Pediatric TB

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  Dr. Nolan has no declared conflicts of interest

Pediatric TB

• Objective:
  – Describe current recommendations for diagnosis and treatment of pediatric TB.
• Content:
  – Diagnosis
  – Treatment strategies
  – Case studies
TB Definitions:

- **Positive tuberculin skin test (TST) result:** indicates possible infection with *M tuberculosis* complex. (Reactivity appears in 2 to 10 weeks; median interval is 3 to 4 weeks after exposure.)
- **Positive interferon-gamma release assay (IGRA):** indicates possible infection with *M tuberculosis* complex.
- **Exposed person:** recent contact with another person with suspected or confirmed contagious pulmonary tuberculosis disease and who has a negative TST or IGRA result, normal physical examination findings, and CXR findings that are not compatible with tuberculosis. Some exposed people become infected (and subsequently, most have a positive TST or IGRA result) and some people do not become infected after exposure (indistinguishable initially).
- **Source case:** person who has transmitted infection with *M tuberculosis* complex to another person who subsequently has either latent tuberculosis infection or tuberculosis disease.
- **Latent tuberculosis infection (LTBI):** *M tuberculosis* complex infection in a person who has a positive TST or IGRA result, no physical findings of disease, and CXR findings that are normal or reveal evidence of healed infection (e.g., calcification in the lung, hilar lymph nodes, or both).

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**TB Definitions:**

**Tuberculosis disease:** infection with symptoms, signs, or radiographic manifestations caused by *M tuberculosis* complex; disease may be pulmonary, extrapulmonary, or both. Infectious tuberculosis refers to tuberculosis disease of the lungs or larynx in a person who has the potential to transmit the infection to other people.

**Directly observed therapy (DOT):** medication is administered directly to the patient by a health care professional or trained third party (not a relative or friend), who observes and documents ingestion of each dose of medication.

**Multiply drug-resistant (MDR) tuberculosis:** TB infection or disease caused by *M tuberculosis* complex resistant to at least isoniazid and rifampin.

**Extensively drug-resistant (XDR) tuberculosis:** infection or disease caused by a strain of *M tuberculosis* complex resistant to isoniazid and rifampin, at least 1 fluoroquinolone, and at least 1 of parenteral drugs: amikacin, kanamycin, or capreomycin.

**Bacille Calmette-Guérin (BCG):** attenuated vaccine strain of *M bovis*. BCG rarely used in United States; most widely used vaccine in the world.

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**Figure 1.** Number of reported cases of tuberculosis, by year or diagnosis—United States, 1982–2003. ATS/CDC/IDSA controlling tuberculosis in the United States. Am J Respir Crit Care Med. 2005 Nov;172(9):1169-227.
Figure 2. Percentage of persons infected with Mycobacterium tuberculosis, by bacteriologic status of and proximity to the source case—British Columbia and Saskatchewan, 1966–1971. Source: Reference 57.


Figure 3. Number and percentage of cases of tuberculosis among foreign-born persons, by year of diagnosis—United States, 1986–2003.


TABLE 2. Tuberculosis rates among five racial/ethnic populations—United States, 2003

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, non-Hispanic</td>
<td>1.4</td>
</tr>
<tr>
<td>American Indian/Alaska</td>
<td>8.0 (5.7)</td>
</tr>
<tr>
<td>Native</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>10.5 (7.5)</td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
<td>11.5 (8.2)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>29.4 (21.0)</td>
</tr>
</tbody>
</table>

- Numbers in parentheses represent risk for tuberculosis compared with white non-Hispanics.
- Per 100,000 population.
**Test** | **Maximum Turnaround Time**
--- | ---
Microscopy for acid-fast bacilli | Onsite 24 h from specimen collection Offsite, 24 h from laboratory receipt (time from collection to lab receipt < 24 h)
Nucleic acid amplification assay | < 48 h from date of specimen collection
Mycobacterial growth detection by culture | < 14 d from date of specimen collection
Identification of cultured mycobacteria | < 21 d from date of specimen collection
Drug susceptibility testing | < 30 d from date of specimen collection
Drug susceptibility testing of second-line drugs | < 4 wk from date of request

*TABLE 3. Essential laboratory tests for tuberculosis control

**Patient and Setting**
**Recommended Evaluation**

| Cough of 2–3 wk duration, with at least one additional symptom, including fever, night sweats, weight loss, or hemoptysis | CXR: if suggestive of TB (or if patient has HIV infection), 3 sputums for AFB smear micro and culture
| High risk for TB* with an unexplained illness, including respiratory symptoms, of 2–3 wk duration | Chest radiograph: if suggestive of TB, 3 sputums for AFB smear micro and culture
| HIV infection and unexplained cough and fever | CXR, 3 sputum specimens for AFB smear microscopy and culture
| High risk for TB* with a diagnosis of community-acquired pneumonia no better after 7 d of treatment | CXR, 3 sputums for AFB smear micro and culture
| High risk for TB* with incidental findings on CXR (infiltrates with or without cavitation in the upper lobes or the superior segments of the lower lobes) suggestive of TB | Review CXR, 3 sputums for AFB smear micro and culture

*TABLE 5. Guidelines for the evaluation of pulmonary tuberculosis in adults in five clinical scenarios
ATS/CDC/IDSA controlling tuberculosis in the United States. AJRCCM. 2005 Nov 1;172(9):1169-227.

**HIGH RISK FOR TB**
- Recent exposure to a person with a case of infectious TB;
- Hx positive test result for *M. tuberculosis* infection;
- HIV infection
- Injection or non-injection drug use
- Foreign birth and immigration in 5 yr from a region in which incidence is high
- Residents and employees of high-risk congregate settings
- Membership in a medically underserved, low-income population
- Medical risk factor for TB (including diabetes mellitus, conditions requiring prolonged corticosteroid and other immunosuppressive therapy; chronic renal failure, certain hematologic malignancies, and carcinomas; weight more than 10% below ideal body weight, silicosis, gastrectomy, or jejunileal bypass).

TB Epidemiology

- Higher in urban, low-income areas
- 2/3rds cases in the U.S. nonwhites
- Foreign-born children > 1/4 newly diagnosed cases ≤ 14 y/o
- Groups with higher LTBI
  - Immigrants/adoptees/refugees/travelers high-prevalence regions (e.g., Asia, Africa, Latin America, and countries of the former Soviet Union)
  - Homeless people
  - Correctional facilities

TB Epidemiology

- Higher risk for progression of LTBI to tuberculosis disease:
  - Infants and post-pubertal adolescents
  - Recent infection (within the past 2 years)
  - Immunodeficiency, especially HIV infection
  - Immunosuppressive drugs, such as prolonged or high-dose corticosteroid therapy or chemotherapy
  - IVDA
  - Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, and malnutrition
  - Treatment with tumor necrosis factor alpha (TNF-alpha) antagonists, such as infliximab and etanercept.

Validated Questions for Determining Risk of LTBI in Children in the United States

- Has a family member or contact had tuberculosis disease?
- Has a family member had a positive tuberculin skin test result?
- Was your child born in a high-risk country (countries other than the United States, Canada, Australia, New Zealand, or Western European countries)?
- Has your child traveled (had contact with resident populations) to a high-risk country for more than 1 week?
Pediatric TB

- Diagnostic and therapeutic challenges
  - Less specific signs and symptoms of disease
  - Paucibacillary resulting in fewer positive cultures
  - Increased risk of progression of disease once infected
  - Increased risk of dissemination

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TB Diagnostic Tests

- **Tuberculin Skin Testing (TST):**
  - Most common method for diagnosing LTBI in asymptomatic people.
  - Mantoux method consists of 5 tuberculin units of purified protein derivative (0.1ml) injected intradermally using a 27-gauge needle and a 1.0-mL syringe into the volar aspect of the forearm;
  - Palpable induration 6 to 10 mm in dia. crucial

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Image 145_21. (A) Sokol ballpoint pen method, 48 to 72 hours placement, slowly approaching site until resistance is felt from induration NOT redness. Repeat on the opposite side.
(B) Distance between the lines in millimeters.
Definitions of Positive Tuberculin Skin Test (TST) Results in Infants, Children, and Adolescents

- **Induration 5 mm or greater:**
  - Close contact with known or suspected TB Case
  - Children suspected to have TB disease
  - Findings on chest radiograph consistent with active or previous TB disease
  - Clinical evidence of tuberculosis disease
  - Children receiving immunosuppressive therapy or with immunosuppressive conditions, including human immunodeficiency (HIV) infection

*Regardless of previous bacille Calmette-Guérin (BCG) immunization; erythema alone at TST site does not indicate a positive test result. Tests should be read at 48 to 72 hours after placement.*

- **Induration 10 mm or greater**
  - Children at increased risk of disseminated tuberculosis disease:
    - Children younger than 4 years of age
    - Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition (see Table 3.80, p 684)
    - Children with likelihood of increased exposure to tuberculosis disease:
      - Children born in high-prevalence regions of the world
      - Children frequently exposed to adults who are HIV infected, homeless, users of illicit drugs, residents of nursing homes, incarcerated or institutionalized, or migrant farm workers
      - Children who travel to high-prevalence regions of the world

*These definitions apply regardless of previous bacille Calmette-Guérin (BCG) immunization (see also Interpretation of TST Results in Previous Recipients of BCG Vaccine, p 685); erythema alone at TST site does not indicate a positive test result. Tests should be read at 48 to 72 hours after placement.*

- **Induration 15 mm or greater**
  - Children 4 years of age or older without any risk factors

*Regardless of previous bacille Calmette-Guérin (BCG) immunization; erythema alone at TST site does not indicate a positive test result. Tests should be read at 48 to 72 hours after placement.*
TB Diagnostic Tests

• *M tuberculosis* complex culture from specimens of gastric aspirates, sputum, bronchial washings, pleural fluid, cerebrospinal fluid (CSF), urine, or other body fluids or a biopsy.

• *M tuberculosis* complex organisms isolated < 50% of children, 75% of infants w/ pulmonary TB diagnosed by other clinical criteria

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TB Specimen Collection

• Hypertonic Saline Sputum induction in ≥ 5 y/o

• Cough is nonproductive or absent
  – Early morning gastric aspirate (GA)
    • Nasogastric tube obtained before ambulation or feeding
    • Aspirates collected on 3 separate days
  – GA AFB smears usually negative
  – False-positive smear results nontuberculous mycobacteria
  – GA highest culture yield on the first day
  – Fluorescent staining of GA smears are more sensitive
  – Diagnostic yield of GA < 50%

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TB Diagnostic Tests

• Immunologic-Based Testing:
  – QuantIFERON-TB Gold and Gold In-Tube and T-SPOT.TB are IGRAs.
  – FDA-approved tests measure ex vivo interferon-gamma production from T lymphocytes
    • fairly specific to *M tuberculosis* complex
    • cannot distinguish between latent infection and disease,
    • negative result cannot exclude tuberculosis infection or disease in a patient with suspicious finding

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Current recommendations for use of IGRAs in children:

- For immune-competent > 5 years of age and older, IGRAs can be used in place of a TST to confirm cases of tuberculosis or cases of LTBI and likely will yield fewer false-positive test results.
- Children with a positive result from an IGRA should be considered infected with M. tuberculosis complex. A negative IGRA result cannot universally be interpreted as absence of infection.
- Because of their higher specificity and lack of cross-reaction with BCG, IGRAs may be useful in children who have received BCG vaccine. IGRAs may be useful to determine whether a BCG-immunized child with a reactive TST more likely has LTBI or has a false-positive TST reaction caused by the BCG.
- IGRAs cannot be recommended routinely for use in children younger than 5 years of age or for immune-compromised children of any age because of a lack of published data about their utility with these groups.
- Indeterminate IGRA results do not exclude tuberculosis infection and should not be used to make clinical decisions.

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Exposure
Household contact with contagious teen or adult
Usually > 4 hours of contact

TB diagnosis

- Risk assessment important
- Diagnosis in children more often based on epidemiology and clinical findings than on smear or culture
TB disease
Clinical and radiographic findings
(1993-2001 11,480 US cases)
• Pulmonary 76.9%
  – Primary
  – Progressive
  – Chronic/reactivation
• Extra-pulmonary
  – Lymphatic 15.5%
  – Meningeal 2.1%
  – Miliary 1.1%
  – Pleural 1.1%
  – Bone/joint 1.4%
• TB in newborns

TST and Pediatric Disease
• Positive TST with TB disease
  – Pediatrics 89%
  – Adults 54%
• Up to 20% of children with TB disease will have a negative TST at diagnosis
• Approximately 5% will be persistently negative

Pediatric TB disease
Laboratory diagnosis
• Adult source isolate can direct treatment
• Cultures need to be obtained from the child if:
  • source case is unknown
  • several possible source cases with different susceptibility patterns
  • if the likely source has drug resistant TB
  • extrapulmonary disease
Pediatric Exposure Treatment

• Window prophylaxis
  – Window period for TST conversion: 2-12 weeks
  – Indicated for those <=4 years
  – Baseline TST – / CXR normal
  – INH prophylaxis recommended
    • Children <=4 yrs
    • Immunosuppressed pts
    • Pts on TNF alpha blockers

• Follow up TST done 10-12 weeks after last exposure to infectious contact
  – Induration less than 5 mm stop prophylaxis,
  – Induration greater than 5 mm treat for LTBI

Pediatric TB Disease

Laboratory Diagnosis

• Childhood pulmonary disease
  • Inpatient early morning gastric aspirate x3 (cx + ~40%)
  • Induced sputum x 3 in cooperative older children-first morning best
  • Bronchoscopy: culture yield is lower than properly obtained gastric aspirate (cx + ~20%)
  • Newer testing modalities are not used for various reasons:
    • PCR sensitivity only slightly better than culture, specificity less, so not widely used in pediatrics
    • NAA and IGRAs not approved for use

• Extrapulmonary disease
  • Culture from affected body site (cx + ~40%)

Clinical Manifestations of TB

Image 145_07. Tuberculosis Mycobacterium tuberculosis infection with paratracheal lymph nodes.
13 yo asymptomatic, identified as part of contact investigation. PPD 20mm

6 yo PPD 15 mm. Contact investigation. CXR hilar and infrahilar fullness.

Chest CT: Multiple pulmonary nodules in the lung bases bilaterally, in the right lower lobe, one in the posterolateral right middle lobe and two in the left lower lobe. Also present is extensive adenopathy.

TB Disease
Clinical and Radiographic Findings

- Progressive pulmonary primary TB
  - Associated with weight loss or FTT, anorexia, fatigue, low grade temp, intermittent cough
  - May cause cavitation or endobronchial disease

- Chronic pulmonary/ reactivation disease
  - Most common in adolescents with primary infection after 7 years of age
  - Present with fever, weight loss, productive cough, hemoptysis, night sweats
  - Xray findings include cavitations, typically upper lobe

US data

<table>
<thead>
<tr>
<th></th>
<th>&lt;10 years of age</th>
<th>10-14 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavitary disease</td>
<td>3.5%</td>
<td>11.8% (p&lt;0.001)</td>
</tr>
<tr>
<td>Sputum smear</td>
<td>1.7%</td>
<td>10.3% (p&lt;0.001)</td>
</tr>
<tr>
<td>Sputum positive</td>
<td>4.2-5.0%</td>
<td>21.3% (p&lt;0.001)</td>
</tr>
</tbody>
</table>
TB Disease
Clinical and Radiographic Findings

• Superficial lymphadenitis
  – Usually the anterior cervical and submandibular nodes
  – Usually presents within 6 months of infection
  – Affects children with median age 31-36 months
  – Nodes are firm, nontender or minimally so
  – No systemic symptoms
  – Chest radiographic findings may be present

Slide: Michelle Hulse, MD


TB Disease
Clinical and Radiographic Findings

• Pleural effusion
  – Most occur 3 months after primary infection
  – Usually affect older children (mean 13.5 years)
  – Present with fever, fatigue, respiratory distress, chest pain
  – CXR shows unilateral pleural effusion
    • Associated parenchymal abnormalities in about half of pts
  – Excellent prognosis

Slide: Michelle Hulse, MD
TB meningitis
8 month old East Indian girl RUL pneumonia, possible abscess or loculated pleural fluid
Slide: Michelle Hulse, MD

8 month old with pulmonary TB and TB meningitis.
Chest CT with RUL dense Consolidation with multiple cavitations.
Superior mediastinum findings consistent with abscess
Slide: Michelle Hulse, MD
TB Disease
Clinical and Radiographic Findings

- Meningeal disease
  - Most within 3-6 months of primary infection
  - Often associated with miliary disease, esp in < 5 yr olds
  - Median age affected 17-23 months
  - Most severe form of disease

- Indolent with symptoms present 1-4 weeks before diagnosis
- Most common symptoms are fever, vomiting, lethargy, headache, seizure (esp in < 2 year olds)
- Hydrocephalus common on presentation
- Brain parenchymal disease (tuberculoma) in 20-37%
- CXR abnormal in 40-86%

- Outcome depends on age and severity of symptoms at presentation
- Mortality <10% with effective therapy
- Long term sequelae are common
  - Mental retardation
  - Seizures
  - hemiparesis

- Mental retardation
Miliary disease in 18 mo Hmong male micronodular infiltrates, hilar fullness
- Similar to meningitis in pathogenesis, time of onset after infection, indolent presentation, and severity
- Median age affected is 6-11 months
- Often present with weeks of fever, cough, weight loss, anorexia, and malaise

TB Disease
Clinical and Radiographic Findings

- Bone/joint disease
  - Onset 6-18 months after primary infection
  - Median age of onset: 6 years
  - Affect vertebrae, knee, hip, and elbow most commonly
  - Present with localized inflammation, pain, swelling, decreased range of motion, and fever
  - Xrays may show spondylitis, arthritis, and osteomyelitis
  - 50% will have abnormal CXR
Image 145_16. Tuberculosis Tuberculosis of the spine with paravertebral abscess (Pott disease).

Image 145_17. Tuberculosis Tuberculosis of the spine with paravertebral abscess (Pott disease) shown on the radiograph. This is the same patient as in image 145_16.

7 yo Hmong refugee
Pott’s disease spine
MRI
Destruction and collapse of L3 and L4 along with inferior L2 and Superior L5.
Kyphosis and gibbus formation, mild
Central stenosis
### Latent Tuberculosis Infection (Positive TST or IGRA Result, No Disease)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 mo of isoniazid, once a day</td>
<td>If daily therapy is not possible, DOT twice a week can be used for 9 mo.</td>
</tr>
<tr>
<td>6 mo of rifampin, once a day</td>
<td>If daily therapy is not possible, DOT twice a week can be used for 6 mo.</td>
</tr>
</tbody>
</table>

*Duration of therapy is longer for human immunodeficiency virus (HIV)-infected people, and additional drugs may be indicated.*

### Pulmonary and Extrapulmonary (Except Meningitis)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mo of isoniazid, rifampin, pyrazinamide, and ethambutol daily, followed by 4 mo of isoniazid and rifampin by DOT for drug-susceptible <em>Mycobacterium tuberculosis</em></td>
<td>If possible drug resistance is a concern, another drug (ethambutol or an aminoglycoside or ethionamide) is added to the initial 3-drug therapy until drug susceptibilities are determined. DOT is highly desirable.</td>
</tr>
<tr>
<td>4 to 12 mo of isoniazid and rifampin for drug-susceptible <em>Mycobacterium bovis</em></td>
<td>If hilar adenopathy only, 6-mo course of isoniazid and rifampin is sufficient.</td>
</tr>
</tbody>
</table>

*Drugs can be given 2 or 3 times/wk under DOT in the initial phase if nonadherence is likely.*

### Meningitis

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mo of isoniazid, rifampin, pyrazinamide, and an aminoglycoside or ethambutol or ethionamide, once a day, followed by 7-10 mo of isoniazid and rifampin, once a day or twice a week (9-12 mo total) for drug-susceptible <em>M. tuberculosis</em></td>
<td>A fourth drug, such as an aminoglycoside, is given with initial therapy until drug susceptibility is known.</td>
</tr>
</tbody>
</table>
| At least 12 mo of therapy without pyrazinamide for drug-susceptible *M. bovis* | For patients who may have acquired tuberculosis in geographic areas where resistance to streptomycin is common, kanamycin, amikacin, or capreomycin can be used instead of streptomycin.*
Commonly Used Drugs for Treatment of Tuberculosis in Infants, Children, and Adolescents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Forms</th>
<th>Daily Dose, mg/kg</th>
<th>Twice a Week Dose, mg/kg/Once</th>
<th>Maximum Dose</th>
<th>Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>Capsules, 300 mg</td>
<td>5-7.5</td>
<td>15</td>
<td>500 mg</td>
<td>Hepatotoxicity, bone marrow depression, hepatitis, peripheral neuritis, hyperesthesia</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Tablets, 500 mg</td>
<td>10-15</td>
<td>20-30</td>
<td>500 mg</td>
<td>Dizziness and gastric irritation caused by vehicle in the spray</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Capsules, 300 mg</td>
<td>5-7.5</td>
<td>10</td>
<td>500 mg</td>
<td>Hypersensitivity, rash, hepatitis, pancreatitis, hepatitis, abnormal hepatic function tests</td>
</tr>
</tbody>
</table>

Less Commonly Used Drugs for Treatment of Drug-Resistant Tuberculosis in Infants, Children, and Adolescents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Forms</th>
<th>Daily Dose, mg/kg</th>
<th>Twice a Week Dose, mg/kg/Once</th>
<th>Maximum Dose</th>
<th>Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>Vial, 25 mg</td>
<td>15-20</td>
<td>45-60</td>
<td>500 mg</td>
<td>Auditory and vestibular effects, nephrotoxic effects</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>Vial, 1 g</td>
<td>15-20</td>
<td>45-60</td>
<td>500 mg</td>
<td>Auditory and vestibular effects, nephrotoxic effects</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Tablets, 500 mg</td>
<td>15-20</td>
<td>45-60</td>
<td>1500 mg</td>
<td>Ocular toxicity</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>Vial, 10 mg</td>
<td>15-20</td>
<td>45-60</td>
<td>500 mg</td>
<td>Auditory and vestibular effects, nephrotoxic effects</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Vial, 500 mg</td>
<td>500-1000 mg</td>
<td>1000-2000 mg</td>
<td>5000 mg</td>
<td>Theoretical risk of Q fever, other gastrointestinal symptoms, rash</td>
</tr>
<tr>
<td>Non-antituberculosis drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PENTAMETHYLPYRROLE</td>
<td>Vial, 1 g</td>
<td>5-7.5</td>
<td>15</td>
<td>500 mg</td>
<td>Auditory and vestibular effects, nephrotoxic effects, rash</td>
</tr>
</tbody>
</table>

LTBI Treatment in Pregnancy

- Positive TST or IGRA result, normal chest radiographic findings, and recent contact index
  - Isoniazid for 9 months
    - Begin after the first trimester
    - Pyridoxine for all pregnant and breastfeeding women
    - Isoniazid safe for nursing; no pyridoxine supplement for infant
TB Disease Treatment in Pregnancy

- Regimen of isoniazid, rifampin, and ethambutol
- Pyrazinamide commonly used in a 3- or 4-drug regimen
  - Safety during pregnancy has not established
- At least 6 months of therapy for drug-susceptible TB if pyrazinamide is used;
- At least 9 months of therapy if pyrazinamide is not used
- Prompt initiation of therapy is mandatory to protect mother and fetus

Infant of Mother w/ TB Disease

- Congenital/Perinatal TB suspected?
- Obtain
  - TST (usually neg)
  - CXR
  - Lumbar puncture
  - Appropriate cultures
- Placenta
  - Histology for granulomas and AFB
  - Cultured for \textit{M} \textit{tuberculosis} complex

Newborn Infant Exposed to LTBI

- Asymptomatic LTBI Exposure, normal CXR
  - no separation infant & mother
- Household members TST or IGRA & Eval
- Do not delay infant's discharge
Newborn Infant Exposed to TB Disease

- Mother w/ TB Disease
- Eval infant for congenital TB
- Infant separated until the mother (contact) evaluated
  - If TB disease confirmed separation until mother (contact) & infant on appropriate anti-TB Rx
- If MDR or poor adherence consider BCG immunization
- Infant may breastfeed after maternal 2 wks Rx and mother not contagious

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Criteria for Determining when a Patient with Pulmonary TB Becomes Noninfectious

- Negligible likelihood of multidrug-resistant TB (no known exposure to MDRTB and no history of prior episodes of TB with poor compliance during treatment).
- Standard multidrug anti-TB therapy for 2–3 weeks. (For AFB smear results that are negative or rarely positive, threshold for treatment is 0–7 days.)
- Complete adherence to treatment (e.g., is receiving directly observed therapy).
- Evidence of clinical improvement (e.g., reduction in the frequency of cough or reduction of the grade of the sputum AFB smear result).
- All contacts identified, evaluated, advised, and, if indicated, treated latent TB infection; critical, especially for close contacts: younger than 4 years; any age immunocompromised
- In hospital pulmonary TB should remain in airborne-infection isolation until
  1. Are receiving standard multidrug anti-TB therapy
  2. Demonstrated clinical improvement
  3. Have had three consecutive AFB-negative smear results of sputum specimens collected 8–24 hours apart, with at least one being an early-morning specimen. Patients returning to a congregate setting (e.g., a homeless shelter or detention facility) should have three consecutive AFB-negative smear results of more than 8 hours apart before being considered noninfectious.


Case

- 20 mo old Somali refugee with 8 mo hx of fever, cough, chronic otitis media, constitutional symptoms
  - +PPD
  - Chest imaging with miliary opacities and extensive mediastinal and hilar adenopathy
  - CNS tuberculomas
  - Splenomegaly, retroperitoneal, and peri-portal adenopathy
  - Mildly increased aminotransferases and inflammatory markers

Slide: Michelle Hulse, MD
20 months, Somali Refugee from Kenya 2 m prior 8 m hx cough, fever, poor appetite, no interest in play 11-15-06

11-17-06 Chest CT

11-17-06 Head CT
Case

• Gastric washings X3
  – 1/3 + MTB pansensitive
• Induced sputum X3 all neg
• Left ear drainage cx +MTB
• Blood culture neg
• Urine culture neg

Case

• Started therapy
  – INH
  – Rifampin
  – PZA
  – EMB
  – B6
  – Steroids
  – Ranitidine
  – Dilantin
• NG feeds

Case

• Rapid improvement in symptoms
  – Defervesced
  – More interactive and playful
  – Improved appetite
• Discharged home on directly observed therapy on hospital day 11
• Follow up CT one month after start of therapy
1. Improved findings of miliary tuberculosis compared to 11-17-06.
2. Mild cylindrical bronchiectasis right upper and middle lobes.
3. Very slight improvement in extensive necrotic mediastinal and right hilar lymphadenopathy.
4. Improved aeration right upper lobe

Case

- Follow up chest CT: improvement in all findings except mediastinal and hilar adenopathy
- Head CT: marked improvement in tuberculomas
- Pt had been seen in clinic prior with verification that all meds were being given, TB meds by TB clinic staff, others by mom

Case

- On repeat questioning steroids were not being given, and had not been given after the pt was discharged from the hospital
- Steroids are an important part of treatment in miliary disease
  - Reduce adenopathy and potential for further airway compression and late pulmonary complications such as collapse-consolidation
  - Bronchial erosion and endobronchial disease
  - Reduce risk of broncho- or tracheo- esophageal fistula
  - Reduce CNS inflammation
Case

• Steroids were started again, with one dose by DOT and the other verified each day
• Treatment for 4 weeks with 3 week taper
• Prolonged rx and taper reduce risk of rebound
• Pt did well thereafter
Chest CT on admit with unilateral pleural effusion
Persistent fever and rising CRP on parenteral antibiotics. BC neg, pleural fluid cx neg

CXR 3 months after starting antimycobacterial meds

THANK YOU!
QUESTIONS?

References
• American Academy of Pediatrics Red Book 2009
• ATS/CDC/IDSA controlling tuberculosis in the United States. Am J Respir Crit Care Med. 2005 Nov 1;172(9):1169-227
• Mandalakas AM, Starke JMC “Current Concepts of Childhood Tuberculosis” Semin Pediatr Infect Dis 2005; 16:93-104