Latent TB Treatment in Primary Care

Kaitlyn Cano, MSN, FNP-BC

Amy Robinson, MD

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Disclosures

- We have no financial conflicts of interest

Our story

Dr. Robinson is a physician working at the UNM LoboCare Clinic and Kaitlyn is a FNP working at LoboCare, as well

Lobo Care is an episodic care clinic for UNM employees and their dependents, and a few retirees

Some employees who were identified as having latent TB during their occupational health screening didn't have PCPs. This made accessing treatment for latent TB difficult for them, so we were asked to facilitate treatment of latent TB for those patients

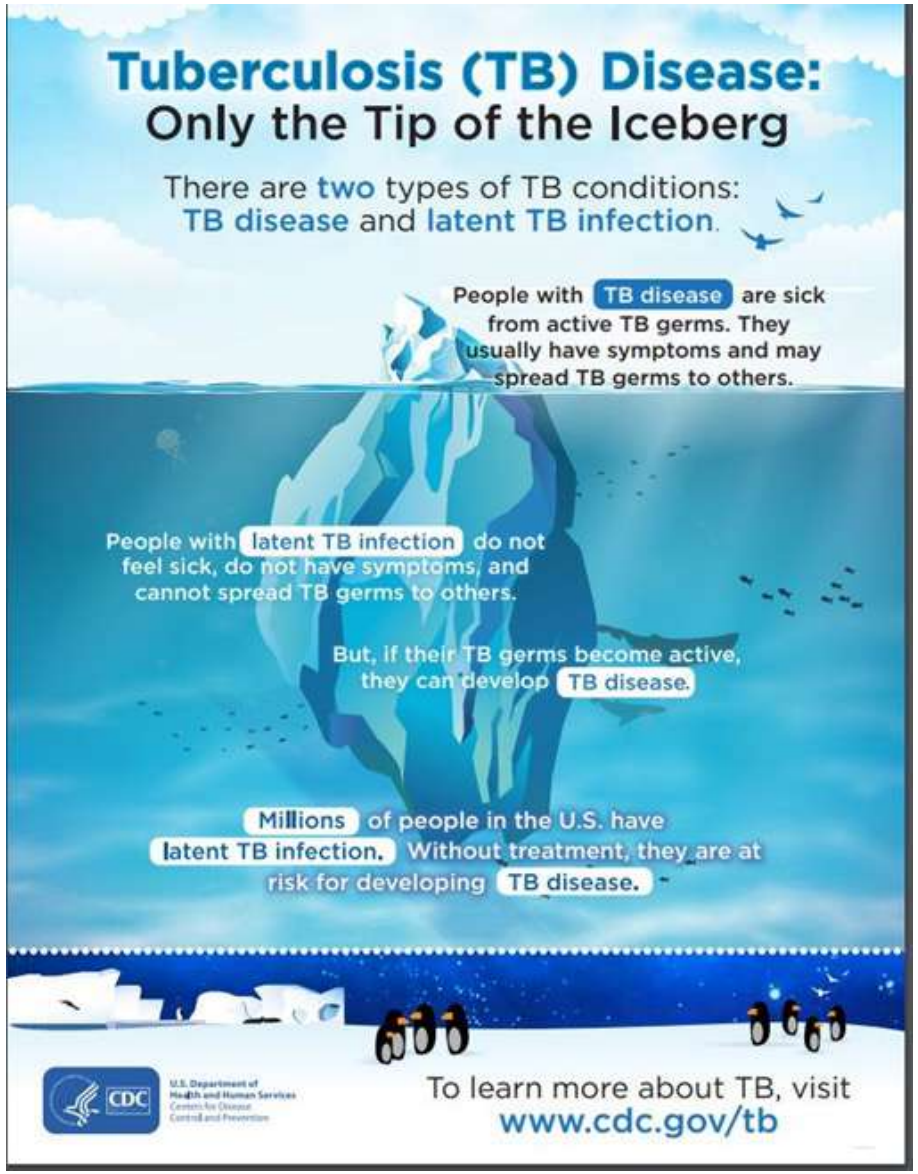
Objectives

- Describe how to diagnose LTBI and who should be tested.
- Identify which patients should be treated for LTBI
- Discuss preferred regimens, risks, benefits, alternatives, and contraindications.
- Manage side effects of treatment

What is LTBI?

Infection with *Mycobacterium tuberculosis (M. tuberculosis*) which is not causing disease. Patients will not have symptoms or radiographic or bacteriologic evidence of TB disease.

Latent Tuberculosis Infection—A Guide for Primary Health Care Providers, CDC Publication Number 22-0468, p. 5



Why is this Important to Healthcare Providers?

About 5-10% of people infected with LTBI will develop TB in their lifetime if not treated.

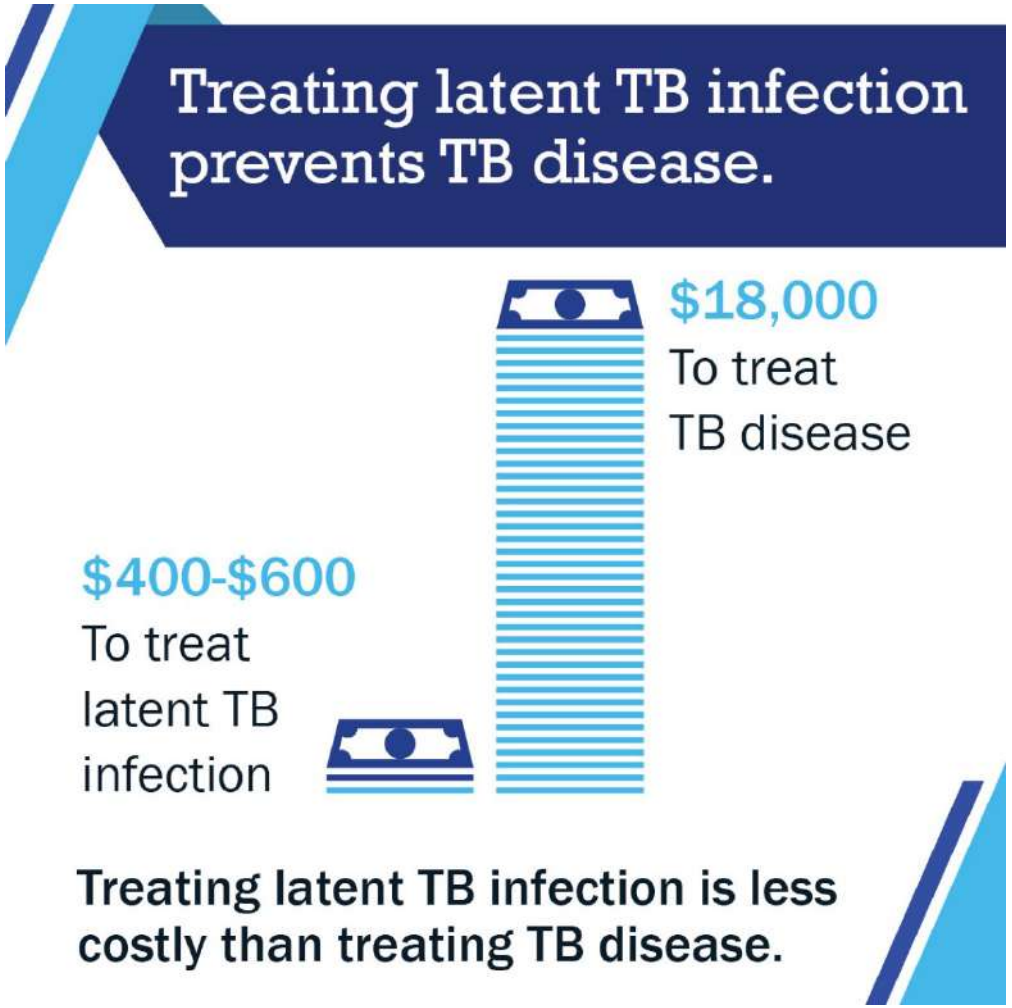
Progression from LTBI to TB accounts for about 80% of US cases.

Approximately half of the people who develop active TB do so within 2-3 years of exposure.

The goal of treatment is to control and eliminate TB.

Up to 13 million people in the US may have LTBI.

CDC booklet, p. 5



Why is this Important to Healthcare Providers?
Risk of Developing TB Disease

TB infection and no risk factors (about 10% over a lifetime)	**TB infection and diabetes** (about 30% over a lifetime)	**TB infection and HIV infection** (a very large risk over a lifetime)
		
For people with TB infection and no risk factors, the risk is about 5% in the first 2 years after infection and about 10% over a lifetime.	For people with TB infection and diabetes, the risk is 3 times greater, or about 30% over a lifetime.	For people with TB infection and HIV infection (not on HIV treatment), the risk is about 7% to 10% PER YEAR, a very large risk over a lifetime.

Why is this Important to Patients?

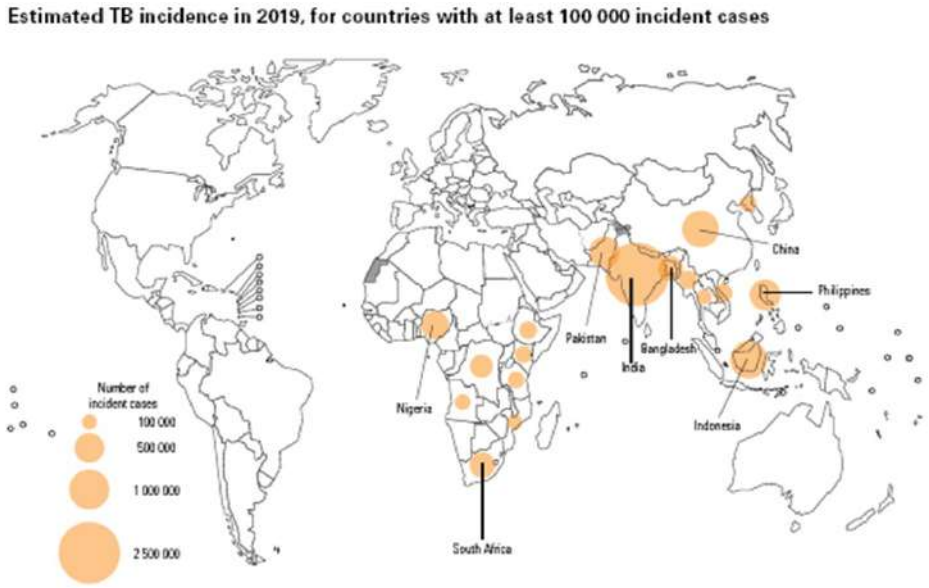
- Transmission: Patient's who develop active TB are now infectious and can make their family members sick.
- Stigma: There is stigma around having active TB disease which could lead to patients feeling isolated or depressed.
- Money lost: Patients who develop active disease may incur unforeseen costs and losses.
  - Patients will have to quarantine and likely miss work resulting in lost wages.
  - More medical appointments and costs of transportation.
- Ease of treatment: Treating Active disease is harder and takes longer.

Who should be tested for Latent TB?

Test only persons at increased risk for TB.

- LTBI testing should be conducted for persons with the following risk factors:
  - Birth or residence in a country with a high or medium incidence rate of TB, regardless of year of arrival. These countries include most countries in Asia, Africa, Latin America, the Pacific Islands, and Eastern Europe.
  - Close contact to someone with infectious TB disease.
  - Immunosuppression, current or planned.
    - This includes HIV infection; organ transplantation; or treatment with tumor necrosis factor-alpha antagonist (e.g., infliximab, etanercept), corticosteroids (equivalent of prednisone ≥2 mg/kg/day, or ≥15 mg/day for ≥1 month), or other immunosuppressive medication.
  - Other medical conditions or social circumstances that meet criteria in state or local recommendations, such as homelessness, incarceration, or occupational risk of TB (e.g., healthcare workers, prison guards).

    - p.6-7



Source: WHO Global TB Report 2020 https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf

TB testing is recommended if any of the 3 boxes below are checked
☐ **One or more sign(s) or symptom(s) of TB disease** • TB symptoms include prolonged cough, coughing up blood, fever, night sweats, weight loss, or excessive fatigue.
☐ **Birth, travel, or residence** in a country with an elevated TB rate for at least 1 month • Includes countries other than the United States, Canada, Australia, New Zealand, or Western and North European countries. • Interferon gamma release assay (IGRA) is preferred over tuberculin skin test (TST) for non-US-born persons.
☐ **Close contact** to someone with infectious TB disease during lifetime
Treat for LTBI if TB test result is positive and active TB disease is ruled out

Differentiating Latent TB from Active TB (p.8)

Latent TB	TB Disease
No symptoms or physical findings suggestive of TB disease	Symptoms may include one or more of the following: fever, cough, chest pain, weight loss, night sweats, hemoptysis, fatigue, and decreased appetite
TB blood test or TST result usually positive	TB blood test or TST result usually positive
Chest radiograph is typically normal	Chest radiograph is usually abnormal, but may be normal in people with advanced immunosuppression or extrapulmonary TB disease
If done, respiratory specimens are smear and culture negative	Respiratory specimens are usually smear and/or culture positive, but may be negative in people with extrapulmonary TB disease or minimal/early pulmonary TB disease
Cannot spread TB bacteria to others	Can spread TB bacteria to others
Should consider treatment for LTBI to prevent TB disease	Needs treatment for TB disease

Selecting a test

In current diagnostic guidelines IGRAs are preferred, but TST is acceptable.

TB blood tests are the preferred method of testing for the following populations:

- Might be less likely to return for Tuberculin Skin Test (TST) reading and interpretation (e.g., homeless people or patients who use recreational drugs)
- Have received or may have received the BCG vaccine
- Are likely to be infected with M. tuberculosis and are at a low to intermediate risk of progression to TB disease
- Those unlikely to be infected with M. tuberculosis (note: those who are unlikely to be infected generally should not be tested for TB; a confirmatory test is recommended if the initial test is positive in people unlikely to be infected)

UNMH uses TB Gold testing.

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Interpretation of TB Blood Test Results

Qualitative

Positive = infection likely

Negative = infection unlikely, but cannot be excluded if pt has s/sx of TB or high risk

Indeterminate (TB Gold) or Invalid (T-Spot) = did not provide useful information; consider repeat blood test or TST

Borderline (T-Spot) = consider repeat testing

p.10

Interpretation of TB Blood Test Results

Quantitative

Numerical responses to the TB antigen and two controls, nil and mitogen

Might help clinical decision-making.

If results are borderline consider patient risk factors. NMDOH is available to discuss cases with providers to determine likelihood of LTBI if questionable.

Tuberculin Skin Test (TST)

- Delayed-hypersensitivity reaction detectable 2-8 weeks after infection
- Do not use if previous + TB test or tx for TB
- >=5 mm **induration** is + for recent contact with infectious TB, HIV infected, CXR suggestive of previous TB, organ transplant, immunosuppressed
- >=10 mm is + for those from TB-endemic countries, resided in high-risk congregate settings, high risk medical conditions (e.g. DM, CKD),low body weight, under age 5, Mycobacteriology lab workers, under 18 exposed to adults in high-risk categories

Tuberculin Skin Test (TST

>= 15 mm **induration** is a positive result in people with no known risk factors for TB

p. 12

Please stand and stretch!

Objective 2: Discuss preferred regimens, risks, benefits, alternatives and contraindications

Who should be treated?

Anyone who has LTBI infection and is interested in treatment and doesn’t have current contraindications to treatment.

p.26

What about Pregnancy?

Pregnancy may not in itself be a risk factor for progression to active TB disease. Pregnant women should only be tested if they have a risk factor.

- If a pregnant women has a positive TB test she should receive a medical evaluation including a CXR with a lead shield.
  - The CXR can be deferred until after the first trimester unless she has HIV, recent contact with a person with active TB, or documented TB infection test conversion in the past 2 years. It should not be deferred until peri- or post-partum.
- Pregnant women can delay treatment until 2-3 months postpartum, but if high risk for progression to active disease or recent TB exposure treatment should not be delayed on the basis of pregnancy alone.
  - Isoniazid and the rifamycins are considered safe in pregnancy.
  - 3HP has not been studied in pregnant women and should not be prescribed for women who are pregnant or expected to be pregnant in the next 3 months
  - Rifampin monotherapy offers the shortest and most tolerable treatment option and should be considered.
  - Isoniazid monotherapy should be used with caution in pregnant women, especially those with HIV.

- NSTC/NTCA Clinical Recommmendaitons, p. 56-57

Before you treat

- Talk to the patient about risks of developing active TB vs risk of adverse event from the treatment
- If unsure, consult your local TB nurse or expert(s)
- Assess the patient's understanding of LTBI—what is it, why treat
- Discuss possible barriers to adherence

- NSTC/NTCA, p. 33

Before you treat

- Obtain a chest radiograph to help rule out pulmonary TB disease
- Take a medical history with symptom review and do a focused physical exam to assess risk of progression to active TB disease
- Possible TB symptoms includes cough >2-3 weeks, fever, chills, hemoptysis, night sweats, unintended weight loss, loss of appetite, fatigue, chest pain
- Focused PE: oropharynx, neck incl. lymph nodes, lungs, abdomen
- Baseline labs: HIV at a minimum

- *Testing and Treatment of Latent Tuberculosis Infection in the United States, NSTC/NTCA Clinical Recommendations*, Feb 2021, p. 28

5 Options—3HP or 4R preferred

Section 4: Deciding Whether to Treat and Choosing a Regimen: Table 3 Recommendations for Regimens

Regimen	Priority Rank	Recommendation	Quality of Evidence (High, Moderate, Low, Very Low)
3HP	Preferred	Strong	Moderate
4R	Preferred	Strong	Moderate (HIV-negative)*
3HR	Preferred	Conditional	Very low (HIV-negative) Low (HIV-positive)
6H	Alternative	Strong^ Conditional	Moderate (HIV-negative) Moderate (HIV-positive)
9H	Alternative	Conditional	Moderate

* No evidence reported in persons with HIV infection.

^ Strong recommendation for persons unable to take a preferred regimen (e.g., because of drug intolerability or drug-drug interactions)

Source: Adapted from Sterling TR, et al. Guidelines for the treatment of latent tuberculosis infection: recommendations from the National Tuberculosis Controllers Association and CDC, 2020. *MMWR Recomm Rep.* 2020 Feb 14;69(1):1-11.

Recommended Regimens

From page 35 of the NSTC/NTCA document/2020 Guidelines

Preferred—excellent tolerability and efficacy, shorter treatment duration, higher completion rates

Alternative—excellent efficacy, but longer treatment duration and lower completion rate

Preferred Regimens—3HP (maybe 10 pills!)

3HP = isoniazid (INH)and rifapentine once per week x 12 doses (take with vitamin B6)

INH dosing: 15 mg/kg, rounded up to the nearest 50 or 100 mg; 900 mg max (usually three capsules, 300 mg each)

Rifapentine >=50 kg—900 mg (usually 6 tabs, 150 mg each)

Vitamin B6 (pyridoxine)--25-50 mg daily

Preferred regimens—4R

120 doses total—one dose daily x 4 months of rifampin

Adults 15-20 mg/kg; 600 mg maximum

Risks

- Medication side effects

Benefits

- Reduction in lifetime risk of developing active TB
- Active TB may spread to others
- Active TB may involve multiple organs, make one very ill, involve isolation

Alternatives and Contraindications

Some patients opt against treatment

Potential drug-drug interactions

Consider referral to TB specialist for patients on multiple medications and/or chronic disease

Possible pitfalls

Problem: WG dispensed only INH to my patient for 12 weeks

I failed to ensure monthly follow up

Solution: She had to repeat tx—this time with rifampin daily

Problem: Patient with nausea and vomiting; otherwise well

Solution: Rx antiemetic 1-2 hours prior to taking weekly tx

Stand and stretch, again!

Objective 3: Manage side effects of treatment

Adverse events and response

Moderate to severe:

hypotension, dizziness, severe nausea, vomiting, syncope, flu-like illness, thrombocytopenia, wheezing, shortness of breath, urticarial, petechiae, conjunctivitis, angioedema, shock

Assess clinically; stop treatment

Mild to moderate:

Rash, fever, pruritis, mild nausea—okay to monitor

Our experience to date

What is your experience?

In summary

- Screen patients at risk
- All health care providers are screened at beginning of employment, usually with blood tests
- Treatment of LTBI represents our best chance to reduce and maybe eventually eliminate TB in the US
- Two short, effective regimens exist: 3HP and 4R
- The NM DOH is ready to help with questions, challenges, and concerns—call if you need help!
- You can do this!

Resources

NTCA:

- Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations
  - www.tbcontrollers.org/resources/ltbi/clinical_recommendations

CDC Resources

- Guidelines for LTBI treatment
  - https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm?s_cid=rr6901a1_w
- Latent Tuberculosis Infection: A Guide for Primary Health Care Providers
  - https://www.cdc.gov/tb/publications/ltbi/default.htm

- NM DOH TB Helpline:
- 505-827-2471
- NM DOH TB Program Manager/TB Nurse Consultant
- Brenda Montoya Denison, BSN, RN
- 505-827-2474

https://www.nmhealth.org/about/phd/idb/tbpp/

Additional resources

Hartman-Adams H, Gerbo RM, George S. Tuberculosis: Common Questions and Answers. Am Fam Physician. 2022 Sep;106(3):308-315. PMID: 36126013.

Thank you for your attention!