Newcomer Tuberculosis Guidance for Health Professionals

Many people who have recently arrived in Minnesota have lived in or traveled through countries in regions with high rates of tuberculosis (TB), such as Latin America (South and Central America, Mexico, and the Caribbean), Africa, Asia, and Eastern Europe. The following concise guide is intended for primary care providers caring for newcomers who may be at risk for TB and is not meant as a substitute for detailed TB guidelines.

Identifying Persons from High TB Burden Countries

Approximately 70% of TB cases in the United States occur in non-U.S. born persons.[1] The top five countries of birth of non-U.S. born persons with TB in the U.S. in 2022 were, in order: Mexico, the Philippines, India, Vietnam, and China. In Minnesota, the highest proportion of TB cases in non-U.S. born persons from 2018-2022 have been seen in persons born in East Africa (Somalia, Ethiopia, Kenya), Southeast Asia (Laos, Vietnam), and South Asia (India); however, we are beginning to see an increase in cases (2023) in new arrivals from Latin America, particularly Ecuador, with cases also seen in arrivals from Colombia, Mexico, Venezuela, and Guatemala.

TB Screening for Newcomers

Screening should be performed for all newcomers who have lived (born in or traveled to for more than a month) in **Latin America, (South and Central America, Mexico, and the Caribbean), Eastern Europe, Africa, or Asia.** The goals of screening are to 1) rapidly identify and refer for treatment those with suspected or confirmed active TB disease and 2) diagnose and prioritize for treatment those with latent TB infection (LTBI).

Screening:

- **History:** prior diagnosis of or treatment for active TB or LTBI, known contact to active TB, HIV or other immunosuppression, congregate setting, health care worker.
- **Symptoms**: fever, persistent cough for three weeks or more, chest pain, lymphadenopathy, unexplained weight loss, night sweats, hemoptysis, fatigue, anorexia.
- **IGRA (interferon gamma release assay) blood test** [e.g., QuantiFERON] or **TST (tuberculin skin test)** [e.g., purified protein derivative or PPD][2]
  - Either IGRA or TST testing is acceptable for children of any age.
  - IGRA is preferred for anyone with a history of bacillus Calmette-Guérin (BCG) vaccine.

[1] CDC: Reported Tuberculosis in the United States, 2022 (https://www.cdc.gov/tb/statistics/reports/2022/default.htm)
[2] MDH: TB Screening (https://www.health.state.mn.us/diseases/tb/hcp/tbscreening.html)

  - A TST should be read within 48-72 hours after administration. If the person is unlikely to return for the TST reading, IGRA testing is preferred.
- **Chest X-ray:** indicated for 1) anyone with positive IGRA or TST OR 2) history of previous active TB, symptoms concerning for active TB, HIV infection, or close contact of known TB case.
  - If chest X-ray is abnormal: send sputum x 3 for PCR and AFB smear and culture to rule out active TB.[3]

Criteria for Positive TST[4]

Tuberculin Skin Test (TST) Result (induration)

≥5mm positive in:	≥10mm positive in:	≥15mm positive in:
HIV infection	Foreign-born from (or extensive travel to) high-prevalence country	No TB risk factors
Close contacts	Children <5 years	
CXR suggestive of previous TB disease	Health care worker or residents/employees in congregate settings	
Immunosuppression	Injection drug use or high-risk clinical condition*	

*Chronic substance use, diabetes mellitus, silicosis, cancer of the head or neck, hematologic or reticuloendothelial disease such as Hodgkin's disease or leukemia, end stage renal disease, intestinal bypass or gastrectomy, chronic malabsorption syndromes, low body weight (i.e., 10% or more below ideal for the given population).

Two IGRAs are commercially available in the U.S.: QuantiFERON Gold and T-SPOT. Results may be positive, negative, indeterminate, or borderline (T-SPOT only).

- Positive results suggest that *M. tuberculosis* infection is likely (cannot distinguish between active TB and LTBI).
- Negative results suggest *M. tuberculosis* is unlikely.
- For indeterminate or borderline results, the IGRA should be repeated and/or a TST performed.

Live virus vaccines might affect TST or IGRA results. **If live vaccines are to be administered, TST or IGRA testing should be performed on the same day or four to six weeks later.[5]**

[3] ISDA: ATS/CDC/IDSA Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children (https://www.idsociety.org/practice-guideline/diagnosis-of-tb-in-adults-and-children/)
[4] MDH: Candidates for Treatment of Latent Tuberculosis Infection (https://www.health.state.mn.us/diseases/tb/candidates.pdf)
[5] CDC: General Best Practice Guidelines for Immunizations. Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP). https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/special-situations.html#administration

Diagnosis of Active TB Disease vs Latent TB Infection (LTBI)[6]

Latent TB Infection (LTBI)	Active TB (disease)
No symptoms or physical findings suggestive of TB disease	Symptoms (may include fever, cough, chest pain, weight loss, night sweats, hemoptysis, fatigue, anorexia)
IGRA or TST usually positive	IGRA or TST usually positive
CXR typically normal	CXR typically abnormal
Respiratory specimens are smear and culture negative	Respiratory specimens usually smear and/or culture positive
Cannot spread TB to others	Can spread TB to others
Consider treatment for LTBI to prevent active TB	**Needs treatment for active TB**

Active TB: Reporting to MDH and Referral to Public TB Clinics

Patients with suspected or diagnosed active TB should be reported to the MDH TB Program by calling 651-201-5414. Reports should be made within one working day. MDH will notify the local public health agency (LPH) where the patient resides to coordinate DOT (directly observed therapy), case management, and contact investigation. **The MDH TB Program can assist with referrals of patients with active TB to care providers and can provide medical consultation.**

The treatment of active TB is beyond the scope of this guidance document. More information for health care providers, including training resources, may be found at TB Information for Health Professionals (https://www.health.state.mn.us/diseases/tb/hcp/index.html). The MDH TB Program can assist providers who have questions. **Patients with active TB living in a county affiliated with one of the public TB clinics (located in Hennepin, Ramsey, and Olmsted Counties) may access care at those clinics regardless of immigration status.**

Children or immunocompromised persons with active TB disease may have atypical clinical and radiological presentations. Young children with positive TST or IGRA results should be promptly evaluated because they can rapidly progress to active TB disease. Pregnant people with a positive IGRA or TST should have a shielded chest X-ray; if asymptomatic, the chest X-ray may be delayed until after the first trimester. **For pregnant people with active TB disease, treatment is recommended**, even during the first trimester[7]; for most pregnant people with LTBI, treatment may be delayed until two to three months postpartum unless they are at high risk for progressing to active TB infection (refer to 'Treatment of LTBI' section below).

Latent TB Infection (LTBI)

Active TB disease must be excluded before treatment of LTBI to avoid inadvertent undertreatment of active TB which can lead to the emergence of drug resistance.

[6] Adapted from CDC: About Tuberculosis (TB) (https://www.cdc.gov/tb/about/index.html)
[7] CDC: Treatment for TB During Pregnancy (https://www.cdc.gov/tb/topic/treatment/pregnancy.htm)

Diagnosing LTBI[8]

- **Laboratory:** positive TST or IGRA.
- **Clinical:** no signs or symptoms of active TB **AND** either chest X-ray (CXR) without abnormalities **OR** abnormal imaging not consistent with active TB with negative microbiological testing (sputum AFB smear and culture x 3).
  - Note: it can be challenging to distinguish LTBI with old, healed disease (e.g., fibrotic changes on CXR) from culture-negative active TB disease. Consultation with MDH is recommended in cases where the diagnosis is uncertain before treating for LTBI.

Treatment of LTBI

The lifetime risk of LTBI progressing to active TB is 5-10% for adults, with an annual risk of 0.1% per year without other comorbid conditions. Persons with HIV have a 10% annual risk of progression. Risk is highest in the first two years after infection. The lifetime risk is also higher in adolescents (15%), children aged 1-5 years (25%), and children <1 year (40%).

Treatment of LTBI to prevent active TB should be considered for all, with special emphasis on the following groups: **current or planned immunosuppression (e.g., HIV, immunosuppressing medications, transplant), recent infection (close contact of active case within the past two years, TB test conversion within two years), and children.** Children under 5 years of age who are contacts of a person with active TB should receive treatment for LTBI even if their initial TST or IGRA is negative, and their last exposure was less than eight to 10 weeks ago; this is called window prophylaxis. Refer to CDC Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis (https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm) for guidance on the management of window prophylaxis in susceptible contacts (children <5 years, immunocompromised); specialist referral is recommended.

The MDH TB Program (651-201-5414) can assist with referrals for any high-risk patient with LTBI (e.g., concern for drug-resistant TB, HIV co-infection, pregnancy, children). LPH can also assist in management of high-risk LTBI patients.

LTBI Treatment Regimens[9, 10]

Considerations for choice of regimen include comorbidities, potential for drug-drug interactions (particularly with rifamycin-based regimens), drug susceptibility of presumed source case, if known, and patient preference and adherence. **Short course three- or four-month regimens are preferred as they are effective, safe, and have higher completion rates than six- to nine-month regimens. Refer to Appendix A for a Quick Reference Guide for LTBI Treatment Regimens.**

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[8] IDSA: ATS/CDC/IDSA Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children (https://www.idsociety.org/practice-guideline/diagnosis-of-tb-in-adults-and-children/)

[9] CDC: Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7041302/)

[10] American Academy of Pediatrics: Tuberculosis | Red Book: 2021–2024 Report of the Committee on Infectious Diseases https://publications.aap.org/redbook/book/347/chapter/5757587/Tuberculosis)

Monitoring on LTBI Treatment[11]

Assess patients at least monthly for side effects and adherence. Common side effects include:

- GI (anorexia, nausea, vomiting, abdominal pain)
- Flu-like symptoms (fever, chills, myalgias)
- Paresthesias
- Hepatotoxicity (jaundice, dark urine)
- Fatigue
- Orange discoloration of body fluids (urine, sweat, saliva, tears) with rifamycins

Baseline laboratory testing (CBC, ALT, AST) is not routinely recommended. Baseline laboratory testing is indicated for those with HIV infection, regular alcohol use, pregnancy, taking other hepatotoxic medication, or if concern for viral hepatitis, chronic liver disease, or cirrhosis.

Laboratory testing should be repeated monthly for those with abnormal results at baseline, those with chronic liver disease or regular alcohol use, and should be checked more frequently when clinically indicated (e.g., signs or symptoms of hepatotoxicity such as nausea, vomiting, abdominal pain, jaundice, or dark urine). Patients should be educated on signs and symptoms of hepatotoxicity and instructed to stop LTBI medications and seek evaluations if they occur. Monitoring flowsheets for providers to use during LTBI treatment are available at MDH Tuberculosis Medications Program (https://www.health.state.mn.us/diseases/tb/meds/index.html).

Directly Observed Therapy (DOT)[12]

DOT is standard for all patients with active TB. DOT should be considered for LTBI treatment for those at especially high risk for active TB (e.g., young children) and those who are either taking an intermittent regimen or who may have difficulty with treatment adherence. Because of the importance of each dose, DOT or video DOT should be used for patients on INH regimens given twice weekly. For the 3HP regimen, MDH recommends using enhanced self-administered therapy (SAT)[13]; this may involve communication via phone, text, or email with the patient on the day of medication administration.

[11] MDH: Evaluation and Monitoring During Treatment of LTBI (https://www.health.state.mn.us/diseases/tb/hcp/monitor.pdf)
[12] MDH: Directly Observed Therapy for the Treatment of Tuberculosis (https://www.health.state.mn.us/diseases/tb/lph/dot.html)
[13] MDH: Updated Latent Tuberculosis Infection (LTBI) Screening and Treatment Recommendations (https://www.health.state.mn.us/diseases/tb/hcp/ltbiguidlines.pdf)

MDH TB Medications Program

The MDH TB Medications Program provides medication for LTBI or active TB disease for those living in Minnesota at no cost, regardless of immigration status. Medications are available at no cost to the patient and will be shipped to the health care provider or local public health. Refer to MDH: TB Medications Program (https://www.health.state.mn.us/diseases/tb/meds/index.html) for eligibility and online application for providers or call the MDH TB Program at 651-201-5414.

References and More Information

- For MDH medical consultation or questions about screening, reporting or additional training, contact the MDH TB Prevention and Control Program at 651-201-5414 or visit MDH: Tuberculosis (TB) (https://www.health.state.mn.us/diseases/tb/index.html)
- MDH: TB data and analysis of TB trends in Minnesota and the United States. TB Statistics (https://www.health.state.mn.us/diseases/tb/stats/index.html)
- CDC: TB Clinical Guidelines (https://www.cdc.gov/tb/hcp/clinical-guidance/)
- CDC: Latent Tuberculosis Infection: A Guide for Primary Care Providers (https://www.cdc.gov/tb/hcp/education/latent-tb-infection-guide-primary-care-providers.html)
- CDC: Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7041302/)
- ISDA: ATS/CDC/IDSA Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children (https://www.idsociety.org/practice-guideline/diagnosis-of-tb-in-adults-and-children/)
- NYC Health: Latent Tuberculosis Infection Screening, Diagnosis and Treatment Guide (https://home.nyc.gov/assets/doh/downloads/pdf/tb/ltbi-treatment-and-management-guide.pdf)
- American Academy of Pediatrics: Guidance for management of tuberculosis in children and adolescents. Tuberculosis | Red Book: 2024-2027 Report of the Committee on Infectious Diseases (https://publications.aap.org/redbook/book/755/chapter/14083107/Tuberculosis)

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To obtain this information in a different format, call: 651-201-5414.

Appendix A: Quick Reference Guide for LTBI Treatment Regimens

LTBI Regimen	Interval, Duration, and Completion	Dosage	This Regimen
4R: Rifampin (RIF)	Daily RIF for four months **Completion:** 120 doses within six months	*Adults*: 10mg/kg (600mg max) *Children*: 15-20mg/kg (600mg max)	**Preferred for people of all ages.** May be used in PLWH not on ART or who are taking ART with acceptable drug-drug interactions with RIF.* Not recommended for people with history of severe RIF-induced reactions and people exposed to RIF-resistant TB.
3HP: Isoniazid (INH)/Rifapentine (RPT)	Weekly INH/RPT for 12 weeks **Completion:** 12 scheduled doses within a 16-week period	**INH:** *Age 2-11 years:* 25mg/kg (900mg max) *Age 12 years and older:* 15mg/kg (900mg max) **RPT:** 10.0-14.0 kg: 300mg 14.1-25.0 kg: 450mg 25.1-32.0 kg; 600mg 32.1-49.9 kg; 750mg ≥50kg; 900mg max	**Preferred for people aged 2 years and older who are not pregnant or breastfeeding** (due to RPT) May be used in PLWH not on ART or who are taking ART with acceptable drug-drug interactions with RPT.* Not recommended for people with a history of severe RIF-, RPT-, or INH-induced reactions and people exposed to INH or RIF-resistant TB.
3HR: Isoniazid (INH)/Rifampin (RIF)	Daily INH/RIF for 12 weeks **Completion:** 90 doses within four months	**INH:** *Adults:* 5mg/kg (300mg max) *Children:* 10-20mg/kg (300mg max) **RIF:** *Adults:* 10mg/kg (600mg max) *Children:* 15-20mg/kg (600mg max)	May be used for people of all ages. May be used in PLWH not on ART or who are taking ART with acceptable drug-drug interactions with RIF.* Not recommended for people with a history of severe RIF- or INH-induced reactions or people exposed to INH or RIF-resistant TB.
6H or 9H: Isoniazid (INH)	Daily INH for six months** **Completion:** 180 doses within nine months Daily INH for nine months** **Completion**: 270 doses within 12 months	*Adults:* 5mg/kg (300mg max) *Children:* 10-20mg/kg (300mg max)	**No longer a preferred regimen due to longer treatment duration** May be used for people of all ages. May be used if RIF or RPT are contraindicated. Not recommended for people with history of severe INH-induced reaction (e.g., hepatic, skin, or allergic reaction) or neuropathy, or people exposed to INH-resistant TB. Twice weekly regimens† may be used but must be administered with DOT.

Table adapted from CDC: Guidelines for Treatment of LTBI, 2020 (https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm?s_cid=rr6901a1_w) and NYC: LTBI Screening, Diagnosis and Treatment Guide, 2022 (https://home.nyc.gov/assets/doh/downloads/pdf/tb/ltbi-treatment-and-management-guide.pdf).

PLWH = People Living with HIV. ART = antiretroviral therapy. DOT = directly observed therapy.

*Not recommended for people taking ART regimens containing protease inhibitors (PI), non-nucleoside reverse transcriptase inhibitors (NNRTIs), integrase strand transfer inhibitors (INSTIs), or tenofovir alafenamide (TAF).

**Nine months of INH daily preferred due to established efficacy but six months provides some protection and may be considered in the setting of difficulty with adherence. Regimens shorter than nine months should not be used for patients with fibrotic lesions on CXR.

†Twice weekly INH is dosed as 15mg/kg for adults (900mg max) and 20-40mg/kg for children (900mg max).