Let's Talk TB

A Series on Tuberculosis, A Disease That Affects Over 2 Million Indians Every Year

Childhood Tuberculosis: Q&A for Primary Care Physicians

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Abstract

GPs frequently see children in their clinical practice, and should be alert to the possibility of pediatric TB, especially in malnourished children. Children with TB often present with vague, non-specific symptoms, and this makes it hard to suspect and diagnose TB. Symptoms could include chronic fever, cough, weight loss, fatigue, loss of appetite, failure to gain weight, and lymph node enlargement. History of contact with an adult with TB is therefore a very important component of history that should be elicited. There is no adequate gold standard test for childhood TB, and diagnosis requires multiple tests. Smears for acid-fast bacilli (AFB) are often negative because of the low numbers of AFB in childhood TB. Therefore, liquid culture and molecular tests (Xpert MTB/RIF) will be most helpful, along with signs, symptoms, chest radiology, evidence of TB infection (e.g. positive Mantoux skin test), and history of contact with active TB. All children who have not been treated previously and do not have other risk factors for drug resistance should receive a WHO-approved first-line treatment regimen for a total of 6 months. The initial phase should consist of two months of isoniazid, rifampicin, pyrazinamide and ethambutol. The continuation phase should consist of isoniazid and rifampicin given for 4 months. Daily treatment is preferable to intermittent therapy. Drug dosages are calculated according to weight (not age). Adherence to the full course of anti-TB therapy is very important to ensure high cure rates. In general, children tolerate first-line anti-TB therapy very well with low risk of toxicity.

Key words: childhood tuberculosis; diagnosis; treatment

Q: WHAT IS CHILDHOOD TB AND WHO IS AT RISK?

India has the largest number of TB cases. GPs frequently see children in their clinical practice, and should be alert to the possibility of pediatric TB. It is estimated by WHO that there are more than half a million cases of TB in children occurring globally each year. Children usually get infected because of adults in the family with active TB. In low and middle income countries, TB is an important cause of morbidity and mortality in children.

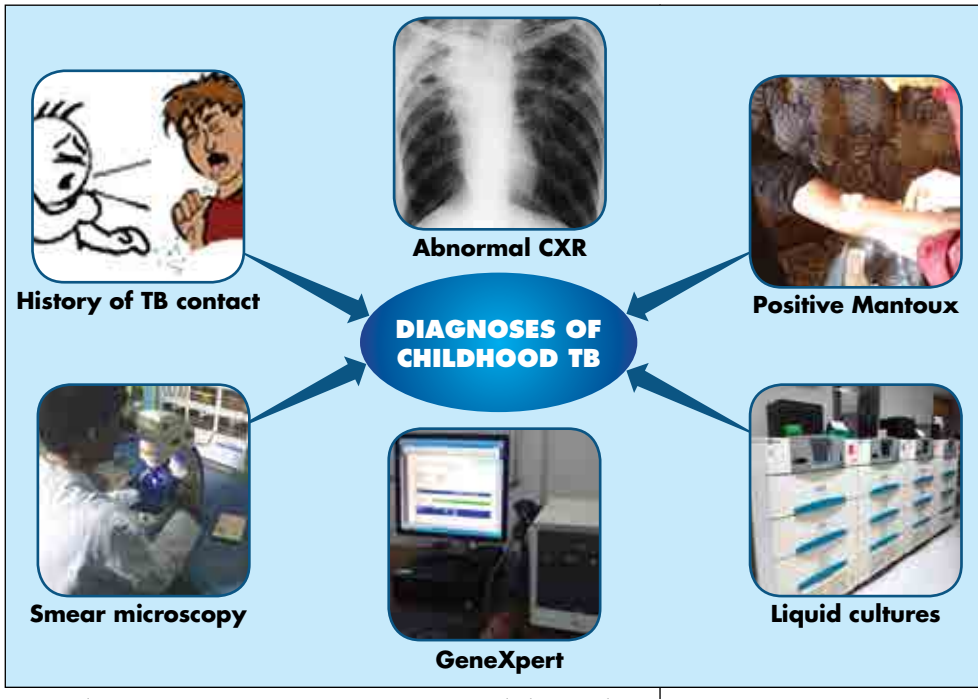
TB in children is difficult to diagnose, and easy to miss. Young children can develop extrapulmonary and severe forms of TB such as TB meningitis and miliary TB, and thus children are a vulnerable population. TB in children can result in malnutrition, while malnutrition itself is a major risk factor for development of TB in children. HIV-infected children are also at high risk of developing TB. In India, malnutrition in children is easily the biggest risk factor for childhood TB, given the high prevalence of under-nutrition in children.[1]

Q: CAN WE PREVENT TB IN CHILDREN?

BCG vaccination at birth is routinely done in many countries including India, and it does have an important role, especially in reducing the risk of severe, disseminated (i.e. miliary) disease in young children that are infected with TB. However, the protective efficacy of BCG is low, and a BCG-vaccinated child cannot be considered to be protected from TB. Multiple does of BCG is not recommended as there is no evidence of increased protection by giving repeat vaccinations.

Q: WHEN SHOULD WE SUSPECT TB IN A CHILD?

Children with TB often pres-



ent with vague, non-specific symptoms, and this makes it hard to suspect and diagnose TB. Symptoms could include chronic fever, cough, weight loss, fatigue, loss of appetite, failure to gain weight, and lymph node enlargement. History of contact with an adult with TB is therefore a very important component of history that should be elicited. If an adult in the family has drug-resistant TB (e.g., MDR-TB), this is critical to know.

Q: HOW IS CHILDHOOD TB DIAGNOSED?

No single test works well in childhood TB. So, the diagnosis of TB in children usually relies on a combination of clinical features, and laboratory tests (see box above). The following clinical history and tests should be done:

- History of contact with an adult with TB disease
- Any symptom suggestive of TB (see above)
- Mantoux (tuberculin) skin test or an interferon-gamma release assay: a positive test provides evidence of TB infection
- Chest X-ray (which can show hilar adenopathy)
- Microbiological tests of sputum or other clinical samples (e.g. gastric juice):

-Smear microscopy (AFB)
-Xpert MTB/RIF (GeneXpert)
-Liquid cultures

A combination of the above can help detect childhood TB. Sometimes, when the above combination fails to detect TB, it may be necessary to empirically treat for TB and assess the clinical response.

Q: WHAT CLINICAL SAMPLES SHOULD BE SENT FOR TB TESTING?

While young children are unable to produce sputum, sputum could be collected from older children and adolescents. At least two sputum specimens must submitted for microscopic examination and Xpert MTB/RIF testing and culture. In young children (<7-8 years of age), the routine specimens collected are two to three fasting gastric aspirates (gastric juice aspirate). However, the collection of 2-3 fasting, early morning gastric aspirate specimens is cumbersome and usually requires hospitalization. The following are basic guidelines for collecting gastric aspirates: 1) Specimens are collected after the child has fasted for eight to ten hours and, preferably, while the child is still in bed; 2) Specimens are usually collected daily for three days.

Extrapulmonary TB can occur in many sites, the most common sites being lymph nodes and meningeal. EPTB cannot be diagnosed with sputum or blood specimens. It is critical to make an effort to collect tissue and fluids from the site of the disease. This may require surgical expertise and referral to a center where biopsies can be done safely. For example, if TB meningitis is suspected in a child, then it is important to refer the child to a hospital where lumbar puncture can be performed for CSF testing.

Q: HOW ACCURATE IS XPERT MTB/RIF (GENEXPERT) IN CHILDREN?

Pooled data from several studies show that compared with culture, the sensitivities and specificities of Xpert for tuberculosis detection is 62% and 98%, respectively, with use of expectorated or induced sputum samples and 66% and 98%, respectively, with use of samples from gastric aspirate.[2] Xpert sensitivity is about 36-44% higher than sensitivity for smear microscopy. Xpert's sensitivity and specificity to detect rifampicin resistance is 86% and 98%, respectively. Thus, Xpert is superior to smear microscopy, and should be routinely used in children, where available. The fact that Xpert performs well

in gastric juice samples is worth underscoring, as gastric aspirates may be easier to collect from young children than sputum samples.

Q: CAN XPERT MTB/RIF (GENEXPERT) BE USED FOR EXTRAPULMONARY TB DIAGNOSIS IN CHILDREN?

Yes, WHO has recommended the use of Xpert MTB/RIF in two extrapulmonary samples: lymph node tissues, and CSF samples. In CSF samples, Xpert has a sensitivity of about 81% and specificity of 98%.[3] In lymph node tissues, Xpert has a sensitivity of about 83% and specificity of 94%.[3]

Q: CAN CHILDREN HAVE DRUG-RESISTANT TB? HOW CAN MDR-TB BE DIAGNOSED IN CHILDREN?

Yes, children in contact with adults with MDR-TB can become infected with drug-resistant strains, and develop MDR-TB. Drug-resistant TB should be suspected in any child that is receiving TB treatment and not improving. Diagnosis of MDR-TB can be achieved by using rapid molecular tests such as Xpert MTB/RIF, and line probe assays (e.g., Hain Genotype MTBDRplus). Liquid cultures can also be used to detect drug resistance. Sputum, gastric aspirate and extrapulmonary samples can be subjected to Xpert, and liquid cultures and DST. Children with suspected or confirmed drug-resistant TB should be referred to a specialist – for additional investigation and specialist management.

Q: ONCE TB IS DIAGNOSED, WHAT IS THE RECOMMENDED TREATMENT IN CHILDREN?

All children who have not been treated previously and do not have other risk factors for drug resistance should receive a WHO-approved first-line treatment regimen for a total of 6 months. The initial phase should consist of two months of isoniazid, rifampicin, pyrazinamide and ethambutol. The continuation phase should consist of isoniazid and rifampicin given for 4 months. Daily treatment is preferable to intermittent therapy. Drug dosages are calculated according to weight (not age). **Table** shows the recommended drug dosages in children.[4]

Table 1– Doses of first-line antituberculosis drugs in children

Drug	Recommended dose in mg/kg body weight (range)
Isoniazid	10 (7-15)
Rifampicin	15 (10-20)
Pyrazinamide	35 (30-40)
Ethambutol	20 (15-25)

Source: Reference 4

Adherence to the full course of anti-TB therapy is very important to ensure high cure rates and to prevent the emergence of drug-resistance. Children with malnutrition should receive adequate nutritional rehabilitation therapy, along with anti-TB treatment. Severely malnourished children with TB may require hospitalization and careful monitoring.

Q: HOW CAN WE MONITOR TREATMENT IN CHILDREN AND WHAT ARE THE LIKELY ADVERSE EFFECTS?

Resolution of symptoms and weight gain are markers of a satisfactory treatment response in sputum smear-negative cases. If a child has smear-positive TB, then it is important to check if the smears become negative at the end of the intensive treatment phase. Xpert MTB/RIF is not recommended for treatment monitoring.

Children tolerate first-line anti-TB therapy very well with low risk of toxicity. Adherence can be a challenge especially during the continuation phase. So, it is important to counsel the parents and the family about importance of completion of full course of anti-TB treatment.

Comprehensive information on childhood TB is available from WHO and IUATLD in the Childhood TB Training Toolkit published in 2014.[5]

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