Treating TB Infection

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Learning Objectives

- Identify recommended treatment regimens for LTBI
- Describe baseline evaluations prior to initiating treatment
- List common side effects to assess throughout LTBI treatment and criteria for determining when to stop/hold treatment and refer patient for further evaluation

What is **always** necessary before starting LTBI treatment?

Ruling out Active TB!

- For patients with TB symptoms or an abnormal chest x-ray, evaluate for active TB disease with a chest x-ray, symptom screen, and if indicated, sputum AFB smears, cultures, and nucleic acid amplification testing. A negative tuberculin skin test or interferon gamma release assay does not rule out active TB disease.

How many common LTBI regimens do you know of?

a) 1

b) 3

c) 5

d) 7

Let's review on the next slide!

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TABLE 3. Recommendations for regimens to treat latent tuberculosis infection

Regimen	Priority rank*	Recommendation	Quality of Evidence (high, moderate, low, or very low)
3HP: 3 mo's of isoniazid and rifapentine once weekly	Preferred	Strong	Moderate
4R: 4 mo's rifampin daily	Preferred	Strong	Moderate (HIV-negative)[†]
3HR: 3 mo's isoniazid and rifampin daily	Preferred	Conditional	Very low (HIV-negative) Low (HIV-positive)
6H: 6 mo's isoniazid daily or twice weekly	Alternative	Strong[§] Conditional	Moderate (HIV-negative) Moderate (HIV-positive)
9H: 9 mo's isoniazid daily or twice weekly	Alternative	Conditional	Moderate

Abbreviation: HIV = human immunodeficiency virus; mo's= months

* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; *Alternative:* excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

[†] 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: NTCA, Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations, 2021

Add B6 with regimens including Isoniazid

If the patient has:

- Diabetes
- Chronic Kidney Disease
- Heavy ETOH use
- Malnutrition
- HIV infection
- Pregnant or post-partum
- Seizure disorder

Then, add B6:

- Adult Dosing:
  25-50mg if given daily
  100mg if given once weekly

Adult Regimen Case

A 37-year-old, working mother of 2 children presents for LTBI treatment. She tells you: her "uncle got very sick taking medications for TB and never completed the treatment; she works in the orchards near your town and takes regular trips back to her home country." What regimen would you recommend *(select all that apply)*?

a) 3HP
b) 4R
c) 3HR
d) 6H
e) 9H

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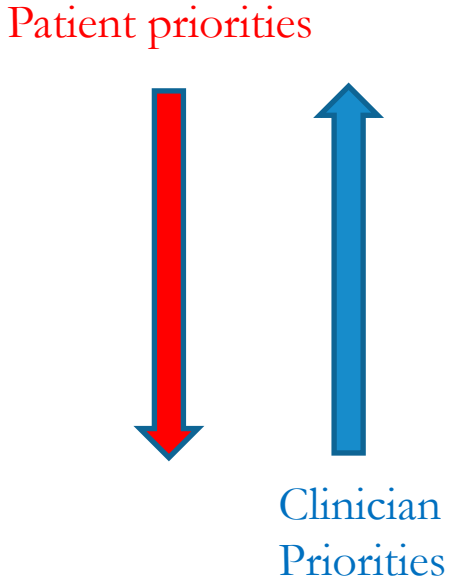
Adult Regimen Case Options

Preferred treatment is **3HP or 4R.** Now, we need more information (pt's order of priority):

- Uncle's baseline health and sickness after medication?
  - Was he coughing or was the TB asleep in his body?
- When's her next trip to her home country?
  - Is it usually around the same time or is it more based on family needs?
- What is an easier routine for her daily or weekly medication?
- Is she breast feeding?
- HIV status?
- Chronic conditions and other medications?



“No, you take the pills”

You have LTBI, which regime would you prefer?

a) 3HP
b) 4R
c) 3HR
d) 6H
e) 9H

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Pediatric LTBI Regimens and Dosage

Therapy	Frequency and Duration	Dosage	Comments
Isoniazid AND rifapentine, administered as directly observed therapy[a]	Once weekly for 12 wk	Isoniazid: 15 mg/kg rounded up to nearest 50 or 100 mg (max, 900 mg) Rifapentine: ▸ 10.0–14.0 kg: 300 mg ▸ 14.1–25.0 kg: 450 mg ▸ 25.1–32.0 kg: 600 mg ▸ 32.1–49.9 kg: 750 mg ▸ ≥50 kg: 900 mg max	▸ Should not be used in children younger than 2 y ▸ Most experts consider isoniazid-rifapentine to be the preferred regimen for treatment of LTBI for children 5 y and older, and some experts prefer isoniazid-rifapentine therapy for LTBI in children 2 y and older.
Rifampin	Daily for 4 mo	15–20 mg/kg (max, 600 mg)	
Isoniazid	Daily for 9 mo	10–15 mg/kg (max, 300 mg)	Contraindications: ▸ Patient received antituberculosis therapy previously ▸ Resistance to isoniazid is suspected or proven in source case ▸ Determine serum transaminase concentrations in patients with underlying liver or biliary disease, during pregnancy or the first 12 weeks postpartum, with concurrent use of other potentially hepatotoxic drugs, or if there is clinical concern of possible hepatotoxicity

LTBI indicates latent *M tuberculosis* infection.

[a] Dosage from Centers for Disease Control and Prevention. Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent *Mycobacterium tuberculosis* infection. *MMWR Morb Mortal Wkly Rep.* 2011;60(48):1650–1653.

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Pediatric Regimen Case

A 3-year-old has been living in a house with exposure to an active TB case (non- resistant to INH) and has tested positive for LTBI with active TB ruled out. What treatment do you recommend for this 15kg (33lbs) patient (select all that apply)?

a) Isoniazid 300mg Daily for 9 months

b) Rifapentine 225mg Daily for 4 months

c) INH 375mg and Rifampin 450mg weekly for 12 weeks

d) None of the above are appropriate for age

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Pediatric Regimen Case Options

Correct answer is D. Preferred treatment is pediatric dosing of **3HP** (INH 350mg-375mg and *Rifapentine* 450mg weekly for 12 weeks).

- Alternative options include- *Rifampin* 225mg-300mg daily for 4 months or Isoniazid 150mg-300mg daily for 9 months
- Consider crushing Rifapentine and Isoniazid or opening Rifampin capsule right before administering and mixing with smallest amount of food possible. Once crushed or opened, administer medication right away.
- Expect to devote a significant amount of face-to-face appointment time to educating parents/guardians and reassurance of med/pill burden vs lifetime risk of activation of LTBI.

LTBI Treatment: Monitoring, Adult and Pediatric

- Routine baseline laboratory testing is not required EXCEPT if…
  - HIV co-infected
  - Pregnant or early postpartum
  - History of liver disease or heavy alcohol use
  - Injection drug use
  - Taking other potentially hepatotoxic medications
  - Prior elevated serum transaminase concentrations
  - History of hematologic condition
  - Other known clinical indication

Then obtain…

→ Baseline AST, ALT & CBC

→ Repeat LFTs if:
- baseline abnormal
- risk for hepatic disease
- signs/symptoms of DILI
- continued heavy or daily use of alcohol

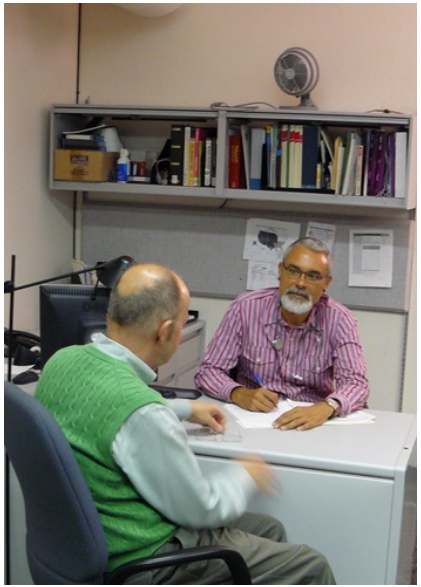
→ Repeat CBC if:
- Flu-like symptoms
- Petechiae

- Offer HIV testing if status unknown
- Baseline hep serologies when indicated (e.g., from high-incidence area)

References: NSTC/NTCA (2021). Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations

LTBI Treatment: Monitoring, Adult and Pediatric (2)

- Face-to-face assessment monthly for:
  - Treatment adherence
  - Symptoms of hepatitis or other side effects
    - Anorexia, nausea or vomiting
    - RUQ abdominal pain
    - Fatigue or weakness
    - Dark urine
    - Rash
    - Numbness/tingling hands or feet (INH only)
- Hold/Stop LTBI treatment when:
  - LFTs are greater than 3x ULN and the patient has symptoms
  - LFTs are greater than 5x ULN
  - patient is intolerant for other reasons



LTBI Treatment Monitoring Case

A 58-year-old patient with liver disease has had baseline AST, ALT, and CBC prior to starting 3HP which were mildly elevated AST/ALT. At the one-month follow up meeting which of these would NOT be a correct course of action:

a) Check current AST, ALT, and CBC to monitor because these labs were elevated at baseline

b) Patient has numbness in their feet, so you redraw an AST, ALT, and CBC

c) Patient is very happy they are being treated and feels great. No need to draw labs

d) Hold treatment as their LFTs are 3x ULN and their feet have been feeling numb. You call the local TB controller for advice

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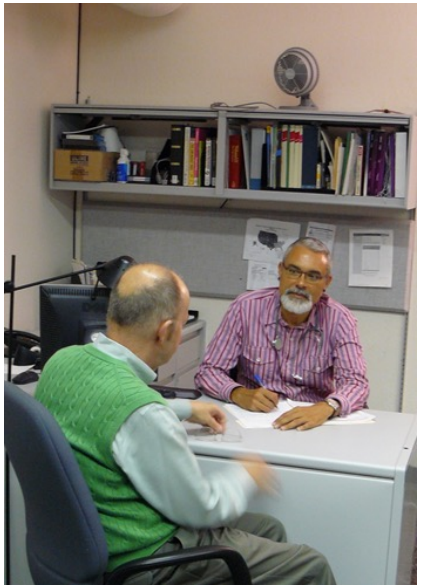

LTBI Treatment Monitoring Case Options

- C is not an appropriate course of treatment due to elevated baseline labs. (A, B, and D are all correct)
- Labs are not necessary to monitor LTBI treatment in most straight-forward, normal cases
- Once you start seeing abnormalities in labs, you usually want to continue to monitor them on at least a monthly basis
- Contact your local TB experts at the county and state levels if treatment and/or monitoring gets confusing or complicated.

Let's talk

- Drive conversations toward addressing patient's concerns and motivations first.
- For demonstration of how to address patient concerns and how to present patient education go to Latent TB Videos for Healthcare Providers at the Curry Center website. (https://www.currytbcenter.ucsf.edu/products/view/latent-tb-videos-healthcare-providers)
- Thank you for treating LTBI in our communities!

Break

- 20-20-20
- The rule says that for every 20 minutes spent looking at a screen, a person should look at something 20 feet away for 20 seconds.