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 Assay (IGRA)
- **TST**: With HIV+ have a 3-16% risk per year for developing active TB.
- **IGRAs**: Use with HIV positive.
- **TST** detects prior infection (booster effect).
- **IGRAs**: Early diagnosis of active TB.

TREATMENT OF TUBERCULOSIS (TB) IN ADULTS WITH HIV INFECTION

References
- Unless otherwise noted, the information contained in this resource has been adapted from the references listed below. For more information, please consult: [www.cdc.gov/tb](http://www.cdc.gov/tb) for additional up-to-date information on the diagnosis and treatment of LTBI and/or active TB.
- **Official American Thoracic Society/Centers for Disease Control and Prevention Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis.** Clin Dis. (2016) 63 (7). Available at: [cid:oxfordjournals.org/content/63/7/e147](http://cid.oxfordjournals.org/content/63/7/e147)
- **LATENT TUBERCULOSIS INFECTION Continued**
- **Regional TB Consultation Services**
- **National HIV Consultation Services**
- **TREATMENT OF TUBERCULOSIS (TB) IN ADULTS WITH HIV INFECTION**
- **Regional TB Consultation Services**
- **National HIV Consultation Services**
- **TREATMENT OF TUBERCULOSIS (TB) IN ADULTS WITH HIV INFECTION**

LATENT TUBERCULOSIS INFECTION CONTINUED

Interpretation of TST Results
- Reaction of 5 mm in diameter is considered positive (TST or IGRA result does not exclude LTBI despite TST reactivity).
- False-negative result is rare. (This condition is not being assessed in this document.)
- False-positive result may be present in:
  - Immune suppression due to medications, malignancy, or HIV (anergy is not recommended).
  - Extremes of age (newborns, elderly).
  - Recent TB infection (2-8 weeks after exposure).
  - Concurrent infections (certain bacterial, fungal, or viral).
  - Overwhelming disease.
  - Immune suppression due to meds, malignancy, or HIV (anergy testing is not recommended).
  - Problem with tuberculin used (e.g., improper storage), poor administration technique (subcutaneous instead of intradermal), impaired reading or result interpretation.
  - Recent live virus vaccination (administer TST at same time as vaccine or wait 4-6 weeks afterwards).

Contraindications to a TST
- Contraindicated for persons with a severe reaction to prior TST (e.g., necrosis, blisters, anaphylactic shock or ulceration).

NOTE: TST is NOT contraindicated in infants, children, pregnant women, persons previously vaccinated with BCG, or persons who have had BCG vaccination.

Interferon (IFN) Gamma Release Assays (IGRAs)
- **IGRAs** are in vitro assays that detect IFN gamma release in response to Mycobacterium tuberculosis specific antigens.
- Specificity of IGRA is 92-97%, compared to 56%-95% for TST.
- Three FDA approved assays are available:
  - **QuantiFERON®** - TB Gold in Tube (Qiagen)
  - **QuantiFERON®** - TB Gold Plus (Qiagen)
  - T-SPOT® TB Test by Oxford & Ayscough Consulting Ltd.
- 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:
  - [www.cdc.gov/tb/publications/fact sheets/testing/IFIRAs.htm](http://www.cdc.gov/tb/publications/fact sheets/testing/IFIRAs.htm)
  - [www.cdc.gov/mmwr/pdf/rr/rr5905.pdf](http://www.cdc.gov/mmwr/pdf/rr/rr5905.pdf)
ACTIVE TUBERCULOSIS DISEASE

- **Initiating ART in Patients with HIV with Active TB**
  - All pts with HIV with active TB should start ART:
    - CD4 < 50: start ART within 2 weeks of starting TB therapy
    - CD4 ≥ 50: start ART at 8 weeks of starting TB therapy

**NOTE:** If TB meningitis is suspected, do not start ART early due to immune Reconstitution Inflammatory Syndrome (IRIS) risk. Corticosteroids recommended with TB therapy. Consult an expert for management.

**Diagnosis of Active Tuberculosis Disease**
- Evaluate all pts at a TB test (TST or IGRA) for active TB
- Test with IGRA, KIT, or TST, in all pts suspected of having active TB; a + test does not rule out active TB, particularly in immunosuppressed pts.

**Symptoms of active pulmonary TB:**
- Prolonged productive cough (usually > 3 weeks), chest pain, hemoptysis, fever/chills, night sweats, decreased appetite/weight loss, fatigue. Tuberculin test can be atypical in pts with HIV.

**Pts with HIV have increased risk of extrapulmonary TB:** Symptoms and clinical presentation depend on the site of infection. Consult a TB/HIV expert for the management of extrapulmonary TB.

**RIF:**
- Should be used if pulmonary or extrapulmonary TB is suspected. Abnormalities often seen in upper lobe. Pts with HIV and TB may have atypical or normal CXR appearance despite pulmonary disease.

**Sputum smear and culture:**
- 3 sputum specimens (3-4 hours apart) should be sent for AFB stain and culture (even if smear is -). Perform a nucleic acid amplification test (NAAT) on at least one sputum sample. Consider sputum induction to obtain good specimen.

**On one respiratory specimen, obtain rapid molecular drug resistance testing (DNA) on at least one sputum sample.**

**As part of the baseline and monthly clinical assessment, assess concurrent medications for drug-drug interactions.**

**Consultation:**
- Rifapentine: RIF (RFB) + PZA + EMB + INH (600 mg vial)
- Rifabutin: RFB (500 mg vial)
- Monitor for antimycobacterial efficacy with HIV.

**Consult a TB/HIV expert for managing these pts**
- Call the 24-hour TB Hotline 1.800.4TB.INFO (1.800.482.4636) for assistance.

**Adverse Effects of TB Drugs:**
- Review the ATS/CDC/IDSA 2016 TB treatment guidelines, product package inserts, the OFFICIAL ATS Statement: Hepatitis on Antituberculosis Therapy and other clinical resources.
- If a drug must be discontinued, a replacement drug is given.

**Consult a TB/HIV expert for management of significant adverse events or cases requiring changes in TB regimen.**

**Immune Reconstitution Inflammatory Syndrome (IRIS):**
- Pts may have worsening or new onset symptoms of active TB following treatment initiation (more common in pts with CD4 < 50 cells/mm³ and pts with higher pre-ART HIV viral load)
- Continue both ART and TB therapy while managing IRIS.
- Mild cases can be treated with NSAIDs while more severe cases may require corticosteroid therapy (such as for TB meningitis).

**Stoeding doxion:** Prednisone 1.5 mg/kg/day for 2 weeks followed by 0.5 mg/kg/day for 2 weeks (some patients may require longer duration of steroid treatment and more gradual tapering).

**Consult a TB/HIV expert as needed for IRIS.**

**Therapeutic Drug Monitoring (TDM):**
- Consider TDM for TB, HIV (NNRTI, PI, integrase inhibitor), and other interacting drugs if signs of ARI, renal or hepatic disease, risk for malabsorption (e.g. diarrheal) or possible treatment failure.
- Consider TDM if 2nd-line TB drugs are used.
- Consult a TB/HIV expert if patient remains culture positive after 2 months of therapy or is clinically slow to improve.
- Consult an TB/HIV expert for assistance in managing these pts.

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

<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>X X X X</td>
<td>X X X X</td>
<td>X X X X</td>
</tr>
<tr>
<td>Sputum smear and culture</td>
<td>X X X X</td>
<td>X X X X</td>
<td>X X X X</td>
</tr>
<tr>
<td>Drug susceptibility testing</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Imaging</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>CXR or other imaging</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Clinical Assessment</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Weight*</td>
<td>X X X X</td>
<td>X X X X</td>
<td>X X X X</td>
</tr>
<tr>
<td>Symptom and adherence review*</td>
<td>X X X X</td>
<td>X X X X</td>
<td>X X X X</td>
</tr>
<tr>
<td>Vision assessment*</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>AST, ALT, bilirubin, alkaline phosphatase</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Platelet count</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Creatinine</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>HIV testing*</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hepatitis B and C screen</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Diabetes Screen*</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Form</th>
<th>Food Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin (RFB)</td>
<td>600 mg, 450 mg, 300 mg, 150 mg</td>
<td>After meals</td>
</tr>
<tr>
<td>Rifabutin (RFB)</td>
<td>300, 150 mg</td>
<td>After meals</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>500 mg, 300 mg, 150 mg</td>
<td>After meals</td>
</tr>
<tr>
<td>Pyrazinamide (PZA)</td>
<td>1500 mg</td>
<td>After meals</td>
</tr>
</tbody>
</table>

**Important Points**
- Most common/severe AEs: hepatitis, peripheral neuropathy, optic neuritis, rare hematologic or dermatologic reactions
- Most common/rare AEs: flu-like syndrome, arthralgias, neuropathy, hepatitis

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

<table>
<thead>
<tr>
<th>Rifampin (RFB) + Regimen</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>INTEGRASE STRAND TRANSFER INHIBITORS (INSTIs)</th>
<th>CRBS INHIBITOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritonavir (RdT)</td>
<td>Boosted</td>
<td>Boosted</td>
<td>Boosted</td>
<td>Boosted</td>
</tr>
<tr>
<td>ATV/c, ETR/c, DRV/c</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Emtricitabine/TAF</td>
<td>Boosted</td>
<td>Boosted</td>
<td>Boosted</td>
<td>Boosted</td>
</tr>
</tbody>
</table>

**Table 2. Adult Dose of Agents for Active TB**

<table>
<thead>
<tr>
<th>Drug (mg/kg)</th>
<th>Isoniazid</th>
<th>Rifampin*</th>
<th>Rifabutin*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily*</td>
<td>45-50</td>
<td>60-75</td>
<td>60-75</td>
</tr>
<tr>
<td>Total</td>
<td>345-420</td>
<td>450-530</td>
<td>450-530</td>
</tr>
</tbody>
</table>

**Dose based on actual weight body if not obese (< 20% above ideal weight).**

**Daily dose of RFB based on other drugs in regimen (consider TDM).**

<table>
<thead>
<tr>
<th>Ethambutol (500 mg)</th>
<th>300 mg</th>
<th>600 mg</th>
<th>900 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily†</td>
<td>600</td>
<td>1200</td>
<td>1800</td>
</tr>
</tbody>
</table>

**Daily dose of PZA**
- 1000 mg tab daily
- 1500 mg cap daily

**Table 1. Adult Dose of Agents for Active TB**

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

**For additional details see the drug-drug interactions tables in the Adult/Adolescent ART guidelines of**


**Active tuberculosis disease (EMB) (RPT)**

**Table 6. Monitoring Treatment for Active Pulmonary TB**

**See the list for 3 recommended baseline and periodic assessments.**

**As part of the baseline and monthly clinical assessment, assess concurrent medications for drug-drug interactions.**

**Consultation:**
- Rifapentine: RIF (RFB) + PZA + EMB + INH (600 mg vial)
- Rifabutin: RFB (500 mg vial)
- Monitor for antimycobacterial efficacy with HIV.

**Consult a TB/HIV expert for 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://idp.cof.ufl.edu), expert interpretation and consultation regarding results are available.**