CD Summary
November 2018 | Volume 67, Number 13
Contact: 971-673-1111 | cd.summary@state.or.us | www.healthoregon.org/cdsummary

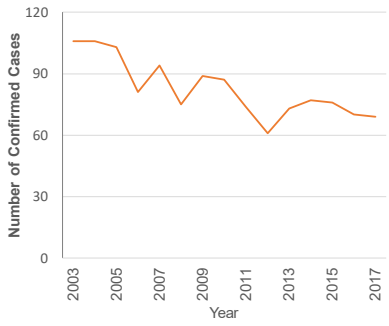
ELIMINATING TUBERCULOSIS: LTBI SCREENING AND TREATMENT

Disease from *Mycobacterium tuberculosis* (TB) was once the leading cause of death in the United States but has now faded from the memory of many Americans. Nonetheless, people in the U.S, (including Oregonians) still suffer and die from this devastating disease (see the personal stories of TB survivors: www.cdc.gov/tb/topic/basics/personalstories.htm). Moreover,TB has overtaken HIV/AIDS as the leading infectious disease killer in the world: an estimated 1.6 million people died from TB in 2017. Multidrug resistant TB (TB disease resistant to isoniazid and rifampin) remains a global public health crisis.[1]

OREGON DATA

In Oregon, 69 cases of TB disease were diagnosed in 2017. The incidence of TB declined from 2003–2011, but has remained relatively stable since then (Figure). Most cases of TB affected the respiratory system, but TB can appear in any location in the body. During 2017, disease sites included the eyes, skin, bones, meninges, GI tract, and lymphatic system. Given the global scope of TB, it's not surprising that 74% of Oregon TB disease cases were among foreign born people, including those from (in decreasing order) Asia, Latin America, Africa, and the Pacific Islands.

Figure. Confirmed tuberculosis cases, Oregon, 2003–2017



LATENT TB INFECTION

The Centers for Disease Control and Prevention (CDC) estimates 13 million people in the U.S. have latent TB infection (LTBI) (N.B. LTBI is not reportable in most states including Oregon). Without treatment, approximately one in ten people with LTBI eventually develop TB disease over their lifetime. Treating LTBI to prevent progression to TB disease is essential to eliminate* TB in the U.S… but…many countries do not diagnose, let alone treat LTBI. What's more, predicting who will progress from LTBI to TB disease remains a major challenge (use The Online TST/IGRA Interpreter from McGill University to get the estimated TB risk for your patient: www.tstin3d.com/en/calc.html).

DIAGNOSING LTBI

Luckily, LTBI diagnostic tests have vastly improved over the past 5 years. Research is underway that should lead to further increases in specificity/sensitivity for LTBI diagnostic tests. Given the possibility of false positives with any of the current tests for LTBI, testing only those with risk factors for TB is important. The CDC and United States Preventive Services Task Force (USPSTF) recommend testing people born in or who frequently travel to countries where TB disease is common, and people who live or have lived in large group settings such as homeless shelters or correctional facilities. CDC additionally recommends TB testing for at risk children, healthcare workers, contacts of people with TB disease†, and people with certain medical conditions.

Although the TB skin test is still a valid test for LTBI, the Oregon Health Authority TB Program encourages the use of interferon gamma release assays (IGRAs) such as QuantiFERON-TB Gold Plus (QFT-Plus®) and the T-SPOT® TB test. These blood tests tend to be more convenient for the patient since only a single office visit and blood draw is needed. IGRAs are also likely to be more specific than the TB skin test because the antigens used in the tests are relatively specific to *M. tuberculosis*.[2] QFT-Plus or T-SPOT are particularly advisable for people from countries where the BCG vaccine is given (check out The BCG World Atlas to find out if your patient may have been vaccinated: www.bcgatlas.org/). Both BCG vaccination and infection by some nontuberculosis mycobacteria can cause false positive TB skin test results. We highly recommend retesting when any patient who lacks TB risk factors tests positive for TB. For example, if your patient is a healthcare worker who tested positive at baseline screening but is a lifelong Oregonian without TB risk factors, retesting is a good idea.

A critical piece of diagnosing LTBI is making certain the patient does not have TB disease. Complete a chest x-ray and physical examination prior to starting LTBI treatment. Obtain baseline liver enzyme tests for all patients with hepatoxicity risk factors.

LTBI TREATMENT OPTIONS

Although some readers may be fond of treating LTBI with 9 months isoniazid (INH), we recommend

* Surprisingly, TB elimination is not defined as zero TB cases: the CDC defines domestic TB elimination as ≤1 case of TB disease/million.

† Although the lifetime risk of developing TB disease is estimated at 10%, half of that risk is within the first 2 years of infection. Progression to disease is highest shortly after infection which is why public health focuses on contacts to TB cases.

treating most patients for LTBI with shorter course regimens. Patients tolerate the shorter courses better, and more often complete treatment when on a short course regimen. However, INH 9 months is still relevant for patients on other medications which might interact poorly with rifampin or rifapentine.

In our opinion, the simplest, safest and most effective regimen for LTBI is 4 months rifampin (RIF) daily.[3] This regimen can be used for patients of any age and is available on most drug formularies. Since rifampin is a potent inducer of cytochrome P450 enzymes, a careful check for drug interactions is essential. RIF can also cause body fluids to turn an orange color, so be sure to warn your patients not to panic if their urine looks like orange Kool-Aid!

Another newer preferred regimen is 12 weekly doses of INH and rifapentine (Priftin®). This regimen is commonly referred to as 3HP. Previously, directly observed therapy (DOT) was advised for all patients on 3HP. CDC recently revised this recommendation stating, "The health care provider should choose the mode of administration (DOT versus self-administered therapy) based on local practice, individual patient attributes and preferences, and other considerations, including risk for progression to severe forms of TB disease."[4]

In Oregon, we agree with CDC that patients and medical providers should determine together when self-administration of 3HP is appropriate. Although 3HP is an excellent regimen, due to the formulation of rifapentine the pill burden for the patient can be high. Also, rifapentine is currently not on all drug formularies. Like rifampin, rifapentine induces cytochrome P450 enzymes, but to a lesser extent. Rifapentine also stains body fluids orange. Due to the risk of INH-induced peripheral neuropathy in this regimen, although less common than during 9 months of INH, we recommend adding vitamin B6 25 mg daily to offset this risk.

No matter which regimen is selected, medical providers should see patients monthly to assess for side effects and adherence to treatment (a pill count is a good idea).

Table. Regimens to treat latent tuberculosis infection (LTBI)

DRUG	INTERVAL & 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(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- 49.9kg (750mg) ≥ 50kg = 900mg max Child 2-11 y.o. see: INH and rifapentine (RPT) dosing table	12 doses within 16 weeks
INH*	Daily x 9 months	Adult: 5 mg/kg (300 mg) Child: 10-15 mg/kg (300 mg max) see link INH 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 molnths
	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.

COMPLETING THE DOSES

To consider LTBI treatment completed, the appropriate number of doses must be taken within a specified timeframe (see table above). If there is a large gap in treatment or the patient cannot complete treatment within the designated timeframe, obtain a new chest x-ray and start treatment again from the beginning. When the patient finishes treatment, give the patient a completion record with their test results and treatment regimen.

WHAT ABOUT THE KIDS?!

We didn't cover testing and treating kids for LTBI in this article. Visit the Curry International TB Center for excellent resources and guidance on kids: www.currytbcenter.ucsf.edu/products/pediatric-tuberculosis-online-presentation

FOR MORE INFORMATION

- TB Program, Oregon Health Authority Obtain clinical consultation on TB disease and LTBI by contacting Heidi Behm (heidi.behm@state.or.us) or 971-673-0169. Patient education materials in multiple languages and clinical guidance available at www.healthoregon.org/tb.

REFERENCES

1. World Health Organization. Global tuberculosis report 2018. Available at: www.who.int/tb/publications/global_report/en/. Accessed 24 October 2018.
2. Centers for Disease Control and Prevention. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection — United States, 2010. MMWR 2010; 59:5–6. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s_cid=rr5905a1_e . Accessed 24 October 2018.
3. Menzies D, Adjobmey M, Ruslami R, et al. Four months of rifampin or nine months of isoniazid for latent tuberculosis in adults. N Engl J Med 2018; 379:440–53. Available at: www.nejm.org/doi/10.1056/NEJMoa1714283#article_citing_articles. Accessed 24 October 2018.
4. Borisov A, Morris S, Njie G, et al. Update of recommendations for use of once-weekly isoniazid-rifapentine regimen to treat latent *Mycobacterium tuberculosis* linfection. MMWR 2018;67:723–26. Available at: http://dx.doi.org/10.15585/mmwr.mm6725a5. Accessed 24 October 2018.

Click for CME credits

Click to sign up for CD Summary

Click to view previous CD summaries

Oregon Health Authority
PUBLIC HEALTH DIVISION

Providence Portland Medical Center designates this enduring material for a maximum of .5 *AMA PRA Category 1 credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity. Portland Providence Medical Center is accredited by the Oregon Medical Association to sponsor continuing medical education of physicians.

You can get this document in other languages, large print, braille or a format you prefer. Contact the Public Health Division at 971-673-1222. We accept all relay calls or you can dial 711 for TTY.