Contact Investigation and Prevention in the USA

George D. McSherry, MD
Division of Infectious Disease
Penn State Children’s Hospital

Pediatric Section
TB Center of Excellence
Rutgers Global Tuberculosis Institute

Annual Meeting of the Child and Adolescent TB working group
The Hague, The Netherlands
October 24, 2018
Control of Tuberculosis in the United States

• Case finding and treatment
  – 2016: 9,272 cases: incidence 2.9 cases/100,000
  – 4.2% in children

• Contact investigations
  – Source case investigations

• Targeted testing of persons with risk
  – Diagnosis and treatment of LTBI is critical to control and elimination of TB in the U.S.
Objectives of the Contact Investigation

- Identify all high and low risk contacts
- Medically evaluate all appropriate contacts
- Identify contacts diagnosed with LTBI and provide appropriate treatment to completion of therapy thus *preventing future disease*
- Identify contacts diagnosed with TB disease and provide appropriate treatment to completion of therapy thus *preventing further transmission*
- Identify contacts at high risk of developing TB disease (e.g., children, immunocompromised) and provide appropriate treatment until infection and disease is ruled out
Control of TB in the United States

• Case finding + 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

High priority contact:
- Household
- Age <5 yrs
- Med risk condition
- Procedure
- Congregate, Time

Red Book 2009
Contact Investigation

- A 39 year-old female was admitted to a New Jersey hospital with fever, decreased appetite, 11 kg weight loss, cough X 1-3 months, night sweats
- Chest radiographs were done
- Sputa were 4+ AFB, later identified as pansensitive M. tbc
- Presumptive case of TB reported to local health department
  - Place of employment-Daycare Center
  - Health department nurse contacted TB controller for the county
Daycare Contact (DCC) Investigation

• 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
  – Daycare is in a church basement
  – Index patient was secretary with “little” contact with the children

• Household and social contacts
  – High priority contacts: 9; field staff felt index pt. did not reveal all contacts
  – 4 are children: 2 are ≤1 year of age with recent history of pneumonia
Church Basement-Daycare

- **PLAY AREA**
- **KITCHEN AREA**
- **COUNTER TOP**
- **SHELVES**
- **Box fan**

Dimensions:
- **CEILING HT: 6'5"**
- **NO WINDOWS**
- **45'**
- **17'**
- **20'**
- **16'**
## Contact Investigation Results: Totals After Initial Testing

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Under 4 yrs old</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daycare Center</strong></td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>(+) TST</td>
<td>14/35</td>
<td>(40%)</td>
</tr>
<tr>
<td>(-) TST</td>
<td>21/35</td>
<td>(60%)</td>
</tr>
<tr>
<td>TB disease</td>
<td>7/35</td>
<td>(20%)</td>
</tr>
<tr>
<td><strong>Household + Social</strong></td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>(+) TST</td>
<td>5/9</td>
<td>(56%)</td>
</tr>
<tr>
<td>(-) TST</td>
<td>4/9</td>
<td>(44%)</td>
</tr>
<tr>
<td>TB disease</td>
<td>2/9</td>
<td>(22%)</td>
</tr>
</tbody>
</table>
TB in Daycare
Contact vs. Source Case Investigation

**CONTACT INVESTIGATION**

- INDEX PATIENT
- TRANSMISSION
  - LTBI
  - TB DISEASE

**SOURCE CASE INVESTIGATION**

- TRANSMISSION
  - LTBI
  - TB DISEASE
- INDEX CASE
## US Contact Investigations Outcomes - Sputum AFB Smear (+)

<table>
<thead>
<tr>
<th>Year</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td># Cases</td>
<td>14061</td>
<td>13727</td>
<td>13282</td>
<td>12895</td>
<td>11520</td>
<td>11163</td>
<td>10517</td>
<td>9951</td>
<td>9550</td>
<td>9406</td>
</tr>
<tr>
<td>Sputum sm (+)</td>
<td>4828</td>
<td>4649</td>
<td>4776</td>
<td>4084</td>
<td>3668</td>
<td>3368</td>
<td>3417</td>
<td>3687</td>
<td>3648</td>
<td>3609</td>
</tr>
<tr>
<td># Contacts ID</td>
<td>73281</td>
<td>75410</td>
<td>76298</td>
<td>69542</td>
<td>66628</td>
<td>63068</td>
<td>72050</td>
<td>73677</td>
<td>69063</td>
<td>64148</td>
</tr>
</tbody>
</table>

### Evaluation Indices

<table>
<thead>
<tr>
<th>Contact index</th>
<th>15.2</th>
<th>16.2</th>
<th>15.5</th>
<th>16.7</th>
<th>18.2</th>
<th>18.7</th>
<th>21.1</th>
<th>20.0</th>
<th>18.9</th>
<th>17.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Objective</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No contacts ID</td>
<td>8%</td>
<td>8%</td>
<td>7%</td>
<td>7%</td>
<td>6%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Evaluated</td>
<td>58624</td>
<td>60010</td>
<td>62630</td>
<td>57306</td>
<td>52259</td>
<td>53019</td>
<td>58785</td>
<td>60189</td>
<td>56464</td>
<td>52029</td>
</tr>
<tr>
<td>Not evaluated</td>
<td>14656</td>
<td>15400</td>
<td>13668</td>
<td>12236</td>
<td>14369</td>
<td>10049</td>
<td>13265</td>
<td>13488</td>
<td>12599</td>
<td>12119</td>
</tr>
<tr>
<td>TB disease</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Infected</td>
<td>24%</td>
<td>23%</td>
<td>23%</td>
<td>22%</td>
<td>20%</td>
<td>19%</td>
<td>19%</td>
<td>19%</td>
<td>19%</td>
<td>17%</td>
</tr>
<tr>
<td>LTBI treatment initiated</td>
<td>69%</td>
<td>72%</td>
<td>71%</td>
<td>74%</td>
<td>67%</td>
<td>74%</td>
<td>70%</td>
<td>68%</td>
<td>71%</td>
<td>72%</td>
</tr>
<tr>
<td>LTBI treatment completed</td>
<td>63%</td>
<td>66%</td>
<td>68%</td>
<td>64%</td>
<td>67%</td>
<td>67%</td>
<td>66%</td>
<td>66%</td>
<td>71%</td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>91%</td>
<td></td>
</tr>
</tbody>
</table>

**National Objective**
Targeted Testing for Tuberculosis in Children and Adolescents

• Children for whom immediate TST or IGRA is indicated:
  – Contacts of people with confirmed or suspected contagious TB (contact investigation)
  – Children with radiographic or clinical findings suggesting tuberculosis disease
  – Children immigrating from high rates of infections (Asia, Middle East, Africa, Latin America, counties of the former Soviet Union)
  – Children with history of significant travel to countries with endemic infection who have substantial contact with the resident population

• Children who should have annual TST or IGRA:
  – Children with HIV infection

• Children at increased risk of progression of TBI to TB disease
  – HIV infection, Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, malnutrition, prolonged or high-dose corticosteroid therapy, chemotherapy, tumor necrosis factor (TNF-alpha) antagonists
Changes in TB Diagnosis Tools in Children: IGRAs and the 2018 “RED BOOK”

• IGRAs recommended in immunocompetent children $\geq 2$ years of age [previously $\geq 5$ years of age] in all situations where a TST would be used
  – Particularly useful for children who have received BCG vaccination
  – Use with caution in immunocompromised children

• TST was acceptable for all age groups and remains the preferred test for those <2 years of age

• In evaluating children for TB disease neither IGRAs nor the TST are perfect; always need clinical judgement

Red Book 2018
Treatment of Tuberculosis Infection in Children: 2018 Red Book and CDC

- Isoniazid + rifapentine (3HP)*
- Rifampin (4R)
- Isoniazid (9H)

*Red Book does not state a preference but says that some experts think 3HP is the preferred regimen

Borisov A, et al, MMWR 2018
LTBI treatment: 3HP for children

- As effective as 9H, shorter course, higher completion rates, safe, DOT or SAT, greater pill burden

- Children >12 years of age: Recommended as equal alternative to 9 months of INH

- Children 2-11 years of age: Recommended as equal alternative to 9 months of INH

- Children <2 years of age:
  - INH-RPT: Not recommended: Lack of safety and pharmacokinetic data in this age group

Dosing: 3HP

• INH (100 and 300 mg tabs):
  – Children age 2-11 years: 25 mg/kg/dose [900 mg]
  – Children older than 12 years of age: 15 mg/kg/dose [900 mg]

• Rifapentine (150 mg tabs):

<table>
<thead>
<tr>
<th>Weight (kgs)</th>
<th>Dose (mg)</th>
<th>Maximum (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>14.1-25</td>
<td>450</td>
<td></td>
</tr>
<tr>
<td>25.1-32</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>32.1-49.9</td>
<td>750</td>
<td></td>
</tr>
<tr>
<td>&gt;50</td>
<td>900</td>
<td>900</td>
</tr>
</tbody>
</table>
Treatment of Latent Tuberculosis Infection

- Rifampin for 15-20 mg/kg/day (max. 600 mg) po daily for 4 months (prior recommended dose 10-15 mg/kg)
  - Acceptable regimen for LTBI treatment
  - As effective as 9H, shorter course, better adherence, higher dose safe
  - INH not tolerated; index patient isolate INH-resistant

- Cruz & Starke, (IJTLD 2014): Rifampin 10-15 mg/kg/day (max. 600 mg) po daily for 4 months: Safe, completion rates similar to 9H by DOPT

- Gaensbauer (PIDJ 2018): No treatment failures: 395 children; well-tolerated; high completion rates

- Diallo (NEJM 2018): Rifampin 10-20 mg/kg/day for 4 months: Effective and safe as 9H
Treatment of Latent Tuberculosis Infection

- INH 10-15 mg/kg (max., 300 mg) PO daily for 270 doses
  - Efficacy approaches 100%; prevents TB meningitis
  - Poor completion rates due to treatment length
- Alternative: Twice weekly directly observed (DOT) INH 20-40 mg/kg (max., 900 mg) PO for 72 doses
- Monitor index case isolate sensitivities
- Hepatotoxicity from INH is rare in children:
  - Monthly assessment for clinical evidence of hepatotoxicity should be made: malaise, loss of appetite or weight, nausea, vomiting, abdominal pain, jaundice
  - Routine monitoring of LFTs is not indicated, except:
    • Concurrent liver disease
    • Pregnancy or first 12 weeks postpartum
    • Concurrently on other hepatotoxic medications
    • Clinical evidence of heptatoxic effects
Summary of contact investigations and LTBI diagnosis and treatment in the U.S.:

- Contact investigations use the concentric circle model and target high priority/high risk contacts first.
- Programs need to improve the number of contacts evaluated, started on and completing LTBI treatment.
- Diagnosis and treatment of LTBI is critical to control and elimination of TB in the U.S.
- Short course treatment regimens (3HP and 4R) for LTBI are safe and effective in children and should lead to increased treatment completion rates which lead to:
  - A decrease in active disease among children following recent infection
  - A reduction of the reservoir of LTBI from which reactivation disease may develop in the future
Tuberculosis Exposure in Children <4 years of age and “Window Prophylaxis”

• 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) or IGRA negative
  – Chest X-ray is normal

• AND IF <4 years of age START: Isoniazid (INH) 10 mg/kg (max., 300 mg) PO once daily

• TST/IGRA repeated 8-10 weeks after contact broken with infectious adult:
  • If TST/IGRA (-), discontinue INH
  • If TST/IGRA (+), re-evaluate child and treat accordingly
Targeted TB Testing Risk-Assessment Questionnaire

• Has a family member or contact had TB disease?
• Has a family member had a positive TB test?
• Was your child born in a high-risk country (i.e. outside US, Canada, Australia, New Zealand, or Western European countries)
• Has your child traveled to a high-risk country and spent significant time with the resident population?

Red Book 2018
Percentage of Pediatric TB Cases by Age Group, 1993–2016

N=21,609

Age 1-4: 49%
Age 5-9: 22%
Age 10-14: 19%
Age <1: 10%