



TREATMENT OF LATENT TUBERCULOSIS INFECTION (LTBI) IN CHILDREN AND ADOLESCENTS

WITH REVISED GUIDELINES FOR RIF-PZA

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WHO TO TEST

Target tuberculin skin testing (TST) for children at high risk for TB:

- Risk of recent TB infection: contact with active TB, foreign birth/residence/travel in TB endemic countries, relative with positive TST, or exposure to high-risk adults
- Clinical conditions with increased risk of progression to active TB.
- TST is not contraindicated in BCG-vaccinated persons. Interpretation of TST is the same in BCG recipients as in those without BCG.

Treat LTBI—it benefits the individual and the community.

Adherence is the key to successful prevention.

WHO TO TREAT

Category of child/adolescent tested	TST <5 mm	TST ≥5 mm	TST ≥10 mm	TST ≥15 mm
Child <5 years and recent contact *†	TREAT	TREAT	TREAT	TREAT
HIV-infected and recent contact*	TREAT	TREAT	TREAT	TREAT
Immunosuppressed and recent contact*	TREAT	TREAT	TREAT	TREAT
HIV-infected	Do Not Treat	TREAT	TREAT	TREAT
Immunosuppressed	Do Not Treat	TREAT	TREAT	TREAT
Recent contact of TB case	Do Not Treat	TREAT	TREAT	TREAT
Fibrotic changes on chest X-ray	Do Not Treat	TREAT	TREAT	TREAT
Recent arrival from endemic country	Do Not Treat	Do Not Treat	TREAT	TREAT
Resident in institutional setting	Do Not Treat	Do Not Treat	TREAT	TREAT
High-risk clinical conditions‡	Do Not Treat	Do Not Treat	TREAT	TREAT
Child <4 years †	Do Not Treat	Do Not Treat	TREAT	TREAT
TST conversion §	Do Not Treat	Do Not Treat	TREAT	TREAT
Exposure to high-risk adults	Do Not Treat	Do Not Treat	TREAT	TREAT
No risk factors (TST discouraged)	Do Not Treat	Do Not Treat	Do Not Treat	Consider Treating

* These groups of contacts should receive a tuberculin skin test (TST) immediately, clinical assessment, and chest X-ray. Even if TST is 00mm, child should be treated and TST placed again 12 weeks after last exposure to TB case. Treatment can be discontinued if second TST is negative in healthy child. For HIV or immunosuppression, continue entire treatment even if TST at 12 weeks is negative.

† In some jurisdictions reporting LTBI in children to health department is mandatory. Health department may conduct a "source case" or "associate" investigation to find the adult who transmitted *M.tb* to the child.

‡ Diabetes mellitus, chronic renal failure, some hematologic disorders (e.g. leukemias and lymphomas), other specific malignancies, weight loss of ≥10% of ideal body weight, gastrectomy, jejunioileal bypass.

§ TST Conversion: An increase in reaction size of ≥10 mm within 2 years should be considered a TST conversion indicative of recent infection with *M.tb*.

¶ Silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g. leukemias and lymphomas), other specific malignancies (e.g. carcinoma of the head and neck or lung), weight loss of ≥10% of ideal body weight, gastrectomy, jejunioileal bypass.

HOW TO TREAT

Drug	Interval and Duration	Pediatric Dosage (max)	Criteria for	Comments Completion
INH*	Daily for 9 mos.	10-20 mg/kg (300 mg)	270 doses within 12 mos.	Preferred regimen for all.
	Twice-weekly for 9 mos.	20-40 mg/kg (900 mg)	76 doses within 12 mos.	DOT must be used with twice-weekly dosing.
RIF	Daily for at least 6 mos.	RIF 10-20 mg/kg (600 mg)	180 doses within 9 mos.	For those who cannot tolerate INH and for contacts of patients with INH-resistant, RIF-susceptible TB.
RIF plus PZA	RIF plus PZA for two months has not been studied in children. This regimen is generally not recommended. Consult TB/LTBI expert.			

Abbreviations: INH = isoniazid, RIF = rifampin, PZA = pyrazinamide, DOT = directly observed therapy, mos. = months

* Pyridoxine (B₆) supplements are also recommended for breast-feeding infants, children and adolescents on milk and meat deficient diets, children who experience paresthesias while taking INH, and those with HIV infection.

For HIV-infected patients and possible multidrug resistant-TB exposure, consult expert.

Pregnancy: Treat during pregnancy if either HIV-infected or recent *M.tb* infection.

HOW TO MONITOR

For all patients:

- Initial clinical evaluation, including radiologic studies to rule out active TB
- Consider possible rifamycin-associated drug interactions, eg. oral contraceptives, antiretrovirals, methadone, oral hypoglycemics, and anticoagulants
- Provider conversant in patient's language should educate patient and family about side effects associated with LTBI treatment and advise to stop treatment and promptly seek medical evaluation if these occur
- Follow-up evaluations at least monthly if receiving INH or RIF alone; at 2, 4, 6, and 8 weeks if receiving RIF and PZA
- Include careful questioning of patient and family about side effects and a brief physical examination checking for evidence of hepatitis or other side effects
- Inform persons considering treatment with RIF-PZA of potential hepatotoxicity

and ask about history of liver disease or adverse effects from INH or other drugs

- If side effects occur, evaluate promptly and change treatment as indicated
- Routine monthly monitoring of liver function tests (LFTs) indicated for:
 - Chronic liver disease
 - Risk for hepatic disease, including other potentially hepatotoxic drugs (eg. anti-convulsants or over-the-counter drugs e.g. acetaminophen)
 - RIF-PZA regimen
 - Pregnancy or immediate postpartum
 - HIV infection

When children taking anti-tuberculosis therapy develop hepatitis, other causes should be sought.

- Therapy should be discontinued for symptomatic hepatitis.
- Therapy should be resumed when LFTs are normal, if appropriate.