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TESTING AND TREATMENT FOR LATENT TB INFECTION

- Target TB testing to those at high risk for infection or development of active TB disease.
- Rule out active TB disease in all people who have a positive test for TB infection.
- Treat high-risk people with latent TB infection, regardless of age.
- Monitor patients monthly and promote adherence to treatment.

Despite dramatic declines in active tuberculosis (TB) cases for more than a decade, many New Yorkers with latent TB infection (LTBI) remain undiagnosed and untreated! Without treatment, approximately 5% to 10% of immunocompetent people with LTBI will develop active TB disease. People with LTBI who are HIV infected have a much higher risk.²⁻⁴ Other groups are also at high risk for developing active TB disease, including those who have recently been infected with *Mycobacterium tuberculosis*.⁵

Although many individuals start treatment for LTBI, more than half do not complete it. It is essential that health care providers promote adherence to increase treatment completion.

In New York City, recent health department data show:

- Approximately 15% of all people with active TB are HIV infected. TB is a common but preventable opportunistic infection among HIV-positive people.
- About one-third of contacts of people with active TB disease have latent TB infection (LTBI).
- People born outside the U.S. account for more than two-thirds of reported TB cases.
- About 40% of all non-U.S.-born adults have LTBI.

TB is a serious and contagious disease.

Toward a Tuberculosis-Free NYC

Guidelines for LTBI Testing and Treatment

The following guidelines and corresponding steps are recommended to improve both diagnosis and treatment of LTBI.

1. Test people at high risk for TB.

Target testing to (1) those who are likely to be recently infected with *M. tuberculosis*; and (2) those who, if infected, are at high risk of developing active TB due to clinical conditions that substantially increase their risk^{5,6} (Step 1).

A decision to test is a commitment to treat! Test for TB infection only in settings where there are effective plans to monitor and ensure treatment.

Routine testing of people at **low risk** for LTBI or TB disease is **not recommended**.⁵ In some instances, however, testing of such individuals may be necessary to meet state and local requirements. LTBI testing is required of certain children and adolescents by the New York City (NYC) Health Code (see “*TB and the Law*” document at: www.nyc.gov/html/doh/downloads/pdf/tb/tb-law.pdf).

2. Test high-risk people regardless of BCG vaccination history.

Do not consider a history of BCG vaccination when deciding to test a patient, or when determining whether

the test result is positive. The individual’s risk factors will determine how to interpret the tuberculin skin test (TST) (Step 2).

Although prior BCG vaccination can cause a false positive cross-reaction to the TST, an individual’s sensitivity to tuberculin is highly variable and tends to decrease over time.⁷ The TST does not distinguish between BCG-induced sensitivity and true LTBI.

3. Explore your testing options.

QuantiFERON®-TB Gold (QFT-G),* a new blood-based test, is a possible alternative to the TST and will be piloted at select NYC Department of Health and Mental Hygiene (DOHMH) Chest Centers during the summer of 2006. Once the QFT-G is widely available, either it or the TST, performed by the Mantoux method, can be used.

The FDA-approved QFT-G measures a cell-mediated immune response to two proteins that are made by *M. tuberculosis*. These proteins are absent from all BCG vaccine preparations and environmental nontuberculous mycobacteria (NTM), except for *M. kansasii*, *M. marinum*, and *M. szulgai*. As a result, the QFT-G should be unaffected by BCG vaccination status and sensitization to most NTMs, and thus may be a more accurate test for TB infection.⁸⁻¹⁰

Table 1. A Comparison of Blood-based Testing and Skin Testing for Diagnosing LTBI

QuantiFERON®-TB Gold	vs.	Tuberculin Skin Test
<ul style="list-style-type: none"> • <i>in vitro</i>, controlled laboratory test with minimal inter-reader variability • TB-specific antigens used • no boosting; 2-step testing not needed • unaffected by BCG or most environmental mycobacteria • usually a simple positive/negative result • blood samples must be processed within 12 hours of blood draw • ability to predict the risk of LTBI progression to TB disease has not yet been determined in high-risk patients • 1 patient visit possible 		<ul style="list-style-type: none"> • <i>in vivo</i>, subject to errors during implantation and interpretation • less specific PPD antigen used • boosting with repeated testing • false positive tests occur after BCG and environmental mycobacteria exposure • interpretation based on patient’s relative risk for TB exposure or development of disease • risk of developing TB if TST is positive extensively studied and well-defined in high-risk groups • 2 patient visits minimum

* Use of brand names is for informational purposes only and does not imply endorsement by the New York City Department of Health and Mental Hygiene.

STEP 1: Know Whom to Test for LTBI

Individuals Who May Have Been Recently Infected

- Test close contacts of people with active TB disease; retesting may be necessary 8 weeks after original test.¹⁸
- Test people who have immigrated within the past 5 years from areas with high TB rates.* These individuals should be tested the first time they enter the health care system in the US.
- Test people with a prolonged stay (>1 month) in areas with high TB rates.* Test these patients 8 weeks after they return.
- Test people who live or work in clinical or institutional settings where TB exposure may be likely (e.g., hospitals, prisons, homeless shelters, SROs, nursing homes, mycobacteriology labs); most CDC and local guidelines recommend testing annually.^{33,34}
- Test children/adolescents exposed to adults in high-risk categories.

Individuals With Clinical Conditions Associated with Progression from LTBI to Active TB Disease

- Test people with HIV infection as soon as possible after diagnosis of HIV infection and at least once a year thereafter.
- Test injection drug users.
- Test people with evidence of old, healed TB lesions on a chest x-ray (CXR).
- Test underweight people ($\geq 10\%$ under ideal body weight, or a BMI <18.5).
- Test people with certain medical conditions (e.g., silicosis, chronic renal failure, diabetes, some cancers, gastrectomy/jejunioileal bypass).
- Test people receiving immunosuppressive therapy (e.g., prolonged corticosteroid therapy [the equivalent of >15 mg/d of prednisone for one month or more], and tumor necrosis factor alpha (TNF- α) blockers. Two-step skin testing may increase yield of people with LTBI.

* Countries/Areas with an Estimated or Reported High Incidence of TB, 2004³⁵

Africa – All countries except Seychelles; **Eastern Mediterranean** – Afghanistan, Bahrain, Djibouti, Egypt, Iraq, Morocco, Pakistan, Qatar, Somalia, Sudan, Yemen; **Europe** – Armenia, Azerbaij n, Belarus, Bosnia & Herzegovina, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan, Ukraine, Uzbekistan; **North, Central and South America** – Belize, Bolivia, Brasil, Colombia, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname; **Southeast Asia** – Bangladesh, Bhutan, India, Indonesia, Korea DPR (North), Maldives, Myanmar (formally Burma), Nepal, Sri Lanka, Thailand, Timor-Leste; **Western Pacific** – Brunei Darussalam, Cambodia, China (including Hong Kong), Guam, Kiribati, Korea South, Lao PDR (Laos), Macao (China), Malaysia, Marshall Islands, Micronesia, Mongolia, New Caledonia, Northern Mariana Islands, Palau, Papua New Guinea, Philippines, Solomon Islands, Vanuatu, Vietnam

Recent guidelines from the Centers for Disease Control and Prevention (CDC) state that the QFT-G can be used to assess for LTBI in anyone who is a candidate for TB testing, including children, pregnant women, and HIV-infected and other immunocompromised people, although these groups have not yet been adequately studied.¹¹

4. Determine if the test result is positive.

Record TST results as millimeters (mm) of induration; if there is no induration, record the result as “0 mm.” The 3 cutoff points for defining a positive TST result are: ≥ 5 , ≥ 10 , and ≥ 15 mm of induration (**Step 2**).

If the QFT-G is used, a positive reaction is determined

by a positive/negative interpretation provided by the laboratory (**Step 2**).

If an individual tests negative for TB infection, it is usually not necessary to retest (**Step 1**). However, if a person develops a new risk factor, retesting may be necessary. Also, people remaining in high-risk settings should be periodically retested.

Provide patients with positive results indicating TB infection and encourage them to keep results for their personal medical records. Repeat testing is not necessary once a TST or blood-based test is determined to be positive. However, patients should be tested if they cannot provide documentation of a prior positive test.

STEP 2: Determine if the Test Result Is Positive

The reaction to *tuberculin skin test (TST)* is classified as positive based on the individual's risk factor(s) and the following size of induration:

≥ 5 mm for

- people with HIV infection
- recent contacts of people with active TB disease
- people with evidence of old, healed TB lesions on CXR
- patients with organ transplants and other immunosuppressed people, such as patients receiving prolonged corticosteroid therapy (the equivalent of >15 mg/d of prednisone for one month or more) and TNF- α blockers

≥ 10 mm for

- people who have immigrated within the past 5 years from areas with high TB rates (**Step 1**)
- injection drug users
- people who live or work in institutional settings where exposure to TB may be likely (e.g., hospitals, prisons, homeless shelters, SROs, nursing homes)
- mycobacteriology laboratory personnel
- people with clinical conditions associated with increased risk of progression to active TB, including
 - silicosis
 - chronic renal failure
 - diabetes
 - gastrectomy/jejunioileal bypass
 - some hematologic disorders such as leukemias or lymphomas, and specific malignancies such as carcinoma of the head, neck, or lung
- body weight $\geq 10\%$ below ideal or BMI <18.5
- children <5 years of age
- children/adolescents exposed to adults in high-risk categories
- people with prolonged stay (>1 month) in areas with high TB rates (**Step 1**)

≥ 15 mm for

- people at low risk for active TB disease for whom testing is not generally indicated

Guidelines for the interpretation of the QuantiFERON®-TB Gold (QFT-G):

Negative

Same interpretation as negative TST. No further TB evaluation is needed unless indicated by clinical judgment.

Positive

Same interpretation as positive TST. Medical evaluation and CXR are needed to exclude active TB disease and confirm LTBI.

Indeterminate

Test failure. Repeat QFT-G or administer TST as diagnostic aide for TB or LTBI. QFT-G results may be indeterminate due to laboratory error or patient energy. If two different specimens from a patient yield indeterminate results, do not repeat QFT-G for that person.

5. Rule out active TB disease in patients who test positive for TB infection.

Eliminate the possibility of active TB disease (pulmonary or extra pulmonary) before treating patients for LTBI. Evaluate patients with a newly identified positive test for active TB disease with a medical examination and a chest x-ray (CXR). If the patient has no symptoms consistent with active TB and the CXR is negative for active TB, evaluate for treatment of LTBI. Evaluate individuals with TB symptoms or an abnormal CXR by obtaining sputum samples for microscopic examination and culture, and performing other tests as indicated.

Report all suspected cases to the NYC DOHMH.

Children younger than 5 years with positive TB tests should also be reported. Reporting requirements and contact information can be found at: www.nyc.gov/html/doh/downloads/pdf/tb/tb-reporting-requirements.pdf.

6. Provide treatment for high-risk individuals diagnosed with LTBI regardless of age.

- **There are 2 recommended regimens for the treatment of LTBI (Step 3).** A 9-month regimen of isoniazid (INH) is the preferred option for treatment of LTBI in all patients.^{5,12} A 4-month rifampin regimen (6 months in children) is the preferred regimen for individuals exposed to INH-resistant TB, and is an acceptable alternative, especially if patients have adverse reactions to INH or are unlikely to complete a 9-month INH regimen.^{5,13}
- **The 2-month regimen containing rifampin and pyrazinamide for LTBI treatment is no longer recommended** due to the unacceptable rates of hepatitis, hospitalization, and death from liver injury associated with this regimen.¹⁴⁻¹⁷
- **People infected with HIV and children younger than 5 years who have had close contact with people with active TB disease** should receive a baseline test, a CXR, and a medical examination immediately after exposure is identified.¹⁸ Even if a baseline test is negative and active TB disease is ruled out, individuals in both groups should begin treatment for presumed LTBI. Because it can take up to 8 weeks after

M. tuberculosis infection for the immune system to respond, close contacts should be retested 8 weeks after their exposure (**Step 1**). If the test result remains negative, treatment for LTBI should be discontinued in children under the age of 5. However, regardless of test result, infants should remain on treatment until they are at least 6 months old and at least 8 weeks have passed since their last exposure to the active TB case before being tested again. Treatment of HIV-infected individuals should continue regardless of age.

- **Individuals with immunosuppressive conditions and those being treated with immunosuppressive agents** should be evaluated and treated for LTBI at the time their condition is diagnosed or before starting treatment with immunosuppressive therapies. Such therapies include prolonged corticosteroids (the equivalent of >15 mg/d of prednisone for one month or more) and tumor necrosis factor alpha (TNF- α) antagonists. Patients awaiting transplants should also be evaluated and treated for LTBI.
- **The risk of INH toxicity increases with age, especially in those 55 and older.**^{19,20} Closely monitor older patients for INH toxicity and consider excluding from treatment those whose only risk factor is recent immigration. However, patients who have had contact with people with active TB disease and/or who have clinical conditions associated with increased risk of progression to active TB disease should be treated regardless of age.
- **Diabetes** has been shown to increase the risk of progressing from LTBI to active TB disease; the data are most convincing for insulin-dependent diabetes and people with poorly controlled disease.^{21,22} Such individuals who test positive for TB infection should be treated for LTBI regardless of age.²³
- **Adults not at high risk** for developing active TB disease but who have inadvertently been tested should generally not be considered for treatment, even if the test result is positive. If subsequent risk factors for developing the disease arise, the patient should be evaluated for treatment. However, treatment for LTBI is generally recommended for children diagnosed with LTBI, regardless of risk factors.²⁴

STEP 3: Treat Latent TB Infection

Drug and Duration	Dosage		Major Adverse Reactions	Comments
	Daily	Twice Weekly		
Isoniazid (INH) Children (C): 9 months <hr/> Adults (A): 9 months	C: 5-10 mg/kg* (max 300 mg) A: 5 mg/kg (max 300 mg) Completion Criteria 270 doses within 12 months	C: 20 mg/kg (max 900 mg) A: 15 mg/kg (max 900 mg) Completion Criteria 76 doses within 12 months	Symptoms include: unexplained anorexia, nausea, vomiting, dark urine, jaundice, persistent fatigue, weakness, abdominal pain (especially right upper quadrant discomfort), easy bruising or bleeding, rash, persistent paresthesias of the hands and feet, and arthralgia. Potential complications include: hepatic enzyme elevation, hepatitis, icterus, rash, peripheral neuropathy, increased phenytoin levels, possible interaction with disulfiram (Antabuse®).	INH is the preferred regimen for most individuals. Vitamin B ₆ (pyridoxine), 25 mg/day may decrease peripheral and CNS effects and should be used in patients who are <ul style="list-style-type: none"> • abusing alcohol • pregnant • breastfeeding infants on INH • malnourished or in patients who have <ul style="list-style-type: none"> • HIV • cancer • chronic renal or liver disease • diabetes • pre-existing peripheral neuropathy Aluminum-containing antacids should be avoided — they reduce absorption of INH.
Rifampin (RIF) C: 6 months A: 4 months	C: 10-20 [†] mg/kg (max 600 mg) Completion Criteria 182 doses within 9 months A: 8-12 mg/kg (max 600 mg) Completion Criteria 120 doses within 6 months	C: Not recommended A: 8-12 mg/kg (max 600 mg) [‡] Completion Criteria 34 doses within 6 months	Symptoms include: nausea, vomiting, loss of appetite, rash, fever or flu-like symptoms, easy bruising. Potential complications include: hepatic enzyme elevation, hepatitis, rash, thrombocytopenia. RIF reduces levels of many drugs, including methadone, warfarin, oral contraceptives, oral hypoglycemic agents, theophylline, dapsone, ketoconazole, protease inhibitors (PIs), and non-nucleoside reverse transcriptase inhibitors (NNRTIs).	RIF may be used to treat persons who have been exposed to INH-resistant, rifampin-susceptible TB, who have severe toxicity to INH, or who are unlikely to be available for monitoring and follow-up for more than 4-6 months. Orange discoloration may occur in contact lenses and body secretions such as tears and urine. Patients receiving methadone will need their methadone dosage increased by an average of 50% to avoid opioid withdrawal. RIF may make glucose control more difficult in diabetics. It is contraindicated for patients taking most PIs and NNRTIs. [§] Patients should be advised to use barrier contraceptives while on RIF.

STEP 3: Treat Latent TB Infection (cont.)

Drug and Duration	Dosage		Major Adverse Reactions	Comments
	Daily	Twice Weekly		
Rifabutin (RBT) C: 6 months A: 4 months	C: 5 mg/kg (max 300 mg) (little data) Completion Criteria 182 doses within 9 months A: 5 mg/kg (max 300 mg) Completion Criteria 120 doses within 6 months	C: Not recommended A: 5 mg/kg (max 300 mg)† Completion Criteria 34 doses within 6 months	Symptoms include: stomach upset, chest pain, nausea, vomiting, headache, rash, muscle aches, eye redness and pain. Potential complications include: hepatic enzyme elevation, hepatitis, neutropenia, thrombocytopenia, uveitis. RBT reduces levels of many drugs including protease inhibitors, NNRTIs, dapsone, ketoconazole, and oral contraceptives. However, some drugs, including protease inhibitors and some NNRTIs increase levels of RBT.	RBT may be used to treat LTBI in HIV-infected persons who fit the criteria for RIF treatment but for whom RIF is contraindicated, or for patients who need a rifamycin but are intolerant to RIF. Orange discoloration may occur in contact lenses and body secretions such as tears and urine. For HIV-infected persons, adjust the daily or intermittent dose of RBT. Monitor patients for decreased antiretroviral activity and for RBT toxicity if taken concurrently with PIs and NNRTIs.§ Methadone dosage generally does not need to be increased. Patients should be advised to use barrier contraceptives while on RBT.

*World Health Organization (WHO), International Union Against TB and Lung Disease (IUATLD), and British Thoracic Society (BTS) recommend 5 mg/kg in children; CDC/ATS and the American Academy of Pediatrics recommend 10 mg/kg (Frieden T, Sterling T, Munsiff S, Watt C, Dye C. Tuberculosis. *Lancet*. 2003 September 13;362(9387):887-899).

†(Ibid.)WHO, IUATLD, and BTS recommend 10 mg/kg in children; CDC/ATS and the American Academy of Pediatrics recommend 10-20 mg/kg.

‡There are very little data or clinical experience on the use of intermittent treatment of latent TB infection with rifampin or rifabutin. These regimens should be used with caution.

§Please see the NYC Bureau of TB Control's HIV/TB "Antiretroviral Drugs and Treatment of Tuberculosis Guidelines" at: www.nyc.gov/html/doh/downloads/pdf/tb/tbanti.pdf.

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7. Take special care when testing and treating HIV-infected individuals.

HIV-infected people are at markedly increased risk for developing active TB disease once infected.^{3,4} Completion of treatment for LTBI is a potentially life-saving intervention.

HIV-positive people who have recently had close contact with an active TB patient should receive treatment for LTBI regardless of age, test results for TB infection, or history of previous treatment for LTBI²⁵ (**Step 3 and Guideline 6**).

HIV-positive individuals with a history of prior untreated

STEP 3a: Adjust Treatment in HIV-positive Patients Taking Antiretroviral Agents

Generic Name	Brand Name	OK with rifampin?	OK with rifabutin?*
Protease Inhibitors (PIs)			
amprenavir (AMP)	Agenerase®	no	yes
atazanavir (TAZ)	Reyataz®	no	yes
fos-amprenavir (fos-AMP)	Lexiva®	no	yes
indinavir (IDV)	Crixivan®	no	yes
lopinavir/ritonavir (LPV/r)	Kaletra®	no	yes
nelfinavir (NFV)	Viracept®	no	yes
ritonavir (RTV)	Norvir®	no	yes
saquinavir (SQV)	Invirase® Fortovase®	no	no
Tipranavir/ritonavir (TPV/r)	Aptivus® and Norvir®	no	yes
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)			
delavirdine (DLV)	Rescriptor®	no	no
efavirenz (EFV)†	Sustiva®	yes	yes
nevirapine (NVP)	Viramune®	yes‡	yes

* When antiretrovirals are used with rifabutin (RBT), the dosage of the PI, NNRTI, and/or rifabutin may need to be adjusted. Please refer to the latest edition of "Antiretroviral Drugs and Treatment of Tuberculosis Guidelines" at www.nyc.gov/html/doh/downloads/pdf/tb/tbanti.pdf.

RBT dosage and frequency vary depending on the PI or NNRTI being used.

With EFV: RBT 450-600 mg daily or 600 mg 2 or 3 times per week. (EFV dose is unchanged with RBT).

With NVP: RBT 300 mg either daily or 2 or 3 times per week.

With IDV, NFV, AMP, TAZ, or fos-AMP: RBT 150 mg daily or 300 mg 2 or 3 times per week.

With LPV/r and TPV/r: RBT 150 mg 3 times per week. (In patients being treated for active TB, the other anti-TB drugs should be given daily in the intensive phase for patients with a CD4 count <100 cells).

With RBT: increase NFV to 1000 mg 3 times/day or use standard BID dose; increase IDV to 1000 mg 3 times/day.

† With rifampin: increase EFV dose to 800 mg daily (EFV dose is unchanged with rifabutin).

‡ Under limited circumstances. Refer to the following Web site: www.nyc.gov/html/doh/downloads/pdf/tb/tbanti.pdf.

Antiretroviral drugs that do not belong to the above categories are considered safe to use with rifampin and rifabutin. These include: abacavir (ABC)– Ziagen®; didanosine (ddI)– Videx®; emtricitabine (FTC)– Emtriva®; enfuvirtide (T-20)– Fuzeon®; lamivudine (3TC)– Epivir®; stavudine (d4T)– Zerit®; tenofovir (TDF)– Viread®; zalcitabine (ddC)– Hivid®; zidovudine (AZT)– Retrovir®; AZT+3TC– Combivir®; ABC+AZT+3TC– Trizivir®; FTC +TDF– Truvada®.

or inadequately treated TB disease should be re-evaluated for active disease regardless of age or test results for TB infection. If active TB disease is ruled out, patients should still receive treatment for old, healed TB, or for LTBI.

The 9-month INH regimen may be administered concurrently with any antiretroviral regimen used to treat HIV infection.²⁶ Rifampin or rifabutin can be used with

selected antiretroviral drugs²⁷ (Step 3a). However, information on interactions between rifamycins and antiretroviral drugs is constantly evolving with the emergence of new drugs and data. Therefore, clinicians should obtain the most current information regarding TB and HIV drug interactions.^{26,27}

8. Carefully consider treatment for the following groups.

Pregnant women

Pregnant women should receive a test for TB infection only if they are in a high-risk category. Although the need for treatment of active TB disease during pregnancy is unquestioned, the treatment of LTBI in pregnant women is controversial because the risk of isoniazid hepatotoxicity must be weighed against the risk of developing active TB. In general, it is recommended that treatment of LTBI be delayed until 2 or 3 months after delivery. However, for women who are HIV-positive or who have been recently infected, therapy should be given regardless of the trimester of pregnancy.⁵

The preferred regimen for treatment of LTBI in pregnant women is INH⁵ (**Step 3**). Extensive use of INH to treat pregnant women has indicated that the drug is not teratogenic, even when given during the first trimester of pregnancy. Pregnant women taking INH should receive vitamin B₆ (pyridoxine), 25 mg for each 300 mg of INH.

Breastfeeding is not contraindicated when the mother is being treated for LTBI. Vitamin B₆ is not indicated in nursing infants unless the baby is also receiving INH.⁵

Children

All children classified as having LTBI should be treated for LTBI after active disease is ruled out.^{24,28} Treatment is recommended for all children and adolescents diagnosed with LTBI because:

- the drugs used are safe in the pediatric population;
- infection with *M. tuberculosis* is more likely to have been recent;
- children 5 years or younger are at higher risk for progression to active TB disease;
- the pediatric population has more years to develop active TB.

The recommended regimen for children with or without HIV infection is 9 months of INH. The risk for isoniazid-related hepatitis is extremely low in infants and

Call the TB Provider Hotline (212) 788-4162 (Mon–Fri 8:30 a.m.–5 p.m.)

- To report cases and obtain forms
- To access patient information from the TB registry for patients in your care
- To obtain expert medical consultation
- To get more information about TB services
- To refer patients for testing or treatment

Call 311

- For free public education materials — pamphlets, brochures, and fact sheets
- To find local Chest Centers and to learn about available services and hours of operation

Visit nyc.gov/health/tb

- To get current clinical guidelines on TB screening, diagnosis, and treatment
- For TB-related reporting forms
- To access online TB reporting

children. Children who have been exposed to a person with INH-resistant, rifampin-susceptible TB, or who are intolerant to INH, should be treated with 6 months of rifampin (**Step 3**). Vitamin B₆ (pyridoxine), 25 mg for each 300 mg of INH, should be given to undernourished or HIV-infected children treated with INH.^{24,28}

New converters

People whose test for TB infection has converted to positive (≥ 10 mm increase is considered conversion for TSTs) within the past 2 years are considered to have been recently infected and are at high risk for developing active TB disease. They should be considered for LTBI treatment once active disease is ruled out.⁵

Close contacts of people with MDRTB

Individuals infected by patients with active multi-drug-resistant TB (MDRTB) should be evaluated for an alternative regimen for LTBI according to their age and immune status. Such patients are unlikely to benefit from treatment with isoniazid or rifampin; there-

fore, a regimen containing other drugs active against the particular strain of *M. tuberculosis* should be considered. Expert consultation should be sought for these patients.^{29,30} All people exposed to MDRTB should be followed for at least two years, irrespective of treatment. For further information please contact the NYC TB provider hotline: (212) 788-4162.

Individuals with evidence of old, healed TB on CXR

For asymptomatic individuals who have a TST reaction ≥ 5 mm or a positive blood test for TB infection, plus a CXR that shows noncalcified fibrotic lesions suggestive of old, healed TB, the decision to treat is based on several factors. These include clinical suspicion for active TB, prior TB treatment history, sputum results, and repeat CXR. These patients should be evaluated for active TB with a physical exam, CXR, and sputum samples obtained for microscopic examination and culture. If active TB is ruled out, they should be treated for old TB with a 4-month multidrug regimen.^{30,31}

9. Monitor all patients carefully during LTBI treatment.

Obtain baseline hepatic enzymes for all patients over the age of 35 being treated for LTBI; all HIV-infected people; pregnant and postpartum women (up to 3 months postpartum); those with history of hepatitis, liver disease, or alcohol abuse; injection drug users; and those being treated with other potentially hepatotoxic agents.^{5,30,32}

Monitor all patients monthly with a directed clinical exam for potential complications (**Step 3**). Monthly liver enzymes should be obtained for all of the above risk groups, excluding all people over the age of 35 with normal baseline liver enzymes. A baseline complete blood count (CBC) with platelets should be done on anyone prescribed a rifamycin-containing regimen.

Patients should be educated about potential complications, symptoms of adverse drug reactions, and the need for clinical evaluation and prompt cessation of treatment if adverse symptoms occur. Appropriate educational materials in the patient's language should be provided at the initiation of treatment (**see Resources**).

10. Promote treatment adherence.

Many people with LTBI do not realize the urgency to continue prolonged treatment due to either a lack of symptoms or to the potential adverse effects of drug treatment.⁶ Patients need to be encouraged to return monthly for follow-up visits, and providers need to educate patients about both the potential adverse effects of treatment and the importance of treatment adherence and completion (**Step 4**).

If interruptions in treatment occur, patients can be given 2 to 3 additional months to complete the regimen.^{5,30} A decision regarding completion of treatment should be based on the total number of medication doses administered as well as the duration of therapy (**Step 3**). For those on INH, treatment may need to be restarted if there is a gap of more than 3 months unless more than 6 months of treatment have already been completed. In that case, treatment should be considered complete. ♦

STEP 4: Promote Adherence during LTBI Treatment

Providers should use various measures to assess and promote adherence during the initial visit and monthly follow-ups.

- Use directly observed therapy (DOT) for LTBI when available, especially for children, contacts of active TB disease cases, and HIV-infected persons. DOT can be performed at many locations such as clinics, schools, homes, work sites, and day care programs.
- Provide written information about potential adverse effects of the medications at the start of treatment.
- Provide incentives and other enablers, such as MetroCards for assistance with transportation.
- Send reminder letters or call patients prior to appointments.
- Follow up promptly on missed appointments to prevent interruption or cessation of treatment.
- Minimize wait time at follow-up visits.
- Ask patients at monthly visits about the number of missed pills in the past week.
- Remind patients to bring in the medication bottle(s) and monitor pill counts.
- During each monthly visit, reiterate the importance of adherence and educate patients about potential adverse effects of medication.

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RESOURCES

For Clinicians

Call 311 for

- Tuberculosis Services in New York City: A quick guide for health care providers (booklet). *Also available at:* www.nyc.gov/html/doh/downloads/pdf/tb/tb-hcp-serviceguide.pdf
- The Mantoux Tuberculin Skin Test A Guide for Providers (laminated 2-page tool). *Also available at:* www.nyc.gov/html/doh/downloads/pdf/tb/tb-hcp-tst-guide.pdf

Online Resources

- Many state-of-the-art clinical guidelines, tools, and resources are available at: www.nyc.gov/html/doh/html/tb/tb-hcp.shtml
- Tuberculin Skin Test: Pediatric and Adolescent Risk Assessment Questionnaire (poster and card). *Available at:* www.harlemtbcenter.org/prods.htm
- Improving Completion Rates for Treatment of LTBI in Children and Adolescents. *Available at:* www.harlemtbcenter.org/prods.htm

For Patients

Call 311 or visit www.nyc.gov/health for

- Learn About Tuberculosis: What Everyone Should Know (Booklet) *Available in English and Spanish, and coming soon in Bengali, Chinese, French, Haitian Creole, Hindi, Korean, Russian, and Urdu*
- Friends Forever: A Triumph Over TB (Comic Book)

Charles P. Felton National TB Center at Harlem
www.harlemtbcenter.org/prods.htm

- Pediatric Calendar for LTBI Completion (booklet)



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CME Activity – Testing and Treatment for Latent Tuberculosis Infection

1. A 35-year-old HIV-infected male receives a TST. At what induration would he be considered to have latent TB infection?

- A. ≥ 0 mm
- B. ≥ 5 mm
- C. ≥ 10 mm
- D. ≥ 15 mm

2. Which of the following statements is NOT true?

- A. Even when the test result is positive, adults should not be considered for treatment unless they are at high risk for developing TB disease.
- B. People who have received the BCG vaccine will always have a positive TST for latent TB infection.
- C. The risk of INH toxicity is greater in persons 55 years and older.
- D. Many people who start treatment for LTBI do not go on to complete treatment.

3. A 55-year-old HIV-infected female has a tuberculin skin reaction of 10mm, a normal CXR, and no symptoms of TB. Patient is on highly active antiretroviral therapy (HAART) regimen of Kaletra® and Combivir®. Which is the preferred LTBI regimen for this patient?

- A. Isoniazid for 9 months.
- B. Rifampin daily for 4 months.
- C. Rifabutin daily for 4 months.
- D. Rifampin and pyrazinamide for 2 months.
- E. Patient does not need treatment.

4. The following statements are all advantages of the QFT-G blood-based test for TB infection EXCEPT:

- A. Results of the QFT-G are usually simple to interpret as positive or negative.
- B. QFT-G has been extensively studied in all groups at high risk for TB infection.
- C. QFT-G is unaffected by BCG.
- D. Blood-based tests are considered more accurate than TSTs.

5. Which of the following patient characteristics place(s) a patient at high risk for LTBI, and therefore is/are an indication for testing? (check all that apply):

- A. Patient recently moved to New York from Mexico.
- B. Patient is a chronic smoker.
- C. Patient has been incarcerated.
- D. Patient has a medical history of asthma.
- E. Patient has a medical history of diabetes.

6. How well did this continuing education activity achieve its educational objectives?

- A. Very well
- B. Adequately
- C. Poorly

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Instructions

Read this issue of *City Health Information* for the correct answers to questions. To receive continuing education credit, you must answer 4 of the first 5 questions correctly.

To Submit by Mail

1. Complete all information on the response card, including your name, degree, mailing address, telephone number, and e-mail address. PLEASE PRINT LEGIBLY.
2. Select your answers to the questions and check the corresponding boxes on the response card.
3. Return the response card (or a photocopy) postmarked **no later than April 30, 2007**. Mail to:

CME/CNE Administrator, NYC Dept. of Health and Mental Hygiene,
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Visit www.nyc.gov/html/doh/html/chi/chi.html to complete this activity online. Your responses will be graded immediately, and you can print out your certificate.

Continuing Education Activity Testing and Treatment for Latent TB Infection

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Objectives

At the conclusion of the course, the participants should:

1. Be familiar with new guidelines and diagnostic options in the prevention of TB.
2. Know the 10 guidelines for testing and treating LTBI.
3. Be able to identify the high-risk groups who should be tested for LTBI, as well as the high-risk groups who are more likely to progress to active TB disease.
4. Know whom to treat for LTBI, as well as the recommended treatment options for LTBI for both HIV-positive and HIV-negative patients.

Accreditation

The DOHMH is accredited by the Medical Society of the State of New York to sponsor continuing medical education for physicians. This continuing medical education activity is designated for a maximum of 2 hours in Category One credit toward the AMA/PRA (Physician's Recognition Award). Each physician should claim only those hours of credit that were spent on the educational activity.

Participants are required to submit name, address, and professional degree. This information will be maintained in the Department's CME program database.

If you request, the CME Program will verify your participation and whether you passed the exam.

We will not share information with other organizations without your permission, except in certain emergencies when communication with health care providers is deemed by the public health agencies to be essential or when required by law. Participants who provide e-mail addresses may receive electronic announcements from the Department about future CME activities as well as other public health information.

The Continuing Nursing Education (CNE) activity is open to nurses. The DOHMH is an approved provider of continuing education by the New York State Nurses Association, which is accredited as an approver of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation. A total of 2.4 contact hours will be awarded to nurses for participation in this activity.

Participants must submit the accompanying exam by April 30, 2007.

CME Activity Faculty:

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Dworkin F, MD.

All faculty are affiliated with New York City DOHMH, Division of Disease Control.

The faculty does not have any financial arrangements or affiliations with any commercial entities whose products, research, or services may be discussed in these materials.



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