Latent Tuberculosis Infection (LTBI) Microlearning Supplemental Information

MINNESOTA CENTER OF EXCELLENCE IN NEWCOMER HEALTH MICROLEARNING SERIES

Screening for LTBI

- Only screen persons with risk factors for tuberculosis (TB).
- Persons who test positive for TB infection should be assessed for active TB disease before initiating LTBI treatment.
- IGRA (T-SPOT.TB and QuantiFERON-TB Gold plus) have a sensitivity of approximately 90%.
- IGRA can be used for children at any age (AAP: Update in the Diagnosis and Treatment of Tuberculosis in Children (https://doi.org/10.1542/pir.2024-006539).
- TST has a sensitivity of approximately 80%.
- TST cutoffs for a positive test:
  - **5 mm:** if also has HIV, close contact of TB case, fibrosis on CXR, immunosuppression (e.g., TNF-alpha inhibitors, chemotherapy, organ transplantation, glucocorticoid treatment).
  - **10 mm:** if is also a recent immigrant, injection drug user, resident/employee of prison, jail, nursing home, hospital, shelter; diabetes, renal failure, leukemia/lymphoma, weight loss, gastrectomy; child < 4 years.
  - **15 mm:** all others.

Contacts to infectious TB

- "Close contact" is defined as someone who shared the same airspace in an enclosed setting with the infected individual (e.g., household member, roommate).
- Close contact has the highest risk of progression to TB disease in the first 2 years after infection.
- AFB smear positivity has the highest urgency for contact tracing as smear-positive cases are 5-10 time more infectious than smear-negative cases. Also, cavitary disease on chest X-ray increases infectiousness, even if AFB smears are negative given presumed higher bacillary load.
- TB is not spread by touching surfaces, sharing food, or casual contact.

Drug-drug interactions

- **Rifamycins** can reduce serum concentration of warfarin, apixaban, rivaroxaban, dabigatran, hormonal contraceptives, levothyroxine, methadone and certain HIV drugs.
- **Isoniazid** can increase serum concentration of carbamazepine, phenytoin, warfarin, disulfiram and others. It can also increase serum concertation of itraconazole and ketoconazole.

Toxicity monitoring

- INH induced peripheral neuropathy can be mitigated by pyridoxine 25-50 mg/day.
- Obtain baseline CBC, ALT, AST for persons with following comorbidities:
  - HIV/AIDS or other immunosuppressive conditions
  - Liver disorders (e.g., HCV, HBV, cirrhosis)
  - Pregnancy or postpartum period (≤3 months after delivery)
  - Regular alcohol use
  - Injection drug use
  - Use of medications with known possible interactions
- Continue laboratory monitoring during treatment if:
  - Baseline testing is abnormal
  - At risk for hepatotoxicity
  - New adverse side effect or hypersensitivity
- Hold medications if a serum AST concentration is ≥5 times the upper limit of normal in the absence of symptoms or ≥3 times the upper limit of normal in the presence of symptoms.
- Adverse reactions to LTBI regimens:

INH + RPT	INH + RIF	RIF	INH
Hypersensitivity 3.8% Rash 0.8% Hepatotoxicity 0.4%	Rash 1-8% Hepatotoxicity 1-6% Unacceptable GI events 0-6%	Hypersensitivity 3.8% Rash 0.2% Hepatotoxicity 0.3% Hematologic toxicity 0.2% Unacceptable GI events 0.1%	Hepatotoxicity 2-3% Rash 0.6% Hypersensitivity 0.5%

[Shah M, et al. Latent Tuberculosis Infection. N Engl J Med. 2021 Dec 9;385(24):2271-2280. PMID: 34879450]

INH = isoniazid; RPT = rifapentine; RIF = rifampin

LTBI treatment completion

- **3HP regimen:** completion of therapy is 12 doses in 16 weeks. If 12 doses cannot be completed, at least 11 weekly doses of treatment within 16 consecutive weeks. Doses must be given at least 72 hours apart.
- **3HR regimen:** 3 months of daily dosing totaling 90 doses. Should be completed within 4 consecutive months.
- **4R regimen:** 4 months of daily dosing totaling 120 doses. Should be completed within 6 consecutive months.
- **6H regimen**: 6 months once daily totaling 180 doses. If gap(s) are >two months, patient should be re-evaluated for signs and symptoms before resuming treatment.
- **9H regimen**: 9 months once daily totaling 270 doses. If gap(s) are >two months, patient should be re-evaluated for signs and symptoms before resuming treatment.
- If not at high-risk for active TB disease and has had repeated interruptions or treatment attempts, therapy may be discontinued and the patient educated on signs and symptoms of active TB disease and instructed to seek medical care immediately, if development any of these symptoms.

Switching of preventive treatment regimens

- When switching between two different regimens, the total duration must follow the new regimen's full length (do not subtract or add previously completed doses). The rationale for this is that different drugs have different mechanisms, half-lives, and effectiveness, and currently no studies are available to support "mixing" regimens.

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11/4/25

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