantitative IGRA or TST results (including induration [in mm] if a TST is performed);
- provide documentation of subsequent evaluation to rule out TB disease, including chest x-ray and other relevant laboratory results; and
- report LTBI treatment regimen and start date.

Laboratories must report all positive, negative, indeterminate, and borderline IGRA results to the NYC Health Department.[55] See Health Code and Rules for an updated version of the NYC Health Code (§11.21) and Tuberculosis: Provider Resources for reporting instructions. In addition, report LTBI to the NYC Health Department if diagnosed among NYC residents applying for adjustment of status for permanent US residence.[56] See the Tuberculosis Technical Instructions for Civil Surgeons for guidance.

The use of brand names is for informational purposes only and does not imply endorsement by the New York City Health Department.

SUMMARY

TB is preventable. Identification, treatment, and management of people with LTBI is key to preventing TB disease and reducing TB rates in NYC.

- Test all patients at high risk for TB infection or disease.
- Prioritize testing and treatment of close contacts of people with infectious TB; people with HIV infection or other immunosuppressive conditions; and people who were born in or have traveled or resided in (≥1 month consecutively) areas with high TB case rates.
- Use TB test results, chest x-ray, and other medical and diagnostic evaluations, as needed, to rule out TB disease before initiating LTBI treatment (**Box 13**).
- Treat patients with LTBI using short-course regimens (eg, RIF, INH/RPT) to ensure timely completion, and monitor closely for adverse effects.
- Report TB infection test results and LTBI treatment as required by the NYC Health Code and other regulations.
- Access the NYC Health Department's TB website and Provider Hotline (844-713-0559) for resources and assistance with TB infection or disease.

BOX 13. ICD-10 CODES RELATED TO LTBI TESTING AND DIAGNOSIS

- Z11.7: Encounter for testing for LTBI
- Z86.15: Personal history of LTBI
- Z22.7: Diagnosis of LTBI
- R76.11: Nonspecific reaction to TST without active tuberculosis
- R76.12: Nonspecific reaction to cell-mediated immunity measurement of gamma interferon antigen response without active tuberculosis

See International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) for the complete list of ICD-10 codes

LTBI, latent tuberculosis infection; TST, Mantoux tuberculin skin test

RESOURCES FOR PROVIDERS

General Information

- Tuberculosis (TB) Provider Hotline: 844-713-0559

  Report cases of TB disease and LTBI per health code requirements, obtain expert medical consultation, refer patients to a TB Clinic
- New York City (NYC) Health Department. Tuberculosis provider resources: https://www1.nyc.gov/site/doh/providers/health-topics/tuberculosis.page

  Reporting requirements and information, information on testing, treatment, and patient follow-up, recent publications and clinical guidelines, discharge planning, referrals for directly observed therapy
- Centers for Disease Control and Prevention (CDC). Tuberculosis education and training: http://www.cdc.gov/tb/education/provider_edmaterials.htm

  Health care provider and TB program materials, patient education materials, continuing education activities, self-study modules, regional training and medical consultation centers

Training

- CDC. TB Education and Training Network: www.cdc.gov/tb/education/tbetn/default.htm
- The Global TB Institute at Rutgers, The State University of New Jersey: globaltb.njms.rutgers.edu

  One of the National TB Centers of Excellence for Training, Education, and Medical Consultation
- National Tuberculosis Controllers Association: http://www.tbcontrollers.org

Telehealth

- CDC. Managing healthcare operations during COVID-19: https://www.cdc.gov/coronavirus/2019-ncov/hcp/facility-planning-operations.html
- NYC Health Department. Telehealth Tips: https://www.familypathways.nyc
- NYC REACH. COVID-19 support for providers: http://nycreach.org/covid-19

Reporting

- NYC Health Department
  - NYCMED: https://a816-healthpsi.nyc.gov/NYCMED/Account/Login

    Reporting platform for NYC
  - Health Code and Rules: https://www1.nyc.gov/site/doh/about/about-doh/health-code-and-rules.page
- CDC. Tuberculosis Technical Instructions for Civil Surgeons: https://www.cdc.gov/immigrantrefugeehealth/civil-surgeons/tuberculosis.html

***City Health Information* archives:** https://www1.nyc.gov/site/doh/providers/resources/city-health-information-chi.page

- Improving Medication Adherence: https://www1.nyc.gov/assets/doh/downloads/pdf/chi/chi28-suppl4.pdf

RESOURCES FOR PATIENTS

General information

- NYC Health Department: Call 311 or visit www1.nyc.gov/site/doh/health/health-topics/tuberculosis.page for information on TB clinics and free patient education materials, including:
  - Taking Control of Your Tuberculosis: What to Expect and How to Stay Healthy

    https://www1.nyc.gov/assets/doh/downloads/pdf/tb/tuberculosis-taking-control.pdf (English)

    https://www1.nyc.gov/site/doh/health/health-topics/tuberculosis.page (other languages)

    Brochure with general information in easy-to-read format and multiple languages
  - You can help stop TB in NYC!

    http://www1.nyc.gov/assets/doh/downloads/pdf/tb/you-can-stop-tb.pdf (English)

    Educational poster with basic TB information, including illustrations with captions. For bulk orders or other languages, email tbtraining@health.nyc.gov or call 844-713-0559
- CDC. Patient and general public materials: https://www.cdc.gov/tb/education/patient_edmaterials.htm

TB testing and medical care site locator

- NYC Health Department. NYC Health Map: https://a816-healthpsi.nyc.gov/NYCHealthMap

Peer support

- National Tuberculosis Controllers Association. We are TB—tuberculosis survivors and advocates page: https://www.wearetb.com
- CDC. TB personal stories: https://www.cdc.gov/tb/topic/basics/personalstories.htm

Mental health and substance use

- NYC Well:
  - English: 888-NYC-WELL (888-692-9355), press 2
  - Spanish: 888-692-9355, press 3
  - Chinese : 888-692-9355, press 5
  - Relay service for deaf/hard of hearing: 711
  - https://nycwell.cityofnewyork.us

    A 24-7 call, text, and chat line for people seeking crisis counseling, including, but not limited to, suicide prevention, substance use services, peer support, short-term counseling, assistance scheduling appointments or accessing other mental health services, and follow-ups to ensure connection to care. Interpreters available in 200 languages

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City Health Information

nyc.gov/health

42-09 28th Street, Long Island City, NY 11101

E-mail *City Health Information* at AskCHI@health.nyc.gov
New York City Department of Health and Mental Hygiene. Testing for and treating latent tuberculosis infection. *City Health Information.* 2021;40(1):1-14.

ASK CHI

Have questions or comments about latent tuberculosis?

Email

AskCHI@health.nyc.gov

CONTINUING MEDICAL EDUCATION ACTIVITY

Instructions

1. Log in to the CME portal at http://bit.ly/3YF8cHH

   If this is your first time logging into the CME portal, you will need to create a user ID and password. To set this up, click on "Existing Account (Non-NYC Health + Hospitals User)". Then click on "Create one now!" Or use this link to go directly to "Create a Profile": bit.ly/3YnpRob
2. Click on "Activity Listing" in the upper right corner and select "Enduring Material (Recorded or written online activity)".
3. Find "City Health Information (CHI): Testing for and Treating Latent Tuberculosis Infection" in the course list.
4. Click on "Enroll" and follow instructions to complete pre-test, view material, and complete post-test and evaluation. To receive CME credit, you must score at least 80% on the post-test and answer all evaluation questions.
5. Click "Print Session Certificate" to claim your credit and access the certificate.

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