Tuberculosis in Children and Adolescents 2012 - Part I

George D. McSherry, MD
Division of Infectious Diseases
Penn State Hershey Children’s Hospital
and
Pediatric Section
Northeastern Regional Training and Medical Consultation Center
NJMS Global Tuberculosis Institute

TB Intensive Workshop
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Classification System for TB

<table>
<thead>
<tr>
<th>Class</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No TB exposure</td>
<td>No history of exposure or negative reaction to tuberculin skin test</td>
</tr>
<tr>
<td>1</td>
<td>TB exposure</td>
<td>History of exposure or negative reaction to tuberculin skin test</td>
</tr>
<tr>
<td>2</td>
<td>TB infection</td>
<td>Positive reaction to tuberculin skin test or negative bacteriologic studies</td>
</tr>
<tr>
<td></td>
<td>No disease</td>
<td>No clinical, bacteriological, or radiographic evidence of active TB</td>
</tr>
<tr>
<td>3</td>
<td>TB, clinically active</td>
<td>M. tuberculosis cultured (if done) Clinical, bacteriological, or radiographic evidence of current disease</td>
</tr>
<tr>
<td>4</td>
<td>TB</td>
<td>History of episode(s) of TB or Abnormal but stable radiographic findings</td>
</tr>
<tr>
<td></td>
<td>Not clinically active</td>
<td>Positive reaction to the tuberculin skin test Negative bacteriologic studies (if done) and No clinical or radiographic evidence of current disease</td>
</tr>
<tr>
<td>5</td>
<td>TB suspected</td>
<td>Diagnosis pending</td>
</tr>
</tbody>
</table>

Epidemiology

- Tuberculosis remains the leading infectious disease in the world
  - Approximately 1/3 of the world’s population (>1.9 billion people) is infected with *M. tuberculosis*
  - In the 1990s:
    - 90 million new cases
    - 30 million deaths
  - Among children <15 years of age:
    - Approximately 13 million cases
    - 5 million deaths

Epidemiology: United States

- Case rates for all ages are higher in urban, low-income areas, and in nonwhite racial and ethnic minorities

- Specific groups with high LTBI and TB disease rates:
  - Immigrants and refugees from high-prevalence regions (Asia, Africa, Latin America, countries of the former Soviet Union)
  - International adoptees
  - Travelers to countries with high-prevalence
  - Homeless people
  - Residents of correctional facilities

Transmission of *M. tuberculosis* to Children

- Children are usually infected by an adult or adolescent in the immediate household

- Casual extra-familial contact is less often the source of infection

- Children rarely infect other children or adults:
  - Tubercle bacilli are relatively sparse in secretions
  - Children with pulmonary TB rarely cough
  - Cough, when present, lacks the force needed to aerosolize bacilli
Significance of Tuberculosis in Children

- Public Health: Diagnosis of LTBI or tuberculosis disease in a child is considered a "SENTINEL PUBLIC HEALTH EVENT" usually representing recent transmission of TB within a community
- Personal Health: High rates of morbidity and mortality

Red Book 2009
American Academy of Pediatrics

Risk of Progression to TB Disease

- Immunocompetent adults: 5-10% lifetime risk of developing disease after infection
- Adults with TB infection and HIV infection: 5-10% annual risk of developing disease
- Children and the risk of TB disease:

Risk of Tuberculosis Disease by Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk of disease following primary infection</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>&lt;1 years</td>
<td>10-20%</td>
<td>30-40%</td>
</tr>
<tr>
<td>1-2 years</td>
<td>2-5%</td>
<td>10-20%</td>
</tr>
<tr>
<td>2-5 years</td>
<td>0.5%</td>
<td>5%</td>
</tr>
<tr>
<td>5-10 years</td>
<td>&lt;0.5%</td>
<td>2%</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>&lt;0.5%</td>
<td>10-20%</td>
</tr>
</tbody>
</table>

Adapted from reference 10.

Table 1: Risk of pulmonary and extrapulmonary disease in children following infection with Mycobacterium tuberculosis

Increased Risk of Progression of LTBI to Tuberculosis Disease

- **Age groups:**
  - Infants and young children
  - Post pubertal adolescents

- **Recent infection:**
  - Highest risk in first 6 months after infection
  - Remains high for 2 years

- **Recent immigration**

- **Immunodeficiency:**
  - HIV infection, Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, malnutrition
  - Immunosuppressive drugs:
    - Prolonged or high-dose corticosteroid therapy
    - Chemotherapy
    - Tumor necrosis factor (TNF-alpha) antagonists used to treat arthritis, Crohn’s disease: Infliximab, etanercept, adalimumab, golimumab

Control of Tuberculosis in the United States

- **Case finding and treatment**

- **Contact investigations**
  - The most reliable TB control program is based upon aggressive and expedient contact investigations, rather than routine screening of large populations
  - Can be complex and may require lots of detective work

- **Targeted testing with tuberculin skin test or IGRA**
  - Red Book 2009

Prevention of TB in Children: Potential Missed Opportunities

- Failure to find and appropriately manage adult source cases (Case finding)
- Delay in reporting the initial diagnosis of TB
- Contact investigation interview failure
- Delay in evaluation of exposed children
- Failure to completely evaluate exposed children
- Failure to prescribe INH “window prophylaxis”
- Failure to maintain a contact under surveillance
- LTBI diagnosed; treatment not prescribed
- Failure to complete treatment for LTBI

Tuberculosis Exposure in Children

- **History, PE, TST/IGRA, CXR are done**
  - CXR is done regardless of TST/IGRA result

- **IF the child is:**
  - Asymptomatic and physical examination is normal
  - TST is negative (<5 mm)
  - Chest X-ray is normal

- **AND IF <4 years of age START:** Isoniazid (INH) 10 mg/kg (max., 300 mg) PO once daily
Tuberculosis Exposure in Children

- Why is INH given as “Window Prophylaxis” even if there is no evidence of TB infection or disease at the initial visit?
  - Child may already be infected
  - Infection more likely to progress to disease
  - Infants and younger children are more likely to develop disseminated disease or meningitis

- TST repeated 8-10 weeks after contact broken with infectious adult:
  - If TST (-), discontinue INH
  - If TST (+), re-evaluate child and treat accordingly

Contact Investigations and TB-Exposed Children:

Case#1: The Need for Speed or Nightmare in Daycare

Opportunities we almost missed but didn’t....

George McSherry, MD
Mark Wolman, MA, MPH
Suzanne Tortoriello, RN, NP, C
Jacqueline Messineo, RN, C,
Patti Restaino
Judy Thomas, RN
June Hare
Rebecca Stephens
Sosamma Methratta, MD
INDEX CASE (Patient)

• 6/14 (Monday): 39 year-old female was admitted to a suburban New Jersey hospital with history of fever, decreased appetite, 23 lb wt loss, cough for 3 months, night sweats

• Chest x-ray:

Index Patient

• 6/17 (Thursday): Sputum was obtained for AFB studies; AFB smear reported as (4+); AFB subsequently confirmed as *M. tuberculosis*

• 6/19 (Saturday): Treatment with INH, RIF, PZA, & Emb started

• 6/21 (Monday): Presumptive case of pulmonary TB is verbally reported to local health department

• 6/21: LHD informed TB Control Program Manager of suspected case adding the following information
  – Index case was a volunteer at a daycare center*
  – Name, address and telephone of daycare center provided
  – Director of center is the sister of index case

• Red flag day: Red flag # 1

Background – 1

• 6/21: Telephone call from TB Control Program Manager to director of daycare center who volunteered information that her aunt (“I know who this is…”) is diagnosed with suspected tuberculosis
  – Director further volunteers that her aunt is a:
    • Secretarial volunteer 1-2 hrs/week
    • Works at desk doing paperwork, filing
    • Little or no contact with children in the daycare
  – Purpose to schedule a meeting to discuss potential exposure to children and staff
    • Conduct on-site exposure assessment of center
    • Provide TB education to the director
    • Identify high-priority contacts during infectious period established at 3/17-6/14

Background - 6

• Near the conclusion of telephone call the following exchange occurred:
  – Director reveals that she has a 6 mo. old infant, exposed to index pt. socially on weekends (10 hrs/wk) but who “does not attend daycare”
    – Director: So, should my daughter be tested?
    – TB Control: Tell me about your daughter and how much exposure she had to your aunt.
    – Director: Not too much. She doesn’t attend the daycare but we do spend some time socially (maybe 5 hours) together on the weekends going to the mall
Background - 7

- TB Control: How old is your daughter?
- Director: 6 months
- TB Control: I’ll make arrangements for your daughter to be tested tomorrow morning
- TB Control: By the way, how is your daughter feeling?
- Director: Well…. she was diagnosed with bronchitis* a few weeks ago and is still coughing
  - Red flag # 2

Contact Investigation - 1

- 6/22: First of 4 TB interviews for contact investigation conducted by HCW in hospital
  - Infectious period confirmed at 3/17-6/14
  - Index case may have spent more time in daycare than originally described
  - Index case indicates not much contact with children at daycare
  - 9 high-priority contacts outside of work are identified
    - 2 household
    - 7 social
  - Despite director being aware of index patient’s identity, written consent obtained by patient to release her identity

Daycare Contact Investigation

- 6/23: On-site assessment of DCC conducted by TB controller:
  - High priority contacts: 35
    - 30 children attend: All ≤4 years of age
    - 5 staff members: Adults and adolescents
  - The Daycare is in a church basement and the index case’s desk is:
6/23: 6 month old infant (Director’s daughter)

- Admission PE: Somewhat lethargic
- LP: 10 wbc: nl protein, nl glucose;
- Gastric aspirates X3: (+) M. tuberculosis

HILAR ADENOPATHY

- Right upper and middle lobe infiltrate with faint miliary pattern
- TST: 20 mm

Contact Investigation - 5

- 6/22-6/25: Process begins in collecting names and locating information of identified contacts in all exposure settings including household, social and workplace
  - Notification process begins for testing
  - Education sessions provided to parents of daycare children
  - During these sessions it is learned that the 6 month old infant was at daycare center on regular basis

Contact Investigation - 6

- 6/23: Field visit to social contact residence by HCW identifies a second 6 mo. old infant not named on initial interview
  - 70 hours exposure per week during infectious period
  - Diagnosed with pneumonia* 3 weeks ago
  - Red flag # 3
  - HCW & TB Control Program Manager consult with Pediatric Nurse Practitioner at Lattimore Practice and infant is referred to ED, evaluated and admitted with diagnosis of suspected pulmonary TB
Contact Investigation - 7

- 6/29 - 6/30: TST administered on all 35 daycare contacts and chest x-ray taken on all 30 children from daycare
- 6 extra clinic sessions scheduled at clinic in addition to 3 evening clinics at local health department to accommodate the medical evaluations of the 30 children

2nd 6 month-old infant

TST: 17 mm
Gastric aspirates X3: (+) *M. tuberculosis*

3 year old

TST: 20 mm

Hilar and probably paratracheal adenopathy with infiltrate

3 year old

TST: 20 mm

RIGHT HLAR AND PARATRACHEAL ADENOPATHY (LOWER ARROW) WITH INFILTRATE (UPPER ARROW)
3 year old
TST: 16 mm
Questionable shadows left hilum on AP + lat films so CT ordered

4 year old
TST: 17 mm
Hilar adenopathy consistent w/ early TB disease

3 year old
TST: 19 mm
Hilar adenopathy consistent w/ early TB disease

4 year old
TST: 0.0 mm
Hilar adenopathy consistent w/ early TB disease
Contact Investigation, Initial Results: Infection and Disease at Daycare

<table>
<thead>
<tr>
<th></th>
<th>Children</th>
<th>Staff</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) TST</td>
<td>30 (≤4 years of age)</td>
<td>5</td>
</tr>
<tr>
<td>(+) TST w/ disease</td>
<td>11/30 (37%)</td>
<td>5/11 (45%)</td>
</tr>
<tr>
<td>(-) TST</td>
<td>19/30 (63%)</td>
<td>19/30 (63%)</td>
</tr>
<tr>
<td>(-) TST w/ disease</td>
<td>2/19 (11%)</td>
<td>2/19 (11%)</td>
</tr>
</tbody>
</table>

No disease in adults or adolescents

Contact Investigation: Totals After Initial Testing

<table>
<thead>
<tr>
<th>Investigation Totals</th>
<th>44</th>
<th>32 ≤4 yrs old</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) TST</td>
<td>19/44 (43%)</td>
<td>All ≤18 yrs old</td>
</tr>
<tr>
<td>(-) TST</td>
<td>25/44 (57%)</td>
<td></td>
</tr>
<tr>
<td>TB disease</td>
<td>9/44 (20%)</td>
<td>All ≤4 yrs old</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Children &lt;4 yrs old</th>
<th>32</th>
<th>7 with disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) TST</td>
<td>13/32 (40%)</td>
<td>2 with disease</td>
</tr>
<tr>
<td>(-) TST</td>
<td>19/32 (60%)</td>
<td></td>
</tr>
<tr>
<td>TB disease</td>
<td>9/32 (28%)</td>
<td></td>
</tr>
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</table>

Observations on Private Pediatrician Involvement in Contact Investigations

- 6 of 30 (20%) of the exposed children were initially evaluated in conjunction with their pediatricians:
  - TSTs read by pediatricians were reported in at least one case as negative, i.e.: Not in millimeters
  - TSTs 0.0 (zero) mm: (3)
    - H & PE, CXR done: None
  - TSTs 0.0 (zero) mm + CXR (-): (2)
    - H & PE done: None
  - INH prescribed for prophylaxis for 6 contacts ≤4 yrs of age: None
  - In each case TCs made to assure proper evaluation were followed by a referral to TB Center for the evaluation
Prevention of Tuberculosis in Children: Missed Opportunities

- Failure to find and appropriately manage adult source cases (Case finding)
- Delay in reporting the initial diagnosis of TB
- Contact investigation interview failure
- Delay in evaluation of exposed children
- Failure to completely evaluate exposed children
- Failure to prescribe prophylactic INH
- Failure to maintain a contact under surveillance
- LTBI diagnosed; treatment not prescribed
- Failure to complete treatment for LTBI (Adherence)

Contact Investigation: Lessons

- Large scale contact investigations require thoughtful planning
  - Don’t want to over test
  - Don’t want to under test
- Importance of on-site assessment
  - Testing recommended?
  - Magnitude of the problem
  - Answer questions of why some convert and not others
- Critical to provide follow-up TB interviews of index patient to allow for:
  - Clarification of previously collected contact information
  - Collection of additional information
  - Provision of additional TB education
  - Different Interviewers if no contacts identified, rapport is an issue

Contact Investigation: Lessons

- Despite the rapidity of the contact investigation 9 cases of TB disease occurred in young children
  - Children develop disease soon after infection so it is imperative to move quickly
- Pediatricians are generally not familiar with standard evaluations of children exposed to tuberculosis and use of INH in such situations
- Radiological expertise with young children is important:
  - In this CI, 7/30 CXRs either needed to be repeated or were interpreted incorrectly
- Education: Parents, students, teachers, media
Case #2. Three generations, two families and a pediatrician....

Or, Source cases, index cases, and contact investigations... you never know what you’ll get if you keep your eyes open... and keep asking questions....

Clinicians are asking

“Could this child have TB?

THE IMPORTANCE OF EPIDEMIOLOGY in childhood TB...

If we could only find an adult source case...
Potential Missed Opportunities in TB Control

- Initially, 5/18 children are diagnosed as TB-exposed
  - Two (Ages 6 & 28 months) identified in the contact investigation have 0.0 mm TSTs and normal CXRS at the health department
  - Mother (same family as above) insists to health department that she would like to see them by their private pediatrician
    - No PE done
    - No INH “window prophylaxis” given
Potential Missed Opportunities in TB Control

• Two children with LTBI from one family see their private pediatrician for evaluation and management after mother insists to health department that she would like them seen by the pediatrician:
  – Receive prescriptions for INH plus 8 refills
    • No follow-up appointments are given
    • Social history: Homeless, 5 children, mother with her own serious health problems, holding down a full-time job
  – Set-up for another missed opportunity? Strong probability
    • Will therapy for LTBI be completed?
    • Was it? Yes, why? DOT of infection (DOTI).
Case History: Final Numbers

- Eighteen children were exposed to a 26-year-old woman with bilateral cavitary pulmonary tuberculosis:
  - 15/18 (83%) children are infected
    - 9/15 (60%) develop TB disease
      - Two after initial negative TST (Missed opportunity)
    - 1 TB meningitis, 2 miliary
  - 6/15 (40%) have LTBI
    - 3/18 (17%) are TB-exposed but not infected
- Through 3 generations: All 2nd and 3rd generation cases preventable
  - TB-infected child of today may become the index pt. of tomorrow without treatment for LTBI

Case #3. The six year-old boy who was not a household contact but was....so says Dr. Kreiswirth....and a memory of LTBI treatment long ago....

The six year old boy....

- A 16 year old male was referred to oncology for evaluation of a lump in the neck
  - There was history of decreased appetite, 20 lb weight loss, and intermittent, nonproductive cough
  - A CXR was done:

The six year old boy....

- A 22-year-old aunt remembered being treated for LTBI about 10 yrs ago
  - An uncle who had a cough and may have had TB but was not sure of the diagnosis
- Using the name provided, the TB controller was able to find the uncle’s medical record
  - Was a highly infectious case 9 years earlier
  - Review of the contact investigation showed 5 household contacts including the niece and 4 work contacts
  - The 6-yr-old boy who spent several hours in the uncle’s apartment each day after school was not mentioned
The six year old boy...

- RFLP analysis was a match between the uncle and the 16 year-old (Dr. Kreiswirth)
- The contact investigation of the now 16 year-old (now a computer whiz) involved evaluation of his H.S. (1600 students) and targeted testing of 50 high priority classmates and teachers