Update In Tuberculosis, Indiana – 2017
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Disclosures
- Medical Consultant, TB Control Program
  Indiana State Department of Health
- Clinical trials with Merck, Genzyme and Romark
- Have personally endured over 36 Tuberculin skin tests (all negative or perhaps misinterpreted?)
  Major thanks to Kelly White, ISDH TB Control Program Epidemiologist, for Indiana data updates!

Outline/Objectives
1) Learn the current Tuberculosis Incidence;
   - World
   - U.S.
   - Indiana
2) Review the definition of Latent Infection versus Active TB Disease
3) Contrast New TB Testing and Screening Guidelines
4) Compare current LTBI Treatment options
5) Review available County and State Support Systems

Pathogenesis of M.tb

- An estimated 10.4 million new TB disease cases globally
- 1.4 million deaths due to TB disease
  - Additional 0.4 million deaths from TB among HIV-positive people
  - The rate of decline remains low at 1.5% per year
  - Must accelerate to 4-5% annual decline by 2020 to reach first milestone of End TB Strategy
- Estimated 10-15 million persons in U.S. TB infected

Source: WHO Global Tuberculosis Report 2016
TB Epidemiology, worldwide

- Africa has the highest incidence rate (275 per 100,000 population, vs. ~ 3.0 U.S.)
  - Some regions of Africa have rates over 500!
- Largest number of cases from Asian Countries:
  - India, Indonesia, China, Nigeria, Pakistan and South Africa account for 60% of global cases in 2015
- Three countries (China, India, and Russian Federation) account for 45% of MDR-TB
- One-third of world population infected with TB

Factors Contributing to the Increase in TB Morbidity: 1985-1992
- Deterioration of the TB public health infrastructure
- HIV/AIDS epidemic
- Immigration from countries where TB is common
- Transmission of TB in congregate settings
  - homeless shelters, prisons, etc.

The Key to Elimination of TB

- Up to 15 million people in the U.S. have LTBI
- 5 – 10% of infected will develop TB disease
- Therefore 750,000 to 1,500,000 will develop TB disease unless they receive LTBI treatment
- Identify and treat those at highest risk for TB disease
- Primary care providers play a key role in the goal of TB elimination because of access to high-risk populations

Remember to check HIV status on EVERY new diagnosis of TB infection.
**Tuberculosis Cases by U.S./Foreign Birth**

- **Indiana, 2016**
  - U.S.-Born: 30.3%
  - Foreign-Born: 69.7%
  - N = 109

**Percentage of Foreign-Born Tuberculosis Cases by Country of Birth, Indiana, 2016**

- **Burma**: 27.6%
- **Mexico**: 39.5%
- **India**: 18.4%
- **Philippines**: 6.6%
- **Other**: 7.9%
  - N = 76

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**Number & Percentage of TB Cases by Risk Factor**

- **Indiana, 2016**
  - Resident of Correctional Facility: 1 (0.9%)
  - Homelessness: 0 (0.0%)
  - Resident of Long-Term Care Facility: 2 (1.8%)
  - Injecting Drug Use: 0 (0.0%)
  - Non-Injecting Drug Use: 7 (6.4%)
  - Excess Alcohol Use: 13 (11.9%)

**Race and Ethnicity-specific Incidence Rates**

- **White, not Hispanic or Latino**: 0.8
- **Black or African-American**: 2.8
- **Hispanic or Latino, all races**: 5.5
- **Asian**: 35.3 (~20x higher than state average)
- **Males**: 2.0
- **Female**: 1.3

  *Per 100,000 population*

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**Percentage of TB Cases by HIV Testing Status & Age Group**

- **Indiana, 2015**
  - 15 years or older: 25-44 years
  - Test Results Known: 90.6%
  - Testing Not Offered: 4.9%
  - Refused Testing: 4.4%
  - 15 years or younger: 25-44 years
  - Test Results Known: 98.0%
  - Testing Not Offered: 2.0%
  - Refused Testing: 0.0%

Thank you for all your hard work in improving our HIV screening rates!

**Tuberculosis Cases by Directly Observed Therapy Utilization**

- **Indiana, 2015**
  - N = 113
  - Total DOT: 90.3%
  - Partial DOT: 8.8%
  - Self-Administered: 0.9%

Kudos to everyone!

Over 90% DOT
Common Sites of TB Disease
• Lungs (75% of 2008 Indiana cases)
  • Extrapulmonary 18% (7% both)
  • Pleura
  • Central nervous system
  • Lymphatic system
  • Genitourinary systems
  • Bones and joints
  • Disseminated (miliary TB)

Treatment of TB Disease
• Consult your friendly TB consultant!!!
  • Infectious Disease, Pulmonary, County or State Health Dept
• Start with four active drugs
• Increased dosing frequency is better
  • 7 or 5 days a week dosing more effective
  • 3 times weekly is acceptable
  • 2 times weekly not routine any more

TB Infectiousness
• Patients with Active pulmonary TB are no longer considered infectious if they meet all of these criteria:
  • Are on adequate therapy
  • Have a significant clinical response
  • Have 3 consecutive negative sputum smears

TB Infection Control in the Home
• Patients can be sent home while infectious if
  • A clear follow-up plan has been made
  • Patient is on standard treatment and DOT
  • No very young (under 4 years) or immunocompromised persons in household
  • All in household previously exposed
  • Patient willing to refrain from travel outside the home except for health-care visits
Risk Factors for Progression from Latent to Active Tuberculosis

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk/Odds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent infection (&lt;1 year)</td>
<td>12.9</td>
</tr>
<tr>
<td>Fibrotic lesions (spontaneously healed)</td>
<td>2–20</td>
</tr>
<tr>
<td>HIV infection</td>
<td>100</td>
</tr>
<tr>
<td>Silicosis</td>
<td>30</td>
</tr>
<tr>
<td>Chronic renal failure/hemodialysis</td>
<td>10–25</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2–4</td>
</tr>
<tr>
<td>Intravenous drug use</td>
<td>10–30</td>
</tr>
<tr>
<td>Immunosuppressive treatment (prednisone)</td>
<td>10</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>2–5</td>
</tr>
<tr>
<td>Jejunoleal bypass</td>
<td>30–60</td>
</tr>
<tr>
<td>Post-transplantation (renal, cardiac)</td>
<td>20–70</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>2</td>
</tr>
</tbody>
</table>

Limitations of Tuberculin Skin Testing

- False positives:
  - BCG vaccination, wanes over time
  - Non-tuberculous mycobacteria, usually < 10 mm
- False negative:
  - Recent TB infection, window period < 6 weeks
  - Immuno-compromised: HIV, Immunosuppressed
  - Poor technique
- No discrimination between Active/Latent ds
- Sensitivity only 75%

BCG Vaccination and Tuberculin Skin Testing

- Bacillus Calmette Guérin – strain of *M. bovis*
- Infant vaccination in high TB endemic areas
- Cross-reactivity of surface proteins
- Immunity wanes over time
  - Under 10% + TST by adulthood
- TST > 10 mm suggests Latent TB infection

Interferon–Gamma Release Assays (IGRAs)

- Advantages of IGRAs:
  - Requires a single patient visit, ready in 24 hrs
  - Do not cause booster phenomenon
  - Not impacted by BCG / most NTB mycobacteria
- Limitations of IGRAs include:
  - Blood processing needed within 8-30 hrs
  - Interpretation of low positive range in low risk pts
  - No discrimination between Active/Latent ds
  - Specificity only 75%

Treatment of LTBI

- INH daily for 9 months
- 3 HP dosing gaining momentum
  - 12 weekly doses by DOT
- INH plus rifapentine
- Other rifampin based regimens coming
Dosage for a combination regimen of isoniazid and rifapentine in 12 once-weekly doses under direct observation for treating latent Mycobacterium tuberculosis infection. MMWR December 9, 2011

- MUST BE DONE WITHIN A DOT PROGRAM***
- Isoniazid
  - 15 mg/kg rounded up to the nearest 50 or 100
  - 900 mg maximum
- Rifapentine
  - 10.0–14.0 kg 300 mg
  - 14.1–25.0 kg 450 mg
  - 25.1–32.0 kg 600 mg
  - 32.1–49.9 kg 750 mg
  - ≥50.0 kg 900 mg maximum

Clever Ideas for 3 HP DOT Tracking

Summary of Key Points

- TB is still out there
- TB needs to be in our differential diagnoses in high risk patient (those born outside the U.S.)
- Detection and treatment of LTBI is a key
- New LTBI treatment options available (3HP)
- LTBI screening tests are not perfect (yet)
- Lean on your friendly TB consultants and Public Health systems to treat your patients
- Treat active disease aggressively with DOT

Questions?

References/Resources

- Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005 MMWR Dec 30, 2005 / 54(RR17);1-141 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm
## References/Resources


- Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection. MMWR December 9, 2011 / 60(48);1650-1653
  [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_e)