LATENT TUBERCULOSIS INFECTION

Latent tuberculosis infection (LTBI) is the presence of Mycobacterium tuberculosis in the body without signs and symptoms, or radiographic or bacteriologic evidence of tuberculosis (TB) disease.

DIAGNOSIS OF LTBI: Tuberculin Skin Test (TST) or Interferon Gamma Release Assays (IGRAs)

• Persons with HIV have a 3-26% risk per year for developing active TB if infected with M. tuberculosis
• Test pts with HIV for LTBI, with either a TST or an IGRA, at time of diagnosis of HIV.
• If the initial test is negative, consider re-testing with a different test when infection, progression, and a poor outcome are indicated.
• All pts with (+) TST result should be evaluated for active TB (i.e., chest x-ray and clinical evaluation for pulmonary and extrapulmonary TB) before starting TB therapy.

Tuberculin Skin Test

The Mantoux TST method is recommended and each step must be properly performed to increase accuracy of results.

- A 5-mm induration (raised palpable, hardened area) must be measured area of induration (raised palpable, hardened area), not injected 0.1 mL of tuberculin purified protein derivative (PPD)
- Pts who may have repeat screening (e.g. healthcare workers, staff / students at risk)

Mantouxwallchart.pdf

Regional TB Consultation Services

TB Hotline - Southeastern National Tuberculosis Center 24-Hour Hotline: 800-4TB-INFO or http://www.cdc.gov/tb/publications/ltbi/ltbiresources.htm

Clinical Consultation

National HIV Clinician Consultation Center Visit site for additional details including online resources, phone numbers and hours of operation.

Community Consultation

HEUDS Management PeriHEUDS
HIV/AIDS 24H-PPD
Healthcare C Management Substance Use Management
HVP - Pre-Exposure Prophylaxis PEP: Post-Exposure Prophylaxis

AETC National Coordinating Resource Center

www.aidsetc.org Supporting HIV Education for Healthcare Professionals. or call 1-800-4TB-INFO Medical Consultation Hotline

LATENT TUBERCULOSIS INFECTION Continued

Interpretation of TST Results

• Reaction of ≥ 5 mm is considered (+) in HIV-infected persons
• A (+) TST or IGRA result does not exclude LTBI as the patient may have a compromised ability to react to tests for TB infection

NOTE: If TB disease ruled out, pts with HIV with significant exposure to persons with pulmonary TB should be treated for LTBI regardless of TST or IGRA result.

• False (+) may result if:
  - Reaction with non-tuberculous mycobacteria
  - Prior Bacillus Calmette-Guérin (BCG) vaccine (reactivity wanes over time; use of IGRA preferred)
• Improper testing or interpretation of results
  - Possible reasons for false (-) (I am not a十足 include:
    - Recent TST infection (2-8 weeks after exposure)
    - Extremes of age (newborns, elderly)
    - Concurrent infections (certain bacterial, fungal, or viral)
    - Overwhelming TB disease
    - Immune suppression due to meds, malignancy, or HIV (energy testing is not recommended)
• Problem with tuberculin used (e.g., improper storage, poor admin technique (e.g., subcutaneous instead of intradermal), improper reading or result interpretation
• Recent live virus vaccine (administer TST at same time as vaccination and wait 4-6 weeks after)

Contraindication to a TST

• Contraindicated for pts with a severe reaction prior to TST (e.g., necrosis, blistering, anaphylactic shock or urticaria)

NOTE: TST is NOT contraindicated in infants, children, pregnant women, persons immunocompromised with BCS, or persons who have been previously tested.

Interferon (IFN)-Gamma Release Assays (IGRAs)

• IGRA results are in vitro tests that detect IFN-gamma release in response to Mycobacterium tuberculosis specific antigens. Specificity of the test is 97%, compared to 96%-98% for TST.
• Three FDA approved assays are available:
  - QUANTIFERON® (Cellebi)
  - T-SPOT® TB Test (Oxford Immunotec Limited)
• It is important that test samples be drawn, transported, processed, and interpreted according to each manufacturer’s recommendations.
• Blood samples must be processed within 8-16 hours after collection. (time requirements differ among assays) so that the white blood cells remain viable.
• Additional information about IGRA can be found online at:

TREATING LTBI (to prevent TB disease)

Treat pts with HIV with the symptoms of active TB and (-) culture for M. tuberculosis: and

• (diagnostic test for TST or IGRA)
  - Close contact with a person with infectious pulmonary TB even if TST or IGRA are (-)

TREATING LTBI (to prevent TB disease)

• Close contact with a person who has been treated for active TB; or
• A recent live virus vaccine;
• Infected with HIV/AIDS;
• Occupational exposure to infectious TB;
• A person with TB meningitis, or
• Pre-Exposure Prophylaxis (PrEP), Non-Occupational Post-Exposure Prophylaxis (nPEP) and Occupational PEP (oPEP)

Visit www.sntc.medicine.ufl.edu/
**ACTIVE TUBERCULOSIS DISEASE Continued**

NOTE: In active tuberculosis, sputum smear and culture are usually (but should always be done even when COT is negative as a (+) culture is helpful for diagnosis and guiding treatment.

**Treatment of Drug-Susceptible Tuberculosis Disease in Patients with HIV**

- Use case management during treatment of pts with TB disease. Case management is defined as patient education and counseling, field and home visits, integration and coordination of care with specialists and medical home care, patient reminders, and incentives and enablers.
- All pts treated for TB disease should receive DOT.
- All pts with presumed or confirmed TB disease should be started on a 4-drug regimen of isoniazid (INH), rifampin (RIF) or rifabutin (RFB), pyrazinamide (PZA), and ethambutol (EMB).
- Rifabutin is often substituted for rifampin in pts with HIV since it is a less potent inducer of drug metabolism and can be used with most ART (See Table 5 for information about drug interactions between rifampins and ART).
- Rifapentine is a long-acting rifampin that is dosed once weekly, but should be used only in pts with HIV due to higher risks of relapse and resistance.
- Initial phase: INH + (RIF or RFB) + PZA + EMB po once daily (5-7 days per week) to 2 months (discontinue EMB prior to 2 months if susceptible to INH, RIF, RFB, PZA).
- Continuation phase: INH + (RIF or RFB) + PZA + EMB po once daily (6-7 days per week) for 4 months.
- Relapse: Continue phase A until at least 7 months (i.e., 9 months total treatment) if the pt is not on ART, or if chest X-ray, and/or the sputum culture remains (+) at 2 months.

**Duration of therapy is based on number of doses received as well as duration**

NOTE: If sputum culture remains positive after 2 months of TB treatment, send repeat sputum for susceptibility testing and consult an expert.

**Table 3. Monitoring Treatment for Active Tuberculosis Disease in Patients with HIV**

- X-recommended in all pts. O-dot recommended in certain situations (see footnotes).

<table>
<thead>
<tr>
<th>Activity</th>
<th>Baseline</th>
<th>Month of Treatment Completed</th>
<th>End of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microbiology</td>
<td>Spumum smear and culture</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Drug susceptibility testing</td>
<td>X</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Imaging</td>
<td>CR or other imaging*</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Clinical Assessment</td>
<td>Weight*</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Symptom and adherence review*</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>HIV care</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory Testing</td>
<td>ART, ALT, bilirubin, alkaline phosphatase*</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Platelet count*</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Creatinine*</td>
<td>X</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>HIV testing†</td>
<td>X</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Hepatitis B and C screens</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Diabetes Screen†</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

* In pts who obtain sputum for smear and culture monthly until 2 consecutive (-) culture results. Obtain sputum more frequently in emergency to assess for treatment response (optional). Test at least one baseline specimen using a rapid molecular test.

† Drug susceptibility testing for INH, RIF, EMB, and PZA is recommended. Repeat susceptibility testing if pt remains culture (+) after completing 3 months of treatment. Monthly resistance testing recommended for pts at risk for drug resistance.

**Table 4. Drugs Used for Treatment of Drug-Susceptible Active TB and LTBI**

See the TB Guidelines and call the 24-hour TB Hotline 1.800.4TB.INFO (1.800.482.4636) for assistance in managing pts with renal and/or hepatic impairment.

**Drug** | **Dosage Form** | **Food Restrictions** | **Important Points**
|-------------|-----------------|-----------------------|-------------------------|
| Isoniazid (INH) | 100, 300 mg tab; 50, 60 mg/mL oral (1:2) | Empty stomach (30 mins before or 2 hours after a meal) | Avoid antagonists for 2 hours before and after INH. Most common/severe AEs: hepatitis, peripheral neuropathy, optic neuritis, rare hematologic or dermatologic reactions (200 mg/100 mL); (Co-admin painkiller (vibranic acid) 25-50 mg once daily to prevent neuropathy
| Rifabutin (RFB) | 150 mg cap | With or without food, milk, and/or 60 mL milk (applesauce) | Most common/severe AEs: red-orange discoloration of body fluids (e.g., urine, sweat, tears), rash, flu-like syndrome, arthralgias, hematologic manifestations (pneumonia, neutropenia, thrombocytopenia, urtis-dose-related), hepatitis, nausea, vomiting, arthralgias, or other sensory manifestations; chemosensitivity testing if INH or RIF are contraindicated. Most common/severe AEs: nausea, vomiting, eosinophilia, rash, fever, arthralgias. Hematologic manifestations including neutropenia or rash, renal manifestations including 
| Ethambutol (EMB) | 150 mg cap; 150 mg injection (600 mg vial) | Empty stomach (1 hour prior to or 2 hours after meal); may take with small cap of milk and/or 60 mL milk (applesauce) | Most common/severe AEs: dose-related discoloration of body fluids (e.g., urine, sweat, tears), rash, flu-like syndrome, hematologic manifestations (pneumonia, neutropenia, thrombocytopenia, hepatopathy, eosinophilia, or other sensory manifestations; chemosensitivity testing if INH or RIF are contraindicated. Most common/severe AEs: nausea and vomiting (usually improves after a few weeks), arthralgias, hematologic manifestations, fever, rash, eosinophilia, rare hematologic reactions (thrombocytopenia, purpura, pancytopenia) |
| Pyrazinamide (PZA) | 500 mg cap | With or without food, milk, and/or 60 mL milk (applesauce) | Most common/severe AEs: nausea and vomiting (usually improves after a few weeks), arthralgias, hematologic manifestations, fever, rash, eosinophilia, rare hematologic reactions (thrombocytopenia, purpura, pancytopenia) |

**Table 5. Drug Interactions with Rifampin and ART**

For additional details, including interactions with rifampin, see the drug-drug interaction tables in the Adult/Adolescent ARV guidelines (www.hivguidelines.org) for information on drugs and classes of drugs.

**Rifampin (RIF)-Based Regimen with ART**

**NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)**

Do not use RIF with tenofovir alafenamide (TAF) containing regimens (i.e. Biktarvy®, Descovy®, Genvoya®, Odyssey®)

**NON-NUCLEOSIDE REVERSE TRANSSCRIPTASE INHIBITORS (NNRTIs)**

- If boosted PI included in regimen, see dosing recommendations listed above.
- Do not use PI if boosted or unboosted containing regimen.
- INTEGRASE STRAND TRANSFER INHIBITORS (INSTIs)

- Increase dolutegravir (DTG) to 50 mg bid. Use alternative to RIF if INSTI-experienced with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance.
- Increase raltegravir (RAL) to 800 mg bid. Do not use once daily RAL with rifampin.
- Do not combine with Bicalutamide (BC) or entecavir (ETV)/TAF (Biktarvy®)
- Do not use RIF with efavirenz (EVR) containing regimens (i.e. Genvoya® or Stridbit®)

**CCRS INHIBITOR**

- Use MVC 600 mg bid with RIF, or 300 mg bid if used with RIF and a strong CYP3A inhibitor

**Rifabutin (RFB)-Based Regimen with ART**

**NRTIs**

Do not use RFB with TAF containing regimens (i.e. Biktarvy®, Descovy®, Genvoya®, Odyssey®, Symtuza®)

**NNRTIs**

- Do not use RFB with PI (boosted or unboosted) containing regimen.

**PROTEASE INHIBITORS (PIs)**

- Do not use RIF with any PI (boosted or unboosted) containing regimen.

**Therapeutic Drug Monitoring (TDM)**

- Consult TDF for TB, HIV, NNRTI, PI integrase, maraviroc, and other interacting drugs if sLED, renal or hepatic disease, risk for malabsorption (e.g. diabetes) or possible treatment failure
- Consult TDF if second-line TB drugs are used
- Consult TDF if patient remains culture positive after 2 months of therapy or is clinically slow to improve
- Consult a TB/HIV expert for assistance in managing these pts
- Call the 24-hour TB Hotline 1.800.4TB.INFO (1.800.482.4636) for assistance

**HIV and TB drug levels are available through the Infectious Disease Pharmacokinetic Laboratory at the University of Florida in Gainesville (http://sasdp.coff.edu), expert interpretation and consultation regarding results are available**