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

http://www.letstalktb.org/
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.

http://www.letstalktb.org/
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

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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

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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

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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

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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 be submitted for microscopic examination and Xpert MTB/RIF testing and culture

http://www.letstalktb.org/
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.

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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

http://www.letstalktb.org/
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.

http://www.letstalktb.org/
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.

http://www.letstalktb.org/
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%

http://www.letstalktb.org/
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

http://www.letstalktb.org/
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

http://www.letstalktb.org/
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

http://www.letstalktb.org/
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)

http://www.letstalktb.org/
Recommended Drug Dosages in Children

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended dose in mg/kg body weight (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>10 (7-15)</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>15 (10-20)</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>35 (30-40)</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>20 (15-25)</td>
</tr>
</tbody>
</table>

Source: Reference 4

http://www.letstalktb.org/
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.

http://www.letstalktb.org/
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.

http://www.letstalktb.org/
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

http://www.letstalktb.org/


