

Appendix 1 (as supplied by the authors): Treatment of TB disease:

Summary and list of resources

Expert consultation and the use of a team with experience in managing TB is recommended for the management of pediatric TB disease. (1,2) Treatment for TB disease should always include multiple drugs to prevent the emergence of resistant strains. The usual first line drugs are isoniazid (INH), rifampin pyrazinamide and ethambutol. Generally all 4 drugs should be used initially, pending sensitivities, unless the source strain is known to be drug sensitive.

Once the strain is known to be fully drug susceptible, ethambutol can be discontinued and treatment with INH and rifampin and pyrazinamide continued. Pyrazinamide is usually discontinued after two months. For uncomplicated intrathoracic and pulmonary TB, six months of therapy is usually adequate though if a patient remains sputum-smear/culture positive after two months, total duration of therapy should be at least nine months. (1, 2) The management of drug resistant TB always requires expert consultation. Recent resources detail side effects of drugs used in the management of drug sensitive and drug resistant TB. (1, 2, 3, 4)

To counteract peripheral INH related neuropathy, supplementary Vitamin B6, available as 25mg tablets that are divided and crushed is given to breastfed infants, those with milk and meat deficient diets and if there is any concern about diet. No dosing data for

Vitamin B6 are available; in general 6.25 mg is used for infants, 12.5 to 25 mg for toddlers and older children respectively. If parasthesiae occur double the dose.

Administering medication to young children is difficult but critical for management. Useful suggestions are provided by the Francis Curry TB center. (5) A commercially available liquid formulation is available for INH and is sometimes compounded for rifampin. The following table is adapted from the Canadian TB Standards. (1, 2,) using supplementary resources (3, 4).

Table: Drugs used for treatment of tuberculosis in children (1,2)

	Daily dose (Range)		Thrice weekly dose† (range)		Available dosage forms	Special characteristics	Principal side effects
	By weight (mg/kg)	Max (mg)	By weight (mg/kg)	Max (mg)			
Isoniazid	10 (10-15)‡	300	20-30	600-900	10 mg/mL suspension 100 mg tablet 300 mg tablet	Best absorbed on an empty stomach . Especially avoid administering with fatty and sugary foods.	Mild liver transaminase elevation Hepatitis Gastritis Peripheral neuropathy Hypersensitivity
Rifampin	15 (10-20)	600	10-20	600	150 mg capsule 300 mg capsule Suspension may be made by compounding pharmacies	Monitor for drug interactions, especially with anti-retroviral therapy, corticosteroids	Orange discoloration of secretions Vomiting Hepatitis Flu-like illness
Pyrazinamide	35 (30-40)	2000	70 (60-80)	*	500 mg scored tablet	Dose adjustment in renal failure. Causes the most severe hepatotoxicity	Hepatotoxicity Hyperuricemia Arthralgia
Ethambutol	20 (15-25)	**	40 (30-50)	***	100 mg tablet 400 mg tablet	Dose adjustment required in renal failure	Optic neuritis with decreased visual acuity and decreased red-green colour discrimination Gastrointestinal disturbance
Pyridoxine	1 mg/kg	25 -50	-	-	25 mg tablet 50 mg tablet	Usual adult dose 25 mg; double dose if parasthesiae develop	

†Intermittent doses should be prescribed only when directly observed therapy is available. In general daily therapy is definitely preferred over intermittent regimens.

‡Hepatotoxicity is greater when INH doses are more than 10-15 mg/kg daily. For older children and adolescents, the optimal dosing of INH is an area of uncertainty.

*For PZA: 3000 mg according to the American Thoracic Society (ATS),⁷⁵ 2000 mg according to the Red Book³³

**For EMB: 1600 mg according to the ATS,⁷⁵ 2500 mg according to the Red Book³³

***For EMB: 2400 mg according to the ATS,⁷⁵ 2500 mg according to the Red Book³³

Note: Information on second-line drugs for multidrug-resistant TB (MDR-TB) is available in various recent reviews⁷⁶⁻⁷⁹ and in Chapter 8. Drug-resistant Tuberculosis.

References

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- 2 Kitai I, Demers AM. Paediatric Tuberculosis. In: Menzies D, ed. *Canadian Tuberculosis Standards*: Public Health Agency of Canada; 2013Public Health Agency of Canada; 2013. Available: <http://www.phac-aspc.gc.ca/tbpc-latb/pubs/tb-canada-7/tb-standards-tb-normes-ch9-eng.php> (accessed 2016 Jun .8)
- 3 Al-Dabbagh M, Lapphra K, Pattar R et al . Drug-Resistant Tuberculosis: A Review of Pediatric Treatment Guidelines. [Pediatr Infect Dis J.](#) 2011 30:501-505
- 4 Curry International Tuberculosis Center and California Department of Public Health, 2016: Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, Third Edition Available: <http://www.currytbcenter.ucsf.edu/products/drug-resistant-tuberculosis-survivalguide-clinicians-3rd-edition>
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