

## Treating TB Infection





#### 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 <u>always</u> 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) *i*

Let's review on the next slide!



### LTBI Regimens and Dosage

	DRUG	DURATION	FREQUENCY	TOTAL DOSES	DOSE AND AGE GROUP
Preferred	ISONIAZID† AND RIFAPENTINE†† (3HP)	3 months	Once weekly	12	Adults and children aged ≥12 yrs INH:  15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT:  10-14.0 kg; 300 mg 14.1-25.0 kg; 450 mg 25.1-32.0 kg; 600 mg 32.1-49.9 kg; 750 mg ≥50.0 kg; 900 mg maximum  Children aged 2-11 yrs
	RIFAMPIN <sup>5</sup>				INH': 25 mg/kg; 900 mg maximum RPT'': See above Adults: 10 mg/kg; 600 mg maximum
	(4R)	4 months	Daily	120	Children: 15–20 mg/kg <sup>ll</sup> ; 600 mg maximum
	ISONIAZID¹ AND RIFAMPIN⁵ (3HR)	3 months	Daily	90	Adults INH <sup>1</sup> : 5 mg/kg; 300 mg maximum RIF <sup>9</sup> : 10 mg/kg; 600 mg maximum
					Children INH <sup>‡</sup> : 10-20 mg/kg <sup>‡</sup> ; 300 mg maximum RIF <sup>§</sup> : 15-20 mg/kg; 600 mg maximum
Alternative		6 months	Daily	180	Adults Daily: 5 mg/kg; 300 mg maximum Twice weekly: 15 mg/kg; 900 mg maximum
	ISONIAZID† (6H/9H)		Twice weekly¶	52	
		9 months	Daily	270	<b>Children</b> Daily: 10-20 mg/kg*; 300 mg maximum Twice weekly: 20–40 mg/kg*; 900 mg maximum
			Twice weekly¶	76	

<sup>\*</sup>For persons with HIV/AIDS, see Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV available at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/367/overview. htsoniazid is formulated as 100-mg and 300-mg tablets.







<sup>††</sup>Rifapentine is formulated as 150-mg tablets in blister packs that should be kept sealed until use.

Untermittent regimens must be provided via directly observed therapy (i.e., a health care worker observes the ingestion of medication).

<sup>§</sup>Rifampin (rifampicin) is formulated as 150-mg and 300-mg capsules.

<sup>||</sup>The American Academy of Pediatrics acknowledges that some experts use rifampin at 20-30 mg/kg for the daily regimen when prescribing for infants and tod dlers (Source. American Academy of Pediatrics, Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, IL: American Academy of Pediatrics, 2018 829-53).

Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, It.: American Academy of Pediatrics; 2018 829-4The American Academy of Pediatrics recommends an INH dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice weekly regimen.

### 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 daily100mg 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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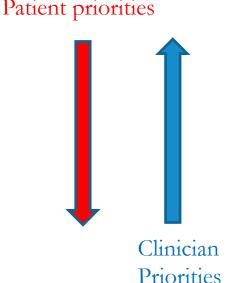
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### Adult Regimen Case Options

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 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

Let's review on the next slide!



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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 INH and Rifampin for 3 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
- Offer HIV testing if status unknown
- Baseline hep serologies when indicated (e.g., from high-incidence area)

#### 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



### 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:

- 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
- 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 straightforward, 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.

