Tuberculosis and Pediatrics

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Mayo Clinic TB Clinical Intensive
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In the past 12 months, I have not had a significant financial interest or other relationship with the manufacturer(s) of the product(s) or provider(s) of the service(s) that will be discussed in my presentation.
Objectives

- To become familiar with the epidemiology and pathophysiology of infection and disease caused by *Mycobacterium tuberculosis* complex (TB)

- To distinguish some key differences between the epidemiology and diagnosis of TB in children and adults

- To incorporate current algorithms for the diagnosis and treatment of TB infection and disease in children
Questions

- How do we recognize TB in infants and children?
- How does disease in children differ from that of adults?
- What are the main diagnostic and treatment algorithms to follow in pediatrics?
Pediatric TB

**Mycobacterium tuberculosis complex** (TB)

- *M. tuberculosis*
- *M. africanum*
- *M. bovis* and *M. bovis* bacillus Calmette-Guérin
- *M. microti* and *M. pinnipedii*
- *M. canettii*, oryx bacillus, and dassie bacillus (proposed)

**Pediatric TB**

- Infection or disease in children or adolescents < 15 years of age

*BMC Infectious Diseases 2010, 10:80*
Incident case of disease

Case verification categories

- Laboratory confirmed cases – “Gold Standard”
  - Positive culture, DNA probe, or nucleic acid amplification test
  - Positive AFB smear when culture not attainable

- Clinical case definition
  - Positive tuberculin skin test
  - Signs and symptoms of TB disease
  - Current treatment for TB disease

- Provider diagnosis
  - Diagnosed by health care provider
  - Does not fulfill all criteria necessary to meet laboratory or clinical case definitions
TB is a Global Disease

- ~ 9 million people developed TB and 1.5 million died in 2013
- ~ 550,000 cases and 80,000 deaths among HIV-negative children
- In 2012, there were > 10 million orphans due to TB parental deaths

Global Tuberculosis Report 2014, WHO
Number of TB Cases in U.S.-born vs. Foreign-born Persons, United States, 1993–2014*

*Updated as of June 5, 2015.
TB Case Rates* by Age Group
United States, 1993–2014

* Updated as of June 5, 2015.
Reported TB Cases by Age Group, United States, 2014

- <15 yrs: 5%
- 15-24 yrs: 10%
- 25-44 yrs: 30%
- 45-64 yrs: 31%
- ≥ 65 yrs: 24%
TB Case Rates by Pediatric Age Groups
1993–2008, N=17,502

Note: Rates presented on a logarithmic scale
TB Case Rates,* United States, 2014

*Cases per 100,000.
<table>
<thead>
<tr>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TB Cases in Franklin County</td>
<td>55</td>
<td>77</td>
<td>85</td>
<td>78</td>
<td>61</td>
<td>41</td>
<td>66</td>
<td>50</td>
<td>42</td>
<td>50</td>
<td>49</td>
</tr>
<tr>
<td>Case rates per 100,000 in Franklin County</td>
<td>5.1</td>
<td>7.1</td>
<td>7.8</td>
<td>7.2</td>
<td>5.5</td>
<td>3.63</td>
<td>5.85</td>
<td>4.3</td>
<td>3.7</td>
<td>4.2</td>
<td>4.04</td>
</tr>
<tr>
<td>TB Cases for Ohio:</td>
<td>219</td>
<td>260</td>
<td>240</td>
<td>252</td>
<td>213</td>
<td>180</td>
<td>190</td>
<td>145</td>
<td>149</td>
<td>148</td>
<td>156</td>
</tr>
<tr>
<td>Case rate per 100,000 for Ohio:</td>
<td>1.9</td>
<td>2.3</td>
<td>2.1</td>
<td>2.2</td>
<td>1.9</td>
<td>1.6</td>
<td>1.64</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>
~35% of household contacts are infected

"LTBI" major focus for PPD screening

Bacteremia and dissemination to multiple body organs

Small & Fujiwara. NEJM 345:189, 2001
## Age-Specific Risk of TB Disease

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Disease</th>
<th>Risk of disease after primary infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>None</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Pulmonary</td>
<td>30–40</td>
</tr>
<tr>
<td></td>
<td>Meningitis or miliary</td>
<td>10–20</td>
</tr>
<tr>
<td>1–2</td>
<td>None</td>
<td>70–80</td>
</tr>
<tr>
<td></td>
<td>Pulmonary</td>
<td>10–20</td>
</tr>
<tr>
<td></td>
<td>Meningitis or miliary</td>
<td>2–5</td>
</tr>
<tr>
<td>2–5</td>
<td>None</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>Pulmonary</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Meningitis or miliary</td>
<td>0.5</td>
</tr>
<tr>
<td>5–10</td>
<td>None</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>Pulmonary</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Meningitis or miliary</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>&gt;10</td>
<td>None</td>
<td>80–90</td>
</tr>
<tr>
<td></td>
<td>Pulmonary</td>
<td>10–20</td>
</tr>
<tr>
<td></td>
<td>Meningitis or miliary</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>
Definition of Positive Mantoux Tuberculin Skin Test (TST) Results in Children

- **Induration ≥ 5 mm**
  - Children in contact with known active TB
  - Children with clinical or radiographic illness consistent with TB
  - Children who are immunocompromised

- **Induration ≥ 10 mm**
  - **Children at increased risk of disseminated disease**
    - Age < 4 years of age or underlying medical illness
  - **Children with increased exposure to TB**
    - Born or parents born in high-prevalence countries
    - Frequent exposure to adults with high risk of TB
    - Travel to high-prevalence countries

- **Induration ≥ 15 mm**
  - Age ≥ 4 years of age without any risk factors

2015 Redbook, 30th edition
Diagnosis of TB infection in Children – Screening Questions

- Exposure to known TB?
- Born in or travel to TB endemic country?
- Family member with risk of TB?
  - Born in or travel to endemic country
  - Chronic cough, hemoptysis, wt loss
  - Time in prison
  - Homeless, HIV infection, or drug abuse
- Visitors from a foreign country?
Diagnostic Evaluation in Children

- Tuberculin skin test (TST) or Interferon gamma release assay (IGRA)
- CXR if one of the above is positive
- Complete physical exam
- Search for contact source
- Treat for LTBI if CXR and PE are negative
- Pursue further evaluation if CXR or PE is abnormal
False negative TST

- Approximately 10% to 20% of children with culture-documented tuberculosis disease may not react initially to a TST:
  - young age
  - poor nutrition
  - Immunosuppression
  - viral infections (especially measles, varicella, and influenza)
  - recent tuberculosis infection
  - disseminated tuberculosis disease

- Co-infected children with HIV and MTB do not react to a TST
- Control skin tests to assess anergy not recommended
TST 6 Months after BCG at Birth in 69 Infants in Peru

Santiago EM et al. Pediatr 2003;112:e298
TST with no Known Exposure to TB
BCG - Vaccinated as Infants

Figure 3  Percentage reactors versus skin test results in mm with 5 TU PPD (576 BCG+, 1145 BCG−).

BCG Scar after Vaccination at Birth

Santiago EM et al. Pediatr 2003;112:e298
“An IGRA may be used in place of (but not in addition to) a TST in all situations in which CDC recommends tuberculin skin testing as an aid in diagnosing *M. tuberculosis* infection . . . .”

“A TST is preferred for testing children aged <5 years.”

“Using both a TST and an IGRA . . . might be useful . . . when additional evidence of infection is required to encourage compliance.”

“For persons who have received BCG and who are not at increased risk for a poor outcome if infected, TST reactions of <15 mm in size may reasonably be discounted as false positives when an IGRA is clearly negative.”

Interferon-γ Release Assay for Detection of TB Infection

Antigens used: ESAT-6, CFP-10, TB 7.7
QuantiFERON-Gold In-Tube

5 easy steps of QFT™ In-Tube

1. Collect 1mL of blood into NIL, Antigen and Mitogen tubes. Shake well. Incubate tubes at 37°C for 16-24 hrs.
2. Centrifuge tubes for 15 minutes.
3. Add conjugate, plasma samples and standards to ELISA. Incubate for 120 minutes at room temperature.
4. Wash and add substrate. Read absorbance after 30 minutes.
5. Software calculates results and prints reports.

Positive when antigen (−) null elisa = ≥ 0.35 IU/ml
<table>
<thead>
<tr>
<th><strong>IGRA</strong></th>
<th><strong>TST</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>in vitro test</em></td>
<td><em>in vivo test</em></td>
</tr>
<tr>
<td><strong>Specific antigens</strong></td>
<td>Less specific PPD</td>
</tr>
<tr>
<td>Not affected by prior BCG</td>
<td></td>
</tr>
<tr>
<td>Does not cause boosting</td>
<td>May cause boosting</td>
</tr>
<tr>
<td>Single patient visit</td>
<td>2 patient visits</td>
</tr>
<tr>
<td>Results possible in 1 day</td>
<td>Results in 2-3 days</td>
</tr>
<tr>
<td>Requires phlebotomy</td>
<td>TST placement skills</td>
</tr>
<tr>
<td>Error in collecting, transporting, lab</td>
<td>Inter-reader variability</td>
</tr>
</tbody>
</table>
# Species Specificity of ESAT-6 and CFP-10

<table>
<thead>
<tr>
<th>Tuberculosis Complex</th>
<th>ESAT</th>
<th>CFP 10</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. tuberculosis</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>M. africanum</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>M. bovis</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>BCG substrains</em></td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-tuberculous Mycobacteria</th>
<th>ESAT</th>
<th>CFP 10</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. kansasii</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>M. marinum</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>M. szulgai</em></td>
<td>+</td>
<td>+</td>
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</table>
Summary of Evidence from 12 Studies Comparing IGRAs vs TST for LTBI in Children

<table>
<thead>
<tr>
<th>IGRA type</th>
<th>IGRA (+)</th>
<th>TST (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QFT-G</td>
<td>33/195 (17)</td>
<td>47/195 (24)</td>
</tr>
<tr>
<td>QFT-GIT</td>
<td>16/210 (8)</td>
<td>98/227 (43)</td>
</tr>
<tr>
<td>QFT-GIT</td>
<td>31/204 (15)</td>
<td>116/207 (56)</td>
</tr>
<tr>
<td>QFT-GIT</td>
<td>65/192 (34)</td>
<td>57/193 (57)</td>
</tr>
<tr>
<td>QFT-GIT</td>
<td>61/184 (33)</td>
<td>80/184 (43)</td>
</tr>
<tr>
<td>TSPOT</td>
<td>36/120 (30)</td>
<td>84/120 (70)</td>
</tr>
<tr>
<td>QFT-GIT</td>
<td>29/97 (30)</td>
<td>46/95 (48)</td>
</tr>
<tr>
<td>TSPOT</td>
<td>25/95 (26)</td>
<td>46/95 (48)</td>
</tr>
</tbody>
</table>

217 immigrant children from Africa or Asia screened in Australia with TST, QFT-GIT and T-SPOT. NONE had known household exposure to TB.

Lucas M et al. Thorax 2010;65:442
Progression to active TB in 104 German children <16 y/o followed for 2-4 yrs without treatment after > 40 hrs contact with an adult with active TB

### Sensitivity of QFT vs TST for TB disease in Children

<table>
<thead>
<tr>
<th>Author, Year*</th>
<th>Test Type</th>
<th>TST Cutoff (mm)</th>
<th>Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okada et al, 2008</td>
<td>QFT-G</td>
<td>10</td>
<td>79%</td>
</tr>
<tr>
<td>Dogra et al, 2006</td>
<td>QFT-G IT</td>
<td>10</td>
<td>63%</td>
</tr>
<tr>
<td>Bianchi et al, 2009</td>
<td>QFT-G IT</td>
<td>10</td>
<td>86%</td>
</tr>
<tr>
<td>Haustein et al, 2009</td>
<td>QFT-G IT</td>
<td>6</td>
<td>72%</td>
</tr>
<tr>
<td>Bramford et al, 2009</td>
<td>QFT-G IT</td>
<td>15</td>
<td>55%</td>
</tr>
<tr>
<td>Kampmann et al, 2009</td>
<td>QFT-G IT</td>
<td>15</td>
<td>60%</td>
</tr>
</tbody>
</table>

**Approach to Diagnosis of TB in Children**

- Child ≥ 5 yrs old with known exposure to TB: IGRA and TST
- Child < 5 yrs old with known exposure to TB: use TST
- Child of any age with suspected TB: TST and IGRA, and aggressively seek TB isolate and epidemiology of exposure
- Child < 5 yrs old immigrating from high risk country without known TB exposure: use TST as screen – follow Redbook guidelines for interpretation
- Child ≥ 5 yrs old immigrating from high risk country without known TB exposure: use TST as screen:
  - If TST ≥ 15 mm, assume TB infection
  - If TST 10-14 mm, obtain IGRA to confirm or refute TB infection

Powell DA. Pediatr Infect Dis J 2009;28:676
Tuberculosis Testing and Treatment

TST Placement

- Interpret TST 48-72 hrs
  - < 10 mm → No Infection
  - ≥ 10 mm → Likely Infection

Likely Infection

- CXR at NCH Radiology
  - No Active Air-Space Disease
    - NCH TB Clinic
  - Active Air-Space Disease
Admit to NCH

> 15 mm

10-15 mm

Blood Draw for QFT

Indeterminate or Equivocal

TB Clinic
LTBI Therapy

Negative (no infection)

Positive (infection)
Adolescent with Latent TB
Question

Which of the regimen(s) would you prescribe for LTBI therapy in a child?

a. 2 months of pyrazinamide and rifampin
b. 3 months of isoniazid and rifapentine (12 weekly doses)
c. 4 months of rifampin
d. 6 months of rifampin
e. 9 months of Isoniazid
Recommend 9 months of INH

Acceptable alternatives
- 6 months of Rifampin
- 12 doses of INH and Rifapentine*
  - Directly Observed Therapy (DOT) only
  - Enrollment 6/01-2/08, follow-up ended 9/30/10
  - 9H, 15/3745 (0.43%) – 69% completion, discontinuation 3.6%
  - 3HP, 7/3986 (0.19%) – 82% completion, discontinuation 4.7%
  - Otherwise healthy patients ≥ 12 years of age

PZA and RIF combination therapy is no longer recommended due to hepatotoxicity and deaths

*MMWR. Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection
## Treatment of LTBI in Children

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration</th>
<th>Daily Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>9</td>
<td>10-15 mg/ kg</td>
<td>270 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(max 300 mg)</td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td>6</td>
<td>10-20 mg/ kg</td>
<td>180 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(max 600 mg)</td>
<td>INH resistant TB</td>
</tr>
<tr>
<td>Isoniazid/</td>
<td>3</td>
<td>H - 15 mg/ kg</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Rifapentine</td>
<td></td>
<td>(max 900 mg)</td>
<td>≥ 12 years old</td>
</tr>
</tbody>
</table>

- **Isoniazid**
  - ≥ 12 years old
  - 10.0-14.0 kg 300 mg
  - 14.1-25.0 kg 450 mg
  - 25.1-32.0 kg 600 mg
  - 32.1-49.9 kg 750 mg
  - ≥50.0 kg 900 mg max
Once weekly Isoniazid-Rifapentine x 12 weeks via DOT for LTBI ≥ 12 years old

- Isoniazid - 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum
- Rifapentine - 10.0–14.0 kg 300 mg, 14.1–25.0 kg 450 mg, 25.1–32.0 kg 600 mg, 32.1–49.9 kg 750 mg, ≥50.0 kg 900 mg maximum
- Isoniazid is formulated as 100 mg and 300 mg tablets.
- Rifapentine - 150 mg tablets packed in blister packs that should be kept sealed until usage.
- New formulations with larger dosage per tablet and fixed-dose INH-RPT combinations are in development.

CDC. MMWR. December 9, 2011 / 60(48);1650-1653
Sterling TR et al. NEJM 2011;365:2155
## Symptoms in Children with Tuberculosis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency (%)</th>
<th>Study A* (47 infants &lt; 1 Yr old)</th>
<th>Study B^ (156 children &lt; 20 yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>79</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>64</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Loss of Appetite</td>
<td>43</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Diarrhea/vomiting</td>
<td>17</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Weight Loss</td>
<td>15</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Night Sweats</td>
<td>NR</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>NR</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>11</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

* Vallejo et al. Pediatr 94:1, 1994

^ Burroughs et al. PIDJ 18:440, 1999
Progressive Primary Pulmonary TB in Children

4-month-old female with RLL consolidation and R hilar lymphadenopathy
10 y/o female with Segmental RLL a/s Disease and Paratracheal Lymphadenopathy
Cavitary TB in an adolescent

17 yr old BF, 2 mo cough, night sweats and 10# wt loss. Born in Virgin Islands; in U.S. x 10 yrs. PPD >20mm; sputum (+) *M. tuberculosis*
Miliary Tuberculosis

3 y/o female exposed to her grandfather with pulmonary TB
Diagnosis of Pulmonary TB

Gastric lavage (GL) is better than bronchoalveolar lavage (BL) for isolation of *Mycobacterium tuberculosis* in childhood tuberculosis  Abadco and Steiner, PIDJ 1992;11:735-738

- 20 children, 4 mo – 7.5 y/o, admitted over 16 months for suspected pulmonary tuberculosis in Brooklyn, NY
- **GL:** 10 (50%) cx + and 0 smear +, **BL:** 2 (10%) cx + and 0 smear +


- 250 children, 1 mo – 5 y/o, admitted 2000-2002 for suspected pulmonary tuberculosis in Cape Town, South Africa; **58 (23%)** cx + and **29 (12%)** smear +
- 1 induced sputum, smear or cx + = **41/62 (66%)**
- 3 gastric aspirates, smear or cx + = **40/62 (64%)**
- **3 induced sputa, smear or cx + = 54/62 (87%) yield, youngest 3 mo**
Any extrapulmonary involvement* (totaling 29.1%)

- Lymphatic: 18.9%
- Meningeal: 3.1%
- Miliary: 1.5%
- Bone & Joint: 1.5%
- Other: 4.1%

*Any extrapulmonary involvement, with or without pulmonary involvement (patients may have > 1 disease site but are counted in mutually exclusive categories for surveillance purposes)
### Percent of Pediatric TB Cases with Extrapulmonary Involvement* by Age Group & Sites of Disease, 1993–2008 (N=17,502)

<table>
<thead>
<tr>
<th>Site of Disease</th>
<th>Age &lt; 1 (n=1,697)</th>
<th>Age 1-4 (n=8,616)</th>
<th>Age 5-9 (n=3,991)</th>
<th>Age 10-14 (n=3,198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphatic</td>
<td>7.8</td>
<td>19.3</td>
<td>22.2</td>
<td>19.4</td>
</tr>
<tr>
<td>Meningeal</td>
<td>7.6</td>
<td>3.6</td>
<td>1.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Miliary</td>
<td>5.5</td>
<td>1.2</td>
<td>0.6</td>
<td>1.1</td>
</tr>
<tr>
<td>Bone &amp; Joint</td>
<td>0.4</td>
<td>1.3</td>
<td>1.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Other</td>
<td>3.5</td>
<td>2.7</td>
<td>4.2</td>
<td>8.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>24.8</strong></td>
<td><strong>28.1</strong></td>
<td><strong>30.1</strong></td>
<td><strong>33.1</strong></td>
</tr>
</tbody>
</table>

*Any extrapulmonary involvement includes extrapulmonary only and both*
Lymphatic TB in Children

13 y/o African male; 2 mo hx neck swelling, fever & 4# wt loss. Born in Somalia; moved to U.S. 9 mo PTA. PPD (+) but no Rx. PPD 25mm
13 month old Honduran male whose grandfather had cavitary tuberculosis diagnosed after this child presented with fever, irritability and nuchal rigidity.

CSF: Glucose 25, prot 108, RBC 13, WBC 39, 100% mononuclear cells.
TB cerebritis of Temporal-Parietal Lobes
Paradoxical Tuberculoma in 3rd Month of Therapy
Pott’s Disease (TB of vertebral bodies)

18 yr old college student from Ghana; known PPD positive in 2001; no RX. Developed 2 mo. back pain and leg weakness during football practice in 2005. PPD 30 mm
Inadequately Treated Pott’s Disease

10 yr old Somali female with severe kyphoscoliosis who was treated with one medication and coining at age 2-3
Vertebral body destruction from inadequately treated Pott’s disease

T1 weighted MRI - destruction and fusion of C5,6,7 & T1 vertebral bodies
16 y/o female immigrated from Somalia 6/04; developed L breast swelling and pain in late 2/05. Aspirate of breast abscess on 3/23/05 (+) for M. TB – INH resistant. PPD 25mm. 12 # wt loss over one month. Tx: with RPE x 9 mo
# DOT TB Disease

<table>
<thead>
<tr>
<th>Stage of TB</th>
<th>RX</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary TB</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Non HIV (+), US born</td>
<td>INH/Rif/PZA*</td>
<td>6 mo**</td>
</tr>
<tr>
<td>• HIV(+) or foreign-born</td>
<td>INH/rifabutin/PZA/eth</td>
<td>6 mo**</td>
</tr>
<tr>
<td>born</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Extrapulmonary TB</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• meningitis</td>
<td>INH/RIF/PZA/eth</td>
<td>9-12 mo**</td>
</tr>
<tr>
<td>• bone, joint, miliary</td>
<td>Same as pulmonary</td>
<td>6-9 mo**</td>
</tr>
</tbody>
</table>

*if INH resistance >4% or high risk of drug resistance in source, add ethambutol until drug susceptibility confirmed/2 months

**PZA for only first 2 months
Pediatric Contacts of Adults with Active Pulmonary TB

- TST or IGRA and CXR; repeat in 8-10 weeks if (-)
- If child is ≥ age 5 years, initial screen is negative, and child is asymptomatic, no therapy needed
- For child ≤ age 4 years, begin INH or rifampin; continue therapy until repeat TST is (-) and index case is on DOT and confirmed to be sputum (-)
- If repeat TST or IGRA positive, repeat CXR and treat as LTBI or active disease
How do we recognize TB in infants and children?
How does disease in children differ from that of adults?
What are the main diagnostic and treatment algorithms to follow in pediatrics?
Conclusions

- A major focus of TB eradication in the US has been to identify and treat patients with LTBI - treatment is prolonged and compliance is difficult.
- Childhood TB is most often pulmonary and may present like many other forms of pneumonia.
- In the U.S., interferon-γ release assays have already replaced TSTs for targeted screening in adults, but their use in children, < 5 years of age in particular, continues to be defined.
- LTBI may be treated with once weekly 12-dose regimen of INH and rifapentine in children > 2 y/o.
- TB disease in children is often more sub-acute and subtle than in adults.