

Choice of Treatment Regimen for TB Infection

Most patients with TB infection should be treated

Because testing of persons at low risk of TB infection should not be done, persons that test positive for TB infection should generally be treated once active TB disease has been excluded with a chest radiograph and, if indicated, sputum smears, cultures, and nucleic acid amplification testing. However, some patients at low risk for TB infection are tested. Clinicians should not be compelled to treat low risk persons with a positive test for TB infection.

Emphasis on short course treatment of TB infection

Shorter regimens of 3 to 4 months for treating TB infection have been shown to be more likely to be completed and use of these shorter regimens is preferred in most patients. Drug-drug interactions and contact to drug-resistant TB are frequent reasons these regimens cannot be used.

Shorter duration TB infection treatment regimens

Preference	Medication	Frequency	Duration
1	INH + rifapentine*	Weekly	12 weeks
2	Rifampin	Daily	4 months
3	INH	Daily	6-9 months

* CDC recommends using DOT

12-dose weekly regimen of Isoniazid (INH) + rifapentine

- Preferred regimen with efficacy similar to 9 months of INH
- Completion rates much higher than with 9 months of INH, up to 85-90%
- Substantially lower risk of hepatotoxicity than with 9 months of INH
- Initially studied and recommended using directly observed therapy (DOT)
- Self-administered therapy (SAT) found to have similar rates of completion to directly observed therapy in U.S. patients (data not yet published)
- Hypersensitivity syndrome (fevers, flu-like symptoms, pre-syncope/syncope, hypotension) observed in some patients. Reactions typically mild and most patients able to continue with regimen

Rifampin for 4 months

- Next preferred regimen if 12-dose regimen cannot be used
- Completion rates are higher than with INH
- Not as much published data on efficacy but there is substantial clinical experience using rifampin
- Substantially less hepatotoxicity than with INH

- Drug interactions are the major contraindications to use
- Rifabutin is a commonly used alternative with significantly lesser degree of drug interactions

Isoniazid (INH) for 6 or 9 months

- Has low completion rates, often less than 50%
- Risk of hepatotoxicity is higher with INH than with rifampin or the 12-dose regimen of INH + rifapentine
- There is a large body of evidence supporting its effectiveness if taken to completion
- INH should be used when patients have significant drug-drug interactions with rifamycins
- Should be used with caution in patients with significant baseline liver disease
- Has significant interactions with anticonvulsant medications including phenytoin and carbamazepine

Children

Ensuring that children, particularly those under 5 who have a high risk for progression to active disease, complete treatment is important.

- Clinical trial data supports the use of the 12-dose INH + rifapentine regimen in children 2 years and older.

Liver Disease

- Rifampin for 4 months or the 12-dose INH + rifapentine regimen have substantially lower risk of hepatotoxicity and are preferred for patients with baseline liver disease or risk of hepatotoxicity
- For those with ALT > 2 to 3 times the ULN, chronic alcohol consumption, or severe liver disease manifested by low albumin, coagulopathy, or encephalopathy, the risks of treating TB infection may outweigh benefits. If TB infection treatment is undertaken, close monitoring is indicated.
- When there is an indication for TB infection treatment in patients with advanced liver disease such as future plans for liver transplantation, TB infection treatment should be conducted with advice of a TB or liver disease expert.

HIV

- Persons living with HIV are a priority group for treatment of TB infection because of a substantially elevated risk for progression.
- Drug interactions might complicate use of a rifamycin-containing regimen. Rifabutin in place of rifampin for 4 months may be an option to avoid certain drug interactions
- Treatment should be pursued with consultation with an HIV TB expert.

Choice of Treatment Regimen for TB infection – *continued*

Immunosuppression (current or planned)

- Immunosuppressed persons are a priority group for treatment of TB infection because of elevated risk for progression
- Organ transplant recipient, treated with TNF-alpha antagonist (e.g., infliximab, etanercept, others)
- Steroids (equivalent of prednisone ≥ 15 mg/day for ≥ 1 month) or other immunosuppressive medication
- Drug-drug interactions, particularly with rifampin, might complicate TB infection treatment and may require additional monitoring.
- For patients with planned immunosuppression, complete TB infection treatment prior to immunosuppressant administration. If this is not feasible, at least one month of TB infection treatment should be completed before immunosuppressant administration.

Pregnancy and Breastfeeding

- Pregnancy is not a risk factor for progression of TB infection to active TB disease.
- Pregnant women with a positive test for TB infection and a risk for rapid progression (e.g., HIV infection, recent exposure and conversion to positive TST/IGRA, such as in the context of a contact investigation) should be considered for TB infection treatment
- For women not at risk for rapid progression, TB infection treatment can be delayed until at least 3 months postpartum
- Both INH and rifampin are considered safe in pregnancy. The INH + rifampentine regimen has not been studied in pregnancy and should be avoided.
- INH and rifamycins are found in breast milk in small quantities but are considered safe.
- Exclusively breastfed infants and their mothers treated with INH should receive pyridoxine (B6) supplementation.

Contact to multidrug-resistant TB (MDR-TB)

Treatment of persons with TB infection who are close contacts to an infectious case of MDR-TB should be offered a regimen selected based on the resistance pattern of the index case. Consultation with a clinician with MDR-TB expertise is essential.

Resources

Los Angeles County TB Control Program

<http://www.publichealth.lacounty.gov/tb>

213-745-0800

California Department of Public Health

Tuberculosis Control Branch (TBCB)

<http://www.cdph.ca.gov/programs/tb/Pages/default.aspx>

510-620-3000

California TB Controllers Association

<http://www.ctca.org/>

510-479-6139

Centers for Disease Control and Prevention

Division of Tuberculosis Elimination

<http://www.cdc.gov/tb/>

800-232-4636

Centers for Disease Control & Prevention, Latent Tuberculosis Infection: Guide for Primary Health Care Providers

http://www.cdc.gov/tb/publications/L_TBI/treatment.htm

Curry International Tuberculosis Center

Warmline Consultation Service

<http://www.currytbcenter.ucsf.edu/>

877-390-6682 or 510-238-5100

Saukkonen et al. ATS hepatotoxicity statement

<https://doi.org/10.1164/rccm.200510-1666ST>

