TUBERCULOSIS INFECTION IN CHILDREN AND ADOLESCENTS: TESTING AND TREATMENT

DAWN NOLT, MD MPH
PROFESSOR, PEDIATRIC INFECTIOUS DISEASES
OREGON HEALTH AND SCIENCE UNIVERSITY
Tuberculosis Infection in Children and Adolescents: Testing and Treatment

Dawn Nolt, MD, MPH, FAAP, Jeffrey R. Starke, MD, FAAP, COMMITTEE ON INFECTIOUS DISEASES
FACULTY DISCLOSURE

- I do not have any financial disclosures
OBJECTIVES OF PRESENTATION

- Epidemiology of pediatric tuberculosis (TB)
- Change in terminology: Tuberculosis infection (TBI)
- Available tests for TBI
- Regimens for treatment of TBI
Mycobacterium tuberculosis (Mtb) is still a problem in pediatrics
TUBERCULOSIS REMAINS AN IMPORTANT DISEASE

- Medical practitioners who care for children and adolescents have questions about tuberculosis (TB) testing and treatment
- High-risk patients who require testing
  - Close contacts of individuals with TB disease
  - Children <2 years and post-pubertal adolescents
  - Individuals with current or planned immunocompromising conditions

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk of Progression from TBI to Disease if Untreated, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 mo</td>
<td>40–50</td>
</tr>
<tr>
<td>1–2 y</td>
<td>25</td>
</tr>
<tr>
<td>School-aged</td>
<td>5–10</td>
</tr>
<tr>
<td>Adolescents</td>
<td>10–15</td>
</tr>
<tr>
<td>Adults</td>
<td>5–10</td>
</tr>
</tbody>
</table>

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®
Call it → Tuberculosis infection (TBI)
CHANGE IN TERMINOLOGY

- A variety of outcomes may occur for an individual who encounters Mtb
  - Rapid progression to symptomatic disease —or—
  - Immune control of the bacilli

- Under immune control, the bacilli are still viable and persistent

- Removal of the term “latent” will
  - Better represents the pathogenesis of tuberculosis —and—
  - Reduce confusion when discussing treatment goals with patients and families

- **Tuberculosis infection (TBI)** will describe asymptomatic individuals who are infected (have a positive test), and have a negative chest radiograph
Available Tests To Detect Mtb
NO “GOLD STANDARD” FOR TB TESTING

- Two available but imperfect methods for identification
  - Tuberculin skin test (TST)
  - Interferon-gamma release assay (IGRA)
- Both depend on cell-mediated immunity and provide immunologic evidence of host sensitization to Mtb
- Neither method can distinguish between TBI and TB disease

This photomicrograph reveals Mycobacterium tuberculosis bacteria using acid-fast Ziehl-Nelsen stain (magnification ×1,000). Courtesy of Centers for Disease Control and Prevention
TUBERCULIN SKIN TEST (TST)

- Intradermal injection of purified protein derivative (PPD), which contains dozens of TB antigens
- Advantages: Wealth of experience in using this test to aid diagnosis
- Disadvantages: Logistical issues are undesirable to medical staff, patients and families
  - False POSITIVE TST results may occur because PPD antigens in environmental NTM and BCG vaccine
  - Experienced personnel are needed for placement and interpretation
  - Results are not binary (need to consider presence of risk factors when interpreting significance of induration)
  - A return visit is needed
IGRA IS PREFERRED FOR CHILDREN \( \geq 2 \) YR

- Test of whole blood that detect interferon-gamma (IFN-\(\gamma\)) release from T lymphocytes
- IGRA is preferred over the TST for several reasons
  - Less false-positive results: TB antigens in the IGRA are NOT found in environmental NTM or BCG vaccine
  - There is one cut-off value for designating a positive vs negative result
  - Only 1 visit is needed (blood draw)

- Caveats
  - Expensive – BUT IGRA may be more cost-effective than TST because only 1 visit is needed for IGRA
  - Experience in children <2 years of age is not as robust as in older individuals

- Neither method has a clear advantage in sensitivity
TUBERCULOSIS

**BCG vaccinated?**

- **No**
  - Age ≥ 2 yrs
  - TST preferred
    - Negative result - Testing complete unless criteria A* are met, then IGRA
    - Positive result - Testing complete unless criteria B** are met, then IGRA

- **Yes**
  - Likely to return for TST reading?
    - **No**
      - TST acceptable, but so is an IGRA
        - Negative result - Testing complete unless criteria A* are met, then IGRA
        - Positive result - Testing complete unless criteria B** are met, then IGRA
    - **Yes**
      - IGRA preferred
        - Indeterminate
          - Repeat IGRA
            - Negative result - Testing complete
            - Positive result - Testing complete
Available treatments for TBI
PRINCIPLES OF TBI TREATMENT

- Reducing risk of TBI progressing to TB disease
  - Treatment reduces the risk of developing TB disease by 90% in children who adhere to therapy

- Risk of disease progression is highest in 3 patient groups
  - Close contacts of individuals with TB disease
  - Children < 2 years of age and post-pubertal adolescents
  - Individuals with current or planned immunocompromising conditions

- ADHERENCE to TBI treatment is inversely correlated to DURATION
  - The shorter the duration, the higher the completion rate of therapy
<table>
<thead>
<tr>
<th>Infection or Disease Category</th>
<th>Regimen</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M tuberculosis</em> infection</td>
<td>12 weeks of isoniazid plus rifapentine, once a week</td>
<td>Most experts consider isoniazid-rifapentine to be the preferred regimen for treatment of TBI for children 2 years and older.</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 mo of rifampin, once a day</td>
<td>Continuous daily therapy is required. Intermittent therapy even by DOT is not recommended.</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 mo of isoniazid plus rifampin, once a day</td>
<td>To be considered if above 2 regimens are not feasible.</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 or 9 mo of isoniazid, once a day</td>
<td>If daily therapy is not possible, DOT twice a week can be used; medication doses differ with daily and twice-weekly regimens.</td>
</tr>
</tbody>
</table>
ASPECTS OF TREATMENT

- Serial evaluations of individuals while on therapy
  - At least monthly, and in-person visits
- Gastro-intestinal upset while on medications
- Interruptions in TBI treatment
RESOURCES

Information for Pediatricians and Pediatric Health Care Providers


- Red Book 2021 Tuberculosis Chapter
  https://publications.aap.org/redbook/book/347/chapter/5757587/Tuberculosis

Information for Patients, Families, and Caregivers

- Healthy Children article Tuberculosis in Children - HealthyChildren.org
THANK YOU

- Members of AAP and medical providers of children and adolescents