

## V. TB and HIV/AIDS

### A. Standards of Treatment and Management

**TB in people who are HIV-positive is an AIDS defining condition. Verify that this has been reported to the HIV/STD section.**

**The majority of TB treatment principles apply to people with HIV/AIDS who require treatment for TB disease. The following points are either unique to co-infected patients or deserve emphasis.**

1. Review all medications individual is taking and assess for potential drug interactions with TB medications
  - Concurrent administration of rifampin (RIF) with certain HIV medications (antiretroviral therapy) may be contraindicated or require dose adjustment.
  - **All HIV/TB patients must have their treatment regimens reviewed by a State TB Medical Consultant**
2. A recent (within 6 months) CD4 lab result must be obtained for all HIV/TB patients.
3. All HIV/TB patients need to be monitored closely for response to treatment and signs of treatment failure or relapse; if failure or relapse is suspected, assume rifamycin resistance until culture-confirmed otherwise. Treatment modification will require consultation with a State TB Medical Consultant
4. Most TB drugs should be calculated according to mg/kg body weight. Calculate on the lower figure in the range and round up to the next available dose supplied by the manufacturer (**see dosage tables in Chapters III & IV**)
5. HIV-positive individuals treated with isoniazid should receive Pyridoxine (B<sub>6</sub>) 25 mg daily or 50 mg twice/thrice weekly on the same schedule as isoniazid
6. All patients with TB/HIV should be initiated on antiretroviral therapy within 8 weeks of TB diagnosis. Patients with CD4 counts of 50 or less should be started on antiretroviral therapy within 2 weeks of TB diagnosis unless they have central nervous system tuberculosis, in which case expert consultation is recommended.
7. All TB patients should be counseled and tested for HIV and a recent (<6 month) CD4 count report obtained if HIV-seropositive

### B. LTBI Screening in People Living with HIV

1. Once HIV infection is diagnosed, all individuals are required by law (10A NCAC 41A .0202) to receive a tuberculin skin test or IGRA
2. Annual risk assessment (screening questionnaire for risk factors) should be performed for all people living with HIV. People with new or ongoing risk of exposure to TB should be tested with a TST or IGRA.

3. For those whose initial TST/IGRA was negative and whose immune function has improved in response to antiviral therapy (i.e., CD4 level has increased to > 200), the TST/IGRA should be repeated.
4. Reactions of  $\geq 5$ mm induration are considered positive

C. Candidates for Treatment of LTBI

**All of the following individuals should receive treatment for LTBI**

1. People with HIV who are TST reactors ( $\geq 5$ mm) or with a positive IGRA who have not previously received treatment for latent TB infection
2. People with HIV who are recent close contacts to known or suspected infectious TB disease regardless of previous LTBI treatment and regardless of TST/IGRA result
  - first evaluate for TB disease, with symptom screen and chest X-ray
  - if chest X-ray is normal, initiate treatment for LTBI in accordance with regimens found under E. of this chapter
  - if chest X-ray is abnormal or the patient has signs/symptoms possibly concerning for tuberculosis, consult provider
3. People with HIV and with fibrotic changes on chest X-ray consistent with prior TB who have received inadequate or no treatment (regardless of TST result) and who have been thoroughly evaluated for active TB

D. Chest X-rays Prior to Treatment of LTBI

1. People with HIV  $\geq 5$  years of age or older should receive a posterior-anterior chest X-ray
2. People with HIV < 5 years of age should receive a posterior-anterior and lateral chest X-ray
3. People with HIV with a previously documented positive TST/IGRA and a negative chest X-ray should have a repeat X-ray only when symptoms for tuberculosis disease are present

E. Latent TB Infection (LTBI) Treatment Regimens for people with HIV/AIDS

1. Acceptable treatment regimens (for dosing/monitoring see chapter III)
  - a. Isoniazid/rifampentine once-weekly for 12 weeks  
This is the preferred regimen for LTBI treatment for people living with HIV. This regimen is not compatible with a number of HIV medications (e.g. protease inhibitors) or may require dose adjustment of HIV medications. Reviewing concurrent medications prior to starting this regimen is essential. Directly observed therapy should be used if adherence is a concern.
  - b. Rifampin daily for 4 months  
This is an alternative regimen for LTBI treatment for people living with HIV who cannot take isoniazid/rifampentine. As with isoniazid/rifampentine, this

regimen is not compatible with several HIV medications, and reviewing concurrent medications prior to starting this regimen is essential.

- c. Isoniazid daily for 9 months  
This is the preferred regimen for people living with HIV who cannot take a rifamycin (rifampin/rifapentine) due to drug interactions or intolerance. This regimen is typically administered daily, but twice-weekly, directly observed therapy is a reasonable alternative if adherence is a concern and program resources are available.
- d. Rifabutin for 4 months  
This is an alternative regimen for patients exposed to isoniazid-resistant TB or who are intolerant to isoniazid. It may also be used for patients whose HIV regimen includes unacceptable drug interactions with rifampin but for whom a 9-month course of isoniazid is unlikely to be completed.
- e. Isoniazid/rifampin daily for 3 months  
This is an alternative regimen for patients if isoniazid/rifapentine is not available or not tolerated, a short-course option is desired, and no unacceptable drug interactions with isoniazid or rifampin are present.

## 2. Treatment of LTBI in pregnant women with HIV/AIDS

- a. Chest X-rays  
Due to the risk of progressive and/or congenital TB, pregnant women should have a PA view of the chest (with appropriate shielding) as soon as possible, even during the first trimester of pregnancy, if they have a positive TST/IGRA
- b. HIV-seropositive, asymptomatic TST/IGRA-positive pregnant women with a negative chest X-ray may be considered for LTBI treatment before delivery after a thorough discussion of risks and benefits (see chapter III for additional information). HIV-seropositive women who are recent contacts to infectious TB should be strongly encouraged to take LTBI treatment before delivery if evaluation reveals no clinical evidence of active TB.
- c. Treatment regimen
  - INH treatment of LTBI has recently been associated with increased adverse birth outcomes in pregnant women with HIV (Gupta A et al., New England Journal of Medicine 2019; 381: 1333). INH treatment of LTBI should probably be deferred for pregnant women with HIV who are on antiretroviral therapy and are not recent contacts to infectious TB
  - RIF is an acceptable alternative for pregnant women in the following circumstances:
    - Intolerance to INH
    - Individual is a close contact to INH-resistant, RIF-susceptible TB
    - Individual is high-risk for progression to active TB but is unlikely to adhere to a full 9-month course of INH

- Individual is at relatively high risk for hepatotoxicity from INH (e.g. excess alcohol use, concurrent hepatotoxic medication)
- RIF interacts with many other medications, including oral contraceptives, warfarin and many antiretrovirals. The patient's medication regimen should be carefully examined for potential medication interactions before prescribing RIF.
- There are limited data for use of rifabutin (RBT) in pregnancy and it should be used with caution

#### F. Tuberculosis Disease in People with HIV

The treatment regimen in people living with HIV may involve different TB drugs, may require daily rather than intermittent dosing, and may require longer treatment duration

1. Drugs used to treat TB in people living with HIV  $\geq$  12 yr.
  - a. If the patient is on antiretroviral therapy, the patient's TB treatment regimen should be reviewed with a State TB Medical Consultant. Further drug information is available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5302a6.htm>
  - b. Individuals should receive the usual 4-drug TB regimen (INH, RIF, PZA, and EMB) if they are not on antiretroviral therapy; if they are receiving only NRTI-class drugs (e.g., tenofovir, emtricitabine, lamivudine, abacavir) or efavirenz or nevirapine, they should also receive a rifampin-based regimen. Individuals taking raltegravir or dolutegravir may receive a rifampin-based regimen with dose adjustment of the raltegravir/dolutegravir.
2. Individuals receiving any other antiretrovirals will need to have rifabutin (RBT) substituted for rifampin; this should be done in consultation with a state TB Medical Consultant.
  - a. Monitoring of patients taking rifabutin should include complete blood counts looking for neutropenia and thrombocytopenia; the patient should also be asked about uveitis (eye pain, visual changes).
  - b. Other drugs (clarithromycin and fluconazole, for example), can increase RBT levels and cause RBT toxicity
3. When switching from a RIF based regimen to a RBT or non-rifamycin based regimen, **wait at least 2 weeks before initiating antiretroviral drugs so that the persistent effects of RIF do not interfere with the antiretroviral drug**
4. Serum drug levels are recommended for anyone with a CD4 count  $<$ 100 and taking INH and/or RIF as part of the treatment regimen. Drug level testing is also indicated for anyone experiencing treatment failure or relapse within 2 years. **(See Chapter XII for further information and specimen collection procedure)**

5. Intermittent versus daily treatment

People living with HIV should generally receive daily treatment during both initial and continuation phase of therapy. For people with HIV and a CD4 count of  $>100 \text{ mm}^3$ , thrice-weekly therapy is an option after the initial phase of therapy (i.e. after two months), but daily therapy is preferred. People with HIV and a CD4 count of  $\leq 100 \text{ mm}^3$  must receive daily therapy for the entire course of treatment. See CDC. Notice to Readers: Acquired Rifamycin Resistance in People with Advanced HIV Disease Being Treated for Active Tuberculosis with Intermittent Rifamycin-Based Regimens. MMWR 2002; 51 No. RR-10; 1-3 for further information.

6 Duration of treatment

The duration of active TB treatment is generally the same for people living with HIV as for people without HIV, with two exceptions:

- a. People living with HIV who are diagnosed with culture-negative tuberculosis should receive 26 weeks of TB treatment (not 16 weeks as for HIV-seronegative people).
- b. People living with HIV who do not consistently take antiretroviral (HIV) medications during TB treatment should receive 39 weeks of TB treatment (extend the continuation phase by 13 additional weeks).

7. Regimens for Pregnant Women

- a. The only difference between treating HIV-positive and HIV-negative pregnant women is the use of PZA. The benefit of optimal treatment of TB disease in HIV-positive pregnant women outweighs the very small risk of PZA in pregnancy. Therefore, for HIV/AIDS and TB in pregnant women, follow the treatment recommendations in Section F.1.b above
- b. SM is contraindicated for pregnant women

G. Antiretroviral Therapy

1. Antiretroviral therapy is indicated for all people living with HIV, regardless of CD4 count
2. Patients with active TB and CD4 count  $>50 \text{ cells/mm}^3$  should be started on antiretrovirals within the first two months of TB treatment
3. Patients with active TB and CD4 count of  $\leq 50 \text{ cells/mm}^3$  should be started on antiretrovirals within the first two weeks of TB treatment unless central nervous system tuberculosis is proven or suspected
4. All patients with HIV should have an identified HIV provider, and frequent communication between the HIV provider and the TB treatment provider is essential (if those two providers are not the same person).
5. Medication interactions between TB and HIV medications are common and significant. Potential interactions must be reviewed prior to starting antiretroviral therapy and/or if any change in antiretroviral therapy is contemplated.

6. Additional information on TB/HIV treatment and drug interactions may be found at <https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/0>