Diagnosis and Treatment of Active TB Disease in Adults

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The Ohio State University
Medical Director, Ben Franklin TB Control Program

**Elderly patient with chronic cough and weight loss**

**HOPI**
- 74 year-old, African American female
- Seen at OSU ER with complaints of shortness of breath and progressive weakness
- Increasing SOB over the last 4 days
- Associated with fevers, chills, cough, with purulent sputum
- Family noted history of cough and weight loss over last several months

**74 YO Female**

- Physical Exam
  - Temp 97.8°F; BP 136/77; Pulse 136; RR 22
  - O₂ Sat. 98% on 3L/min NC O₂
  - NAD
  - Chest: crackles R base

**LAB:**
- WBC 9,700
  - PMN 86.5%, Lymph 8.2% Mono 5.2%
- Hb 9.3 gm/dL; Platelets 570K;
- BUN/Creat 12/0.84 mg/dL

**CXR**

- Admission
- 8 months prior to admission
Hospital Course

- Admitted to floor – Community Acquired Pneumonia
- Treated: ampicillin/sulbactam/azithromycin
- Respiratory failure → Intubated 24 hours later
- Blood and routine sputum cultures negative.
- Bronchial alveolar lavage (BAL)

- 5/5 Sputa “Heavy acid fast bacilli (AFB)-Positive”

Estimated TB incidence rate

- 9 million new TB cases each year
- 2 million deaths
- One life every 20 seconds

WHO
The hidden Epidemic – Latent TB Infection

- Every one second someone is newly infected with TB
- Two billion people, 1/3 of the world’s total population, are infected with TB
- One in 10 people infected with TB bacilli will develop active TB

USA: 1953  84,304 cases of TB  Rate 52.6 Cases per 100,000

U.S. Public Health Campaign

Reported TB Cases United States, 1982–2010*

- 11,182 cases (3.6 cases per 100,000 persons)

TB Case Rates,* United States, 2010

*Updated as of July 21, 2011

CDC photo image and A public health campaign poster, lungsNcog.org
Historical Collections and Services, The Claude Moore Health Sciences Library, University of Virginia
Ohio TB Cases by County for 2010
190 Total Cases

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>1.6</td>
<td>190</td>
</tr>
<tr>
<td>2009</td>
<td>1.6</td>
<td>180</td>
</tr>
<tr>
<td>2008</td>
<td>1.9</td>
<td>213</td>
</tr>
<tr>
<td>2007</td>
<td>2.2</td>
<td>252</td>
</tr>
<tr>
<td>2006</td>
<td>2.1</td>
<td>239</td>
</tr>
<tr>
<td>2005</td>
<td>2.3</td>
<td>260</td>
</tr>
<tr>
<td>2004</td>
<td>1.9</td>
<td>219</td>
</tr>
<tr>
<td>2003</td>
<td>2.0</td>
<td>229</td>
</tr>
</tbody>
</table>

Clinical Case

HOPI
- 28 year old Chinese female, 32 week pregnant
- Presented to OSH ER with hemoptysis
- C/O cough X 2 days, associated with mild SOB
- No fever, chills, night sweat, appetite loss, fatigue, or weight loss
- Denies any history contact with known active tuberculosis
- History positive TST, no latent TB therapy
- Received BCG vaccine in China as a child

Cases and Rates of Incident TB Disease in Franklin County, OH by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Cases</th>
<th>Rate/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Franklin Co.</td>
<td>USA</td>
</tr>
<tr>
<td>2002</td>
<td>41</td>
<td>4.5</td>
</tr>
<tr>
<td>2003</td>
<td>42</td>
<td>4.6</td>
</tr>
<tr>
<td>2004</td>
<td>46</td>
<td>4.8</td>
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<td>2005</td>
<td>48</td>
<td>5.0</td>
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<tr>
<td>2006</td>
<td>50</td>
<td>5.2</td>
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<tr>
<td>2007</td>
<td>52</td>
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<td>2008</td>
<td>54</td>
<td>5.6</td>
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<tr>
<td>2009</td>
<td>56</td>
<td>5.8</td>
</tr>
<tr>
<td>2010</td>
<td>58</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Hospital course

Laboratory
- WBC 6.1, Hgb 10.1gm/dL, Platelets 192, Cr. 0.5, AST 41, ALT 51, HIV negative

Radiology
- CXR - Mild asymmetric patchy LUL opacity
- CT - No PE
- Extensive diffuse nodular disease
Hospital course

- Admitted for Community Acquired Pneumonia and
  - Azithromycin and ceftriaxone
- Rule out TB - in Negative Air Isolation
  - Sputum AFB and smear X 3
  - Tuberculin Skin Test
  - Interferon gamma release assay

<table>
<thead>
<tr>
<th>AFB SMEAR and CULTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziehl-Neelsen</td>
</tr>
<tr>
<td>X 1,125</td>
</tr>
<tr>
<td>AFB smear</td>
</tr>
<tr>
<td>&lt; 24 hours</td>
</tr>
<tr>
<td>X 1440</td>
</tr>
</tbody>
</table>

- PPD 17mm
- Interferon gamma release assay
  (QuantiFERON-TB Gold®)
  - Positive

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Smear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum day 1</td>
<td>Negative</td>
</tr>
<tr>
<td>Sputum day 2</td>
<td>Negative</td>
</tr>
<tr>
<td>Sputum day 3</td>
<td>Negative</td>
</tr>
<tr>
<td>BAL day 4</td>
<td>Negative</td>
</tr>
</tbody>
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<td>Negative</td>
</tr>
<tr>
<td>BAL day 4</td>
<td>Negative</td>
</tr>
</tbody>
</table>

• Discharge home on INH for Latent TB Treatment
• Follow up at the Health Department

Is there another test you can order to help you make a diagnosis sooner?

NAAT: Nucleic acid amplification test
Mycobacterium tuberculosis Direct Test (MTD) or Amplicor

Nucleic Acid Amplification Test (NAAT)

• Direct, rapid, detection of *M. tb* complex (rRNA)
  – Patients suspected of TB
  – Takes about 4 to 5 hours
  – Approved for respiratory specimens only
  – Smear positive and smear negative
  – Non-respiratory specimen (validated by labs)
  – Can detect fewer than 10 organisms
  – Does not distinguish live vs dead organism
**CDC Guidelines - 2009**

**Nucleic Acid Amplification Test**

- Collect specimen for AFB, culture, & NAAT
- Interpret results with AFB smear.

<table>
<thead>
<tr>
<th>NAAT</th>
<th>AFB</th>
<th>Recommend</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>Start treatment. PPV &gt;95% NAAT in AFB+ cases</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>Repeat NAAT test. Presume TB if &gt;=2 NAA (+)</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>Presume nontuberculous mycobacteria (NTM)</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>Use clinical judgment. NAAT sensitivity 50-80% in detection AFB (-) Culture (+) pulmonary TB</td>
</tr>
</tbody>
</table>

**PPD 17mm**

- Interferon gamma release assay (QuantIFERON-TB Gold+)
  - Positive
- Nucleic acid amplification test:
  - Positive

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Smear</th>
<th>Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum day 1</td>
<td>Negative</td>
<td><em>M. tb</em></td>
</tr>
<tr>
<td>Sputum day 2</td>
<td>Negative</td>
<td><em>M. tb</em></td>
</tr>
<tr>
<td>Sputum day 3</td>
<td>Negative</td>
<td><em>M. tb</em></td>
</tr>
<tr>
<td>BAL day 4</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Sputum day 9*</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

*All subsequent sputum smear and culture negative

**Antimyobacterial Drugs**

**First-Line Drugs**

- Isoniazid (INH)
- Rifampin (RIF)
- Pyrazinamide (PZA)
- Ethambutol (EMB)

**Second-Line Drugs**

- Streptomycin
- Cycloserine
- p-Aminosalicylic acid
- Ethionamide
- Amikacin or kanamycin*
- Capreomycin
- Levofloxacin*
- Moxifloxacin*
- Linezolid*

*Not approved FDA for TB Treatment

**Vitamin B6**

**Other Drugs**

- Ethionamide
- Pyrazinamide
- Ethambutol
- Isoniazid
- Rifampin
Treatment of Culture-Positive TB

Initial Phase
2 months - INH, RIF, PZA, EMB daily (56 doses, within 8 weeks)

Continuation Phase
Options:
1) 4 months - INH, RIF daily (126 doses, within 18 weeks)
2) 4 months - INH, RIF twice / week (36 doses, within 18 weeks)
3) 7 months - INH, RIF daily (217 doses, within 31 weeks)*
4) 7 months - INH, RIF twice / week (62 doses, within 31 weeks)*

• Continuation phase increased to 7 months
  • chest x-ray shows cavitation and cx positive at 2 months
  • Or NO PZA in initial phase

Drug Susceptibility testing

MDR (Multi-drug resistant) TB
= Resistant to isoniazid and Rifampin
XDR (Extensive Drug Resistance) TB
MDR + Resistance fluoroquinolone + Resistance injectable (amikacin, capreomycin)

Rapid Molecular Detection of Drug Resistance for M. tuberculosis


Common Adverse Reactions to Drug Treatment

<table>
<thead>
<tr>
<th>Caused by</th>
<th>Adverse Reaction</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any drug</td>
<td>Allergy</td>
<td>Skin rash</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Eye damage</td>
<td>Blurred or changed vision, Changed color vision</td>
</tr>
<tr>
<td>Isoniazid,</td>
<td>Hepatitis</td>
<td>Abdominal pain, Abnormal liver function test results, Fatigue, Lack of appetite, Nausea, Vomiting, Yellowish skin or eyes, Dark urine</td>
</tr>
<tr>
<td>Pyrazinamide,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Common Adverse Reactions to Drug Treatment

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<tr>
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<th>Adverse Reaction</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>Peripheral neuropathy</td>
<td>Tingling sensation in hands and feet</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Gastrointestinal intolerance</td>
<td>Upset stomach, vomiting, lack of appetite</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>Arthritis</td>
<td>Joint aches</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Ear damage</td>
<td>Balance problems</td>
</tr>
<tr>
<td></td>
<td>Kidney damage</td>
<td>Abnormal kidney function test results</td>
</tr>
</tbody>
</table>

**LTBI**
- **TST positive**
- **CXR Negative**
- **No symptoms or physical findings suggestive of TB disease**

**Pulmonary TB Disease**
- **TST and IGRA may be positive**
- **CXR may be abnormal**
- **Symptoms may include one or more of the following: fever, cough, night sweats, weight loss, fatigue, hemoptysis, decreased appetite**
- **Respiratory specimens may be smear or culture positive**
- **NAAT may be positive**

LTBI = Latent TB Infection; TST = Tuberculin skin test, IGRA = interferon gamma release assay, NAAT = nucleic acid amplification test

### What to do if you suspect TB?
- Airborne Infection Isolation/precautions –
  - Negative airflow room and N-95 respirator mask
- CXR
- Respiratory AFB smear and culture
- Tuberculin skin test/IGRA -TB blood test
- HIV Test
- Smear and culture from other sites
- Nucleic Acid amplification test on sputum smear
- Drug Susceptibility
- REPORT ALL TB SUSPECTS to TB Control Program
Pediatric Tuberculosis Update

W. Garrett Hunt, MD, FAAP
Associate Professor of Pediatrics
The OSU College of Medicine
Nationwide Children’s Hospital

Objectives

- To become familiar with the epidemiology of infection and disease caused by *Mycobacterium tuberculosis* complex (TB) in children
- To understand current algorithms for the diagnosis of TB infection and disease in children
- To know the treatment regimens for latent TB infection (LTBI) in children

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*
TB Case Definitions and Verification

- 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

TB Case Rates* by Age Group
United States, 1993–2010

TB Case Rates by Pediatric Age Groups
1993–2008, N=17,502

Note: Rates presented on a logarithmic scale
~35% of household contacts are infected

95% of bacteremia hearing in 5 months

Progression to TB within 2 years, 5%

Progression with severe cutaneous TB, 10% each year

Bacteremia and dissemination to multiple body organs

"LTBI" major focus for PPD screening

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, Pulmonary</td>
<td>30</td>
</tr>
<tr>
<td>1-2</td>
<td>None, Pulmonary, Menigitis or miliary</td>
<td>30-40</td>
</tr>
<tr>
<td>2-5</td>
<td>None, Pulmonary, Menigitis or miliary</td>
<td>2-5</td>
</tr>
<tr>
<td>5-10</td>
<td>None, Pulmonary</td>
<td>0.5</td>
</tr>
<tr>
<td>&gt;10</td>
<td>None, Pulmonary</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Reproduced with permission from Marais et al. IJTL 2004; 8:392-402
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
- Induration ≥ 15 mm
  - 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

TST 6 Months after BCG at Birth in 69 Infants in Peru

![Graph showing TST results]  
Santiago EM et al. Pediatr 2003;112:e298

BCG Scar after Vaccination at Birth

- 2 months after birth
- 6 months after birth

Santiago EM et al. Pediatr 2003;112:e298

Updated CDC Guidelines 2010

Updated CDC Guidelines 2010

“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

<table>
<thead>
<tr>
<th>Antigen Presenting Cell (APC)</th>
<th>Antigen specific T cell</th>
<th>APC presents Antigen to antigen specific T cell</th>
<th>Antigen - specific T cell produces IFN-γ</th>
</tr>
</thead>
</table>

Antigens used: ESAT-6, CFP-10, TB 7.7

### IGRA vs TST

<table>
<thead>
<tr>
<th>IGRA</th>
<th>TST</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>

### QuantiFERON-Gold In-Tube

**Stage One – Blood incubation and Harvesting**
- Place blood samples in Quantiferon Gold In-Tube immediately
- Incubate for 24 hours at 37°C
- Harvest at least 200 µl plasma

**Stage Two – Human IFN-γ ELISA**
- Add solution of antigen
- Incubate at 37°C
- Read plate on time
- Results available
- Calculate according to manufacturer’s instructions

Positive when antigen (-) null elisa = 2.0-35 IU/mL

### 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>BCG substrains</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<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>
</tr>
</tbody>
</table>

### Tuberculosis Testing and Treatment

- Place TST
- Interprete TST 48-72 hrs
- < 10 mm: No infection
- ≥ 10 mm: Likely Infection
  - CXR at NCH Radiology
  - NCH TB Clinic
  - No Active Air-Space Disease
  - Active Air-Space Disease

### 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
**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

**Answers – b, d, or e**

- 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


**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 (max 300 mg)</td>
<td>270 doses</td>
</tr>
<tr>
<td>Rifampin</td>
<td>6</td>
<td>10-20 mg/kg (max 600 mg)</td>
<td>180 doses</td>
</tr>
<tr>
<td>Isoniazid/</td>
<td>3</td>
<td>H – 15 mg/kg (max 900 mg)</td>
<td>≥ 12 years old</td>
</tr>
<tr>
<td>Rifapentine</td>
<td></td>
<td></td>
<td>P - 10.0–14.0 kg 300 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14.1–25.0 kg 450 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25.1–32.0 kg 600 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>32.1–49.9 kg 750 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥50.0 kg 900 mg max</td>
</tr>
</tbody>
</table>

**Progressive Primary Pulmonary TB in Children**

4-month-old female with RLL consolidation and R hilar lymphadenopathy
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%)
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

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- GL: 10 (50%) cx + and 0 smear +, BL: 2 (10%) cx + and 0 smear +
- Induced sputum versus gastric lavage for microbiological confirmation of pulmonary tuberculosis in infants and young children: a prospective study  

- 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

Pediatric TB Cases by Site of Disease, 1993–2008

<table>
<thead>
<tr>
<th>Site of Disease</th>
<th>Age &lt; 1 (n=1,697)</th>
<th>Age 1-4 (n=8,816)</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>Total</td>
<td>24.8</td>
<td>28.1</td>
<td>30.1</td>
<td>33.1</td>
</tr>
</tbody>
</table>

*Any extrapulmonary involvement includes extrapulmonary only and both

Percent of Pediatric TB Cases with Extrapulmonary Involvement* by Age Group & Sites of Disease, 1993–2008 (N=17,502)

- Pulmonary 70.5%
- Extrapulmonary 29.1%
- 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)
### Symptoms in Children with Tuberculosis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency (%)</th>
<th>Study A*</th>
<th>Study B^</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(47 infants &lt; 1 Yr old)</td>
<td>(156 children &lt; 20 yrs)</td>
<td></td>
</tr>
<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>


### 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 appear 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
- Pediatric LTBI and TB disease treatment mirrors that in adults - a weekly 12-dose regimen of INH and rifapentine has been approved recently by the CDC for LTBI