Management of Pediatric Tuberculosis in New Jersey

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December 15, 2011

This presentation is in part adapted from Pediatric Tuberculosis by Ann Loeffler, MD: Francis J Curry National TB Center San Francisco, Ca

Why is there a general complacency about pediatric tuberculosis?

• Pediatric TB is uncommon in the US
  – In 2008, 786 Pediatric TB cases in US
• Young children with TB are usually not contagious
• Children with TB are difficult to diagnose...unlike adults who are easier to diagnose because they are more symptomatic

Curry Center, 2010
Reasons not to be complacent about pediatric TB

- Worldwide, approximately 500,000 die annually from TB
- Compared to the US, children in developing countries are disproportionately burdened with TB. Children represent up to 30% of TB cases globally, compared to 6% in the US
- Children with TB or LTBI must have been recently infected so they serve as sensitive indicators of contagious adolescents or adults with TB in the community
- Finding and treating TB infected children is a public health priority in the US

Curry Center, 2010

Pediatric TB Morbidity in New Jersey (2010)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>14</td>
</tr>
<tr>
<td>5-14</td>
<td>12</td>
</tr>
<tr>
<td>15-24</td>
<td>30</td>
</tr>
<tr>
<td>TOTAL</td>
<td>56</td>
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NJDHHS, 2001-2010
How are cases found?

In the United States:

- 26-80% of children with TB are identified during contact investigation
- 17-44% present because of symptoms
- 3 -25% of cases are identified by routine screening

In developing countries:

- No screening of asymptomatic children
- Children are identified only if they are symptomatic

Curry Center, 2010

Clinical Scenarios to Evaluate Children for TB

- Health Maintenance care for well children
  - Screen risk factors for TB at each well child visit
  - Ask 4-6 simple questions

- Children who are contacts to adults with potentially contagious TB
  - Rapid evaluation and intervention are required

- Children with signs and symptoms of TB or radiographic findings suggesting TB
  - High index of suspicion is required
Risk-Assessment Tools

- Risk of exposure to TB should be assessed at routine healthcare evaluations
  - USE Risk Assessment Questionnaire
- Only children with an increased risk of acquiring TB infection or disease should be tested for TB infection

Using the Risk Assessment Questionnaire

- At first contact with child and every 6 months until age 2 years
- After age 2 years, ask risk assessment questions every year if possible
- Anytime the risk of TB is determined, a TST should be performed

AAP Red Book, 2009
• Was your child born outside the United States?
  – Africa, Asia, Eastern Europe, Latin America

• Has your child traveled outside the United States?
  ≥1 week

• Has your child been exposed to anyone with TB disease? TB or LTBI, nature of contact

• Does your child have close contact with a person who has a positive TB skin test?

Pediatrics 2004;114:1175, supplement
Targeted TB Skin Testing
Practical clinical guidelines

• Don’t skin test someone who you won’t treat if his or her skin test is positive
• If a child doesn’t have TB exposure risks, don’t skin test them!
• “A decision to test is a decision to treat if skin test result is positive”

Positive TST Results:
Infants, Children and Adolescents

≥5 millimeters
• In close contact with known or suspected contagious cases of tuberculosis
• Suspected to have tuberculosis disease:
  ➢ CXR consistent with active or previously active tuberculosis
  ➢ Clinical evidence of tuberculosis
• Receiving immunosuppressive therapy
• With immunosuppressive conditions
• With HIV infection

≥10 millimeters
• At increased risk of disseminated disease:
  ➢ Young age: <4 years of age
  ➢ Other medical conditions: Hodgkin disease, lymphoma, diabetes, etc.
• Born or whose parents were born in high-prevalence regions of the world
• Frequently exposed to adults who are HIV-infected, homeless, users of illicit drugs, residents of nursing homes, incarcerated or institutionalized persons, migrant farm workers
• Travel and exposure to high-prevalence regions of the world

≥15 millimeters
• At > 4 years of age with no risk factors

AAP Red Book, 2009
**BCG and a positive TST**

- National guidelines recommend ignoring the history of receipt of BCG when placing or interpreting the TST.
- Likely that a positive TST is due to BCG:
  - If child received BCG as an older infant or child
  - Received multiple BCG’s
  - Received BCG in the recent past
- Treat as LTBI or TB according to breakpoints outlined in prior slide.

**BCG – Myth vs Fact**

<table>
<thead>
<tr>
<th>MYTH</th>
<th>FACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• BCG protects against getting TB infection</td>
<td>• BCG will not protect against becoming infected with TB</td>
</tr>
<tr>
<td>• BCG provides lifetime protection against developing active TB</td>
<td>• BCG protects against severe complications of TB disease in young children, but provides little or no protection in adolescents and adults</td>
</tr>
<tr>
<td>• BCG causes the tuberculin skin test (TST) to be positive for life</td>
<td>• BCG causes the TST to be positive for a few years; then wanes with time. Generally, no reaction is present after 5 years.</td>
</tr>
</tbody>
</table>

A positive TST in a BCG-vaccinated person is most likely due to BCG

- QFT-G, not a (+)TST can delineate if TB infection is due to MTB or due to BCG.

A positive TST in a person of any age from any country is most likely due to BCG, not TB infection

- A positive TST in an adolescent or adult from a TB high-burden country is likely due to TB infection, not BCG.

There is no need for a BCG-vaccinated person with a positive TST to be treated

- Persons with a positive TST from TB high-burden countries are at high risk of developing active TB and should be treated.
AAP Recommendations: Tuberculin Skin Testing

• Only the following children who should have an annual TST:
  – Children with HIV infection
  – Incarcerated adolescents

AAP Red Book, 2003

• Some experts recommend that these children should be tested every 2-3 years:
  – Children exposed to the following persons:
    • HIV-infected
    • Homeless
    • Residents of nursing homes
    • Institutionalized or incarcerated adolescents or adults
    • Users of illicit drugs
    • Migrant farm workers
  
  – Foster children with exposure to adults in the preceding high risk groups
Use of Interferon gamma release assays (IGRAs) in children

• Approved for use in adults in all circumstances where a TST would be used
  – QuantiFERON®-TB
  – QuantiFERON®-TB-Gold In-Tube
  – T-SPOT®.TBDue to lack of data in use in children, AAP (2009 Red Book) only recommends use in children ≥5 years
  – Positive results = infected with *M. tuberculosis*
  – Negative results = cannot universally exclude TB infection
  – Indeterminate results = does not exclude TB infection
  – May be useful in children with history of BCG vaccine

Are IGRAs recommended for children?

• IGRAs can be used in place of TST for immunocompetent children 5 years and older

• Negative IGRA cannot rule out TB infection or disease

• Can distinguish true TB infections from those caused by nontuberculous mycobacteria and BCG vaccination

• IGRAs may be useful in BCG vaccinated children and yield fewer false positive results than do TSTs

• IGRAS cannot be routinely recommended for children younger than 5 years of age because of a lack of published data
TB or LTBI?

- TB means the child has metabolically active *M. tuberculosis* bacteria in some part of the body
  - Children are usually completely or relatively asymptomatic at time of diagnosis

- LTBI (latent TB infection) means that the organism is dormant and physical exam and radiograph are normal

- To decide TB or LTBI, a focused history, physical exam, and a chest radiograph are necessary

Increased Risk of Progression from LTBI to TB Disease

- Age groups:
  - Infants and young children
  - Postpubertal adolescents

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

- Immunodeficiency:
  - HIV infection
  - Immunosuppressive drugs:
    - Prolonged or high-dose corticosteroid therapy
    - Chemotherapy
    - Tumor necrosis factor (TNF-alpha) antagonists used to treat arthritis: Infliximab, etanercept
  - Injection drug use
  - Medical conditions: Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, malnutrition
LTBI in Children

- Source case investigation must be initiated in children < 2 years of age
- 70% of source cases can be identified
- Children are treated for LTBI with INH:
  - daily dosing: 10-20 mg/kg (max 300 mg/day)
  - intermittent dosing: 20-30 mg/kg (max 900 mg) twice weekly (Monday/Thursday or Tuesday/Friday)
  - Vitamin B₆ not need in children on INH
- Alternate regimen for those exposed to INH-resistant organisms: 6 months rifampin
- Efficacy of INH approaches 100% in children if there is appropriate adherence
- All children with a positive TST but no evidence of TB disease should receive isoniazid because it prevents development of disease
- Only exceptions are possibility of INH resistance or a specific contraindication to the use of INH

Diagnosis of Tuberculosis

Even in developed countries, the “gold standard” for the diagnosis of tuberculosis in children is the triad of:

1. Positive TST
2. Abnormal CXR and/or physical exam
3. History of recent contact to an infectious adult case of TB
Evaluating a Child suspected to have TB

- History: must include information about the child’s health as well as information about where the child might have acquired TB i.e., a coughing household member

- Focused physical exam
  - Disseminated disease: fevers, growth parameters
  - Meningitis: alertness, meningeal signs
  - Scrofula: peripheral lymph nodes
  - Peritonitis: abdominal exam
  - Bone and joint disease: palpate back, ROM of extremities

Circumstances that increase TB suspicion

- Exposure to person with TB
- Several people in child’s environment with (+) TST
- CXR changes common in pediatric TB including intrathoracic lymphadenopathy and calcified granulomatas
- Paucity and chronicity of symptoms in comparison to CXR changes
Mycobacteriologic Diagnosis of Tuberculosis

• Adults: 70-90% have a sputum that is (+) for *M. tuberculosis*

• Children:
  – Tubercle bacilli are relatively few in number
  – Sputum generally cannot be obtained from children <10 yrs old
  – Gastric aspirates in children with PTB
    • 30-40% sensitive in children
    • 60-70% sensitive in infants
  – Bronchoalveolar lavage (BAL): Sensitivity may be less than gastric aspirates

Lung Findings

• Lung findings are relatively minimal and modest even with an impressively abnormal chest radiograph

• Of all age groups, infants and adolescents are most likely to have rales, decreased breath sounds, and increased work of breathing
Pediatric Treatment Regimens

- TB disease = 1st 2 months INH, RIF, PZA – followed by an additional 4 months of INH and RIF

- In some types of extrapulmonary TB or coinfection with HIV, the length of treatment is extended to 9-12 months

- No longer routine practice to supplement with Vitamin B6 (Pyridoxine)

- Who should receive Vitamin B6
  - Exclusively breastfed children
  - Malnourished children
  - Children with HIV disease
  - Children with symptoms of periphereral neuropathy

Vitamin B6 Dose

<table>
<thead>
<tr>
<th>Age of child</th>
<th>Pyridoxine dose</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>6.25 mg</td>
<td>¼ of 25 mg tab</td>
</tr>
<tr>
<td>Toddler</td>
<td>12.5 mg</td>
<td>½ of 25 mg tab</td>
</tr>
<tr>
<td>School Age</td>
<td>25 mg</td>
<td>1 25 mg tab</td>
</tr>
</tbody>
</table>
Transmission of M. tuberculosis to Children

- Children are usually infected by an adult or adolescent in the immediate household
- Casual extra-familial contact is much 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

Child Contact to a TB case

- Contact Investigation: evaluation of contacts to active contagious TB
- Young children: very high priority for evaluation
  - Increased risk of developing active TB
  - May develop active TB within weeks of being infected
- Children < 5 years need immediate evaluation for TB with CXR, history, focused physical exam
- Evaluation must be completed even before obtaining a (+) TST
Treatment of Contacts

• If TST is (+), begin a nine month course of INH for LTBI

• If TST is (-) start “window prophylaxis”
  – Repeat TST after 8-10 weeks of no further exposure to contagious case, i.e., contact is broken
  – If TST still (-), and child is immunocompetent, has no new TB symptoms, stop INH. No further evaluation needed
  – If contact is not broken, or another adult contagious source case is present, repeat evaluation and/or extend INH treatment
  – If TST becomes (+), extend INH to complete 9 months

Child contacts > 4 years

• Place a TST and obtain a symptom review

• If TST (-), and child is asymptomatic CXR is not imperative

• Individualize use of “window prophylaxis” based on:
  – Repeat TST 8–10 weeks after contact broken and re-evaluate

• If TST (+), obtain CXR and evaluate if TB or LTBI
Summary: Screening a well child

- No longer performed by routine or universal TB skin test (TST)
- Targeted Testing includes reviewing TB exposure and population risk factors. *TST only for children with new risk factors since last TST*
- If TST is (+)
  - Discern whether child has LTBI or TB

Referral

- Refer the following patients to the Pediatric TB Clinic:
  - All pediatric patients diagnosed to have Tuberculosis
  - All pediatric patients suspected to have Tuberculosis
  - Pediatric patients with doubtful LTBI diagnosis
Summary

- Pediatric TB is relatively uncommon in the US and is therefore sometimes missed
- Screen healthy children with risk factor questionnaires and reserve Tuberculin Skin testing for those children at high risk of exposure
- Evaluate those children exposed to active cases of TB promptly and thoroughly because they are at highest risk of infection and disease
- Not all children with (+) TST and radiographic abnormalities have TB and not all children with TB will have (+) TST

References


Curry International TB Center
http://www.nationaltbcenter.ucsf.edu/pediatric_tb/index.cfm

Pediatric Tuberculosis Collaborative Group
*Pediatrics* 2004; 114; 1175-1201.

New Jersey Department of Health & Human Services (NJDHSS) - Tuberculosis Control Program
TB Cases by Age Group 2001-2010
http://www.state.nj.us/health/tb/tbstats.shtml
Thank you for your attention
Don't take life so seriously!

DANCE!

KISS A LOT!