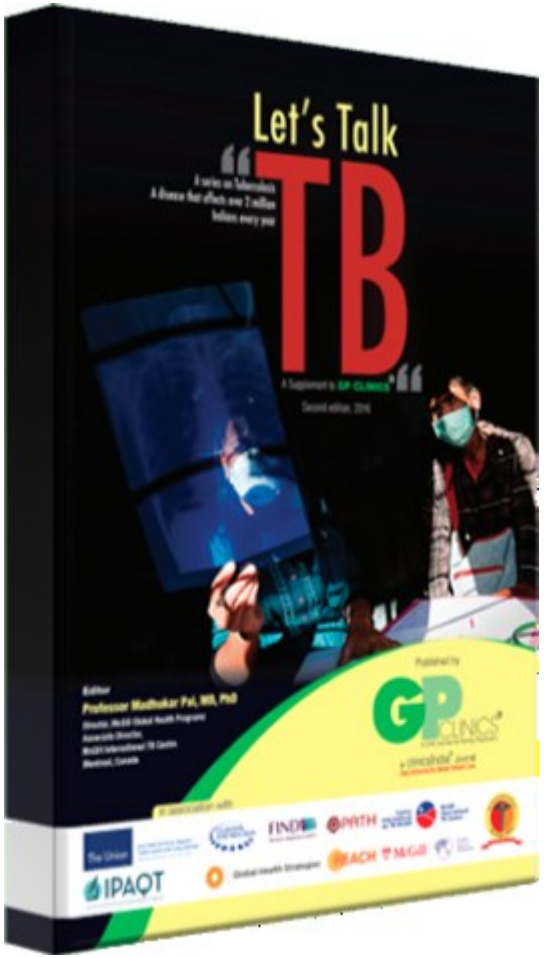

Let's Talk TB:

A Supplement to GP CLINICS

Chapter 10: Childhood Tuberculosis:

Q&A For Primary Care Physicians

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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
- Estimated by WHO that there are more than 500,000 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

What is Childhood TB and who is at risk?

- 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
  - 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 undernutrition in children

Can we prevent TB in children?

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

When should we suspect TB in a child?

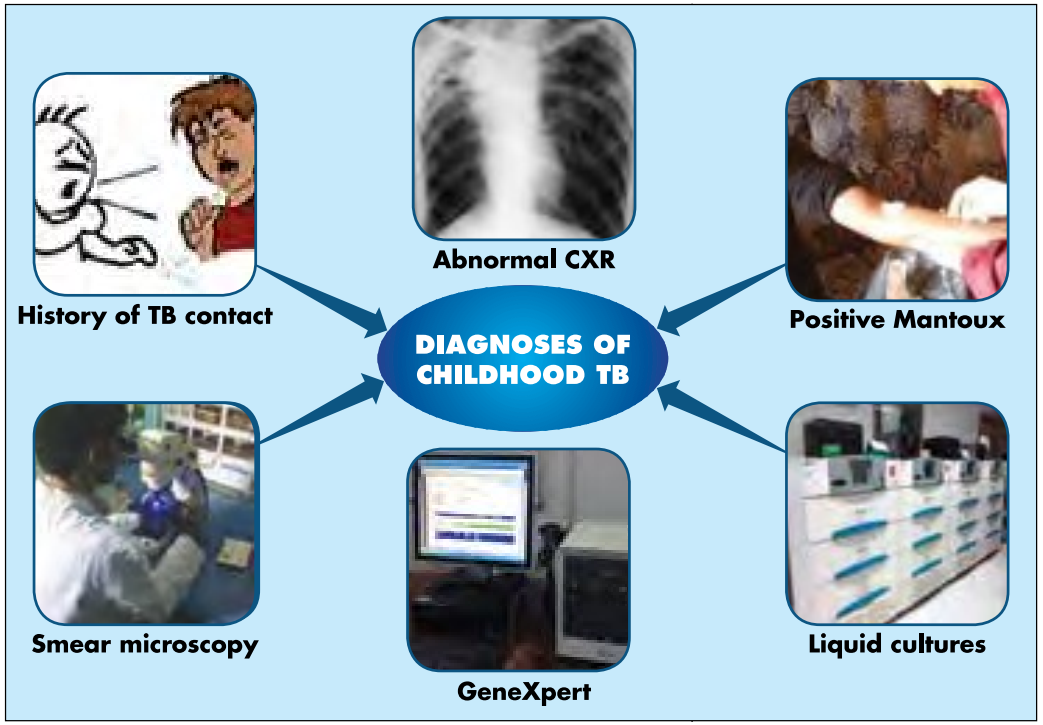
- Children with TB often present with vague, non-specific symptoms
  - Makes it hard to suspect and diagnose TB
- Symptoms could include:
  - Chronic fever
  - Cough,
  - Weight loss
  - Fatigue
  - Loss of appetite
  - Failure to gain weight
  - Lymph node enlargement

When should we suspect TB in a child?

- History of contact with an adult with TB is a very important component of history that should be elicited (CRITICAL TO KNOW)
  - If an adult in the family has drug-resistant TB (e.g. MDR-TB)

How is Childhood TB diagnosed?

- No single test works well in childhood TB
- The diagnosis of TB in children usually relies on a combination of clinical features and laboratory tests



How is Childhood TB diagnosed?

- The following clinical history and tests should be done:
  - History of contact with an adult with TB disease
  - Any symptom suggestive of TB
  - 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

How is Childhood TB diagnosed?

- A combination of clinical history and tests can help detect childhood TB
  - If fails to detect TB it may be necessary to empirically treat for TB and assess the clinical response

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

What Clinical Samples should be sent for TB testing?

- In young children (<7-8 years of age), the routine specimens collected are 2 to 3 fasting gastric aspirates (gastric juice aspirate)
  - However, the collection of 2-3 fasting, early morning gastric aspirate specimens is cumbersome and usually requires hospitalization

What Clinical Samples should be sent for TB testing?

- The following are basic guidelines for collecting gastric aspirates:
  - 1) Specimens are collected after the child has fasted for eight to ten hours (preferably while the child is still in bed)
  - 2) Specimens are usually collected daily for three days

What Clinical Samples should be sent for TB testing?

- Extrapulmonary TB can occur in many sites
  - 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

How Accurate is Xpert MTB/RIF (GeneExpert) in Children?

- Pooled data from several studies show sensitivities and specificities of TB detection
- Use of expectorated or induced sputum samples
  - Sensitivity = 62%
  - Specificity = 98%
- Use of gastric aspirate
  - Sensitivity = 66%
  - Specificity = 98%
- Xpert sensitivity is about 36-44% higher than sensitivity for smear microscopy
- Xpert's sensitivity and specificity to detect rifampicin resistance
  - Sensitivity 86%
  - Specificity 98%
- Thus, Xpert is superior to smear microscopy, and should be routinely used in children, where available.

How Accurate is Xpert MTB/RIF (GeneExpert) in Children?

- 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

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%
- In lymph node tissues: Xpert has a sensitivity of about 83% and specificity of 94%

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 MTBDR plus)
  - Liquid cultures can also be used to detect drug resistance

Can children have drug-resistant TB? How can MDR-TB be diagnosed in children?

- 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
  - Additional investigation and specialist management

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

Once TB is diagnosed, what is the recommended treatment in children?

- Initial Phase: 2 months of isoniazid + rifampicin + pyrazinamide + ethambutol
- Continuation Phase: 4 months isoniazid + rifampicin
- Daily treatment is preferable to intermittent therapy
- Drug dosages are calculated according to weight (not age)

Recommended Drug Dosages in Children

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

Once TB is diagnosed, what is the recommended treatment in children?

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

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

How can we monitor treatment in children and what are the likely adverse effects?

- Children tolerate first-line anti-TB therapy very well with low risk of toxicity
- Adherence can be a challenge especially during the continuation phase
- 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

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