CD Summary
December 2023 | Volume 72 Number 7
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HASN'T TUBERCULOSIS BEEN ERADICATED IN THE UNITED STATES?

For many people in the United States, the memory of tuberculosis (TB) has faded even as its impact as a leading global cause of sickness and death endures. Both drug-sensitive and multidrug-resistant TB, which by definition is resistant to both isoniazid and rifampin, remain pressing public health concerns. TB is relatively rare in Oregon, but it hasn't gone away.

In 2022, Oregon reported 73 cases of TB disease, a figure that has remained relatively stable since 2010. Although transmission of the causative agent *Mycobacterium tuberculosis* (*Mtb*) is via the respiratory route, TB disease can develop anywhere in the body, including the eyes, skin, bones, central nervous system, gastrointestinal tract, and lymphatic system. Given the global distribution of TB, it's not surprising that three-fourths of TB disease in Oregon affects people born outside of the U.S., with most originating from Asia, Latin America, Africa, and the Pacific Islands.

TB INFECTION ≠ DISEASE

Approximately 30% of persons exposed to *Mtb* will develop latent TB infection (LTBI). If left untreated, about 5% to 10% of healthy, immunocompetent persons will progress to active tuberculosis disease.* Risk of progression may be higher in persons with medical conditions that weaken the immune system like HIV/AIDS, diabetes, or severe kidney disease.

*Although the lifetime risk of developing TB disease is estimated at 10%, half of that risk occurs within the first two years of infection. The highest risk of progression to disease is shortly after infection, which is why public health focuses on contacts to TB cases.

To eliminate TB, it is essential to treat LTBI. Unfortunately, lack of public health resources means that in many countries, LTBI is not diagnosed or treated. Furthermore, predicting which LTBI cases will progress to TB disease is an inexact science. The Online TST/IGRA Interpreter from McGill University can help you interpret the results of tuberculin skin testing (TST) and interferon gamma release assays (IGRAs) and estimate your patients' risk for progression to TB disease.

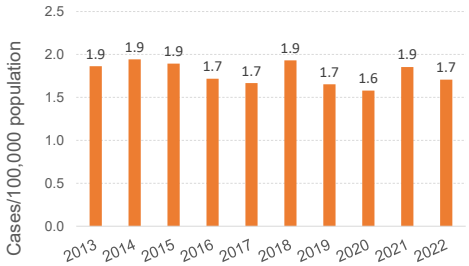
THE FIRST STEP: DIAGNOSIS

Fortunately, diagnostic tests and treatment regimens for LTBI have significantly improved over the years. Ongoing research promises even greater specificity and sensitivity for LTBI diagnostic tests and shorter treatment durations. Given the potential for false positivity with the current LTBI tests, it is important to focus testing on individuals with risk factors for acquiring TB infection.

The United States Preventive Services Task Force (USPSTF) recently released updated guidance on screening for LTBI in adults.[1] After a rigorous review of published evidence, the USPSTF recommends screening for LTBI in asymptomatic adults ≥18 years of age with risk factors including:

- birth or residence in countries with high TB prevalence (this includes most countries other than the U.S., Canada, Australia, New Zealand, or a country in western or northern Europe).
- residence in high-risk congregate settings such as correctional facilities or shelters for the homeless.

Figure 1. Incidence rate of TB in Oregon, 2013–2022



Additionally, CDC recommends LTBI screening for children with TB risk factors, healthcare workers, contacts of TB disease patients, and individuals with specific medical conditions.[2]

The USPSTF found no evidence for the optimal frequency of screening for LTBI. Given the lack of evidence, a reasonable approach is to repeat screening based on specific risk factors; screening frequency could range from one-time screening of persons at low risk for future *Mtb* exposure to annual screening among those at continued risk of exposure.[3]

Although the TST is an acceptable LTBI screening test, the Oregon Health Authority TB Program encourages the use of IGRAs such as QuantiFERON-TB Gold Plus (QFT-Plus) and the T-SPOT.TB test. IGRAs are preferable due to increased specificity (i.e., fewer false positives) and a single blood draw.

QFT-Plus or T-SPOT.TB is particularly advised for individuals from countries where the BCG (*bacille* Calmette-Guérin) vaccine (a live, attenuated strain of the closely related *Mycobacterium bovis*) is administered. Both BCG vaccination and infection by certain nontuberculous mycobacteria

Table 1. Regimens to treat latent tuberculosis infection

REGIMENS TO TREAT LATENT TUBERCULOSIS INFECTION			
DRUG	**INTERVAL AND DURATION**	**ORAL DOSAGE (MAXIMUM)**	**CRITERIA FOR COMPLETION**
RIF	Daily x 4 months	Adult: 10 mg/kg (600 mg max) Child: 15–20 mg/kg (600 mg max) see: Provider fact sheet: LTBI - RIF	120 doses within 6 months
INH†- RPT weekly (3HP)	Once-weekly x 12 weeks	INH 15 mg/kg round up to nearest 50 mg or 100 mg (900 mg max) Rifapentine • 10–14 kg (300mg) • 14.1–25 kg (450mg) • 25.1–32 kg (600mg) • 32.1–49.9 kg (750mg) • ≥50kg = 900mg max Child 2–11 y.o. see INH and rifapentine (RPT) dosing table (2–11 yrs)	12 doses within 16 weeks
Coming Soon! INH† RPT daily (1HP)	Daily x 4 weeks	Age ≥13 years (regardless of weight) Isoniazid 300 mg day Rifapentine • 300 mg daily for weight <35 kg) • 450 mg daily weight for 35-45 kg • 600 mg for weight > 45 kg	28 doses within 4 weeks
INH†	Daily x 9 months	Adult: 5 mg/kg (300 mg) Child: 10–15 mg/kg (300 mg max) see: INH daily dosing table	270 doses within 12 months
	Twice-weekly by DOT x 9 months	Adult: 15 mg/kg (900 mg) Child: 20–30 mg/kg (900 mg max)	76 doses within 12 months DOT
INH†	Daily x 6 months	Adult: 5 mg/kg (300 mg)	180 doses within 9 months
	Twice-weekly by DOT x 6 months	Adult: 15 mg/kg (900 mg)	52 doses within 9 months DOT

†For patients on INH, 25–50 mg daily pyridoxine (vitamin B6) is recommended.

Abbreviations: INH = isoniazid, RIF = rifampin, RPT = rifapentine (Priftin), DOT = direct observed therapy, CXR = chest x-ray

can produce false-positive TB skin test results.[4] We strongly recommend retesting when a patient without TB risk factors tests positive for LTBI. For example, if a healthcare worker tests positive during initial screening but is a lifelong Oregon resident without TB risk factors, retesting is advisable.

A critical aspect of LTBI diagnosis is ensuring that the patient does not have TB disease. Before initiating LTBI treatment, ask about symptoms, examine the patient, and check a chest x-ray.

TREATMENT OPTIONS FOR LTBI

In the past, the 6- or 9-month isoniazid (INH) regimen was the only available treatment for LTBI. INH for 9 months remains relevant for patients who cannot take rifampin or rifapentine due to potential drug interactions or intolerable side effects. For most patients, however, shorter drug regimens are recommended due to higher completion rates and less hepatotoxicity. It should also be noted that isoniazid continues to be in short supply.

Although engaging in shared decision-making with the patient about LTBI treatment options is always important, in our opinion, the simplest LTBI regimen is rifampin (RIF) daily for four months.[5] This “4R” regimen is suitable for patients of all ages, and rifampin is available on most drug formularies. However, as rifampin strongly induces cytochrome P450 (CYP) enzymes, a thorough check for drug interactions is necessary. Rifampin can also turn bodily fluids orange, which patients should be forewarned about to avoid unnecessary concern.

Another newer regimen we like is 12 weekly doses of INH and rifapentine (Priftin®), commonly referred to as “3HP”.[5] Despite its effectiveness and short duration, 3HP can be burdensome for

patients due to the number of pills, and rifapentine may not be available on all drug formularies. Like rifampin, rifapentine induces CYP enzymes, though to a lesser extent. Rifapentine also discolors bodily fluids; and due to the risk of INH-induced peripheral neuropathy, we recommend adding 25 mg of vitamin B_6 daily to mitigate this risk.

Irrespective of the chosen regimen, medical providers should monitor patients monthly for side effects and treatment adherence through pill counts.

A NEW, EVEN SHORTER TREATMENT FOR LTBI: 1HP

Although CDC has not issued guidance on its use, the Oregon Health Authority TB Program and World Health Organization (WHO) endorse using one month (28 doses) of daily isoniazid and rifapentine ("1HP") to treat LTBI.[6] According to WHO, both 1HP and 3HP have shown efficacy in preventing TB disease similar to that of 6 months of INH. Due to lack of data on appropriate dosing of 1HP for young children, WHO currently recommends the use of 1HP only among people ≥13 years of age. 1HP will require patients to take 5 pills daily, which may be difficult for some patients. Note that although the 1HP regimen is shorter, the total number of doses increases from 12 in 3HP to 28 in 1HP. The shorter course may be helpful in situations where treatment must be completed quickly.

COMPLETING TREATMENT: THE NUMBER OF DOSES

To consider LTBI treatment completed, the patient must take the appropriate number of doses within a specified timeframe (refer to the table above). If there is a significant treatment gap or the patient cannot complete treatment within the designated timeframe, a new chest x-ray should be obtained, and treatment started anew. When treatment is complete, provide patients with a completion record that includes their test results and treatment regimen.

FOR MORE INFORMATION

- Obtain clinical consultation on TB disease and LTBI by contacting Heidi Behm at heidi.behm@oha.oregon.gov or 503-358-8516.
- Patient education materials in multiple languages and clinical guidance available at www.healthoregon.org/tb.

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