Mayo Clinic Center for Tuberculosis

TB Transmission, Pathogenesis & Infection Control

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Disclosures

• Medical Consultant, TB Control Program Indiana State Department of Health

• Past clinical trials with Merck, Genzyme and Romark

• AMA Accelerating Change in Medical Education grant

• Personally endured over 36 Tuberculin skin tests
  (all negative - or perhaps misinterpreted)
Learning Objectives

• Describe the pathogenesis of *M. tuberculosis*
• Explain how drug-resistant TB disease develops
• Explain how *M. tb* is transmitted
• Describe the components of an effective infection control program
• Explain administrative, engineering controls, and respiratory protection
• Describe ways healthcare workers can protect themselves and others from infection with *M.tb*

• An estimated 10.4 million new TB disease cases
• 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
2 billion infected with TB worldwide
~ 1/3 of the world population!
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.
We must not let down our guard! – note flattening of decline in 2015
Remember to check HIV status on EVERY new diagnosis of TB infection.
TB Case Rates Among U.S.-Born versus Foreign-Born Persons, United States, *1993–2015†

- **U.S. overall**
- **U.S.-born**
- **Foreign-born**

<table>
<thead>
<tr>
<th>Year</th>
<th>U.S. overall</th>
<th>U.S.-born</th>
<th>Foreign-born</th>
</tr>
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<tbody>
<tr>
<td>1993</td>
<td>10.0</td>
<td>1.0</td>
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<td>2009</td>
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<tr>
<td>2013</td>
<td>0.0</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2015</td>
<td>0.0</td>
<td>2.1</td>
<td>0.9</td>
</tr>
</tbody>
</table>

* Includes the same data as previous slide, but rates are presented on a logarithmic scale.
† As of June 9, 2016.
2016
Cases = 109
Incidence Rate
= 1.7/100,000

Contrast rate to:
U.S. – 3.0
Global - 160

Tuberculosis Cases & Case Rates
Indiana, 2010 - 2016

UNITE TO END TB

Mayo Clinic Center for Tuberculosis
Tuberculosis Cases by U.S./Foreign Birth
Indiana, 2016

N = 109

69.7%
30.3%
State of Indiana Tuberculosis - 2016

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 rate than state average)
Males = 2.0
Female = 1.3

*Per 100,000 population
The Key to Elimination of TB

• Up to 15 million people in the U.S. have LTBI
• 5 – 10% of infected people will develop TB disease if not treated
• This equates to 750,000 to 1,500,000 people who will develop TB disease at some point, unless they receive adequate LTBI treatment
• Identifying and treating those at highest risk for TB disease will help move toward elimination
• Primary care providers play a key role in achieving the goal of TB elimination because of their access to high-risk populations

Describe the pathogenesis of *M. tuberculosis*

- Person-to person spread
- Aerosol via *droplet nuclei*
  - Generated by cough or other airway flow from infected lungs or larynx
  - Can persist in the air for several hours
- Transmission affected by
  - Infectiousness of patient
  - Environmental conditions – air exchange
  - Duration of exposure
- Most exposed persons *do not* become infected
TB Transmission/Pathogenesis

• Once inhaled, bacteria travel to lung alveoli
  • Easily ingested by alveolar macrophages but not killed (intracellular pathogen)
  • Establish localized infection

• 2–12 wks after infection, immune response limits activity; infection is detectable

• Some bacteria survive and remain dormant but viable for years within the inflammatory tissue/granuloma (latent TB infection, or LTBI)
Pathogenesis of *M. tb*

Adapted from Behar 2010

Nature Reviews | Microbiology

Taken from Max Planck Institute for Infection Biology /Volker Brinkmann: http://www.mpg.de/496841/cooperation-new-tb-vaccine-2004
TB Pathogenesis
Latent TB Infection

• Persons with LTBI are
  • Asymptomatic
  • Not infectious

• LTBI formerly diagnosed only with TST

• Now blood-based interferon–gamma release assay test can also be used to detect the immune response to *M. tb*
TB Pathogenesis
Active TB Disease

LTBI progresses to TB disease in

• Small number of persons soon after infection
• 5%–10% of persons with untreated LTBI sometime during lifetime
• About 10% of persons with HIV and untreated LTBI per year
~ 30% of heavily exposed persons will become infected

X – potential intervention points to prevent TB disease

Small, NEJM 2001
Explain how drug-resistant TB disease develops

• Fortunately, highly resistant strains of TB are not common in the Midwest

• Unfortunately, they typically cost the state $500,000 to 1 million dollars to treat
  • Intensive nature and duration of treatment
  • Monitoring for adverse effects of injectable medications
  • High cost of second and third-line agents
Drug-resistant TB

- Drug-resistant strains emerge when bacteria are exposed to low levels of an antimicrobial agent that fails to kill all of the bacteria it targets.
- Surviving bacteria are likely to become resistant to that class of drugs.
- Drug-resistant strains of tuberculosis can also be acquired at the time of infection.
Drug-resistant TB

- Strains of TB have also developed resistance to drugs such as fluoroquinolones and injectable medications such as amikacin, kanamycin and capreomycin.

- "Multidrug-resistant TB" (MDR-TB) refers to isolates that are resistant to at least isoniazid and rifampin and possibly additional agents.

- The clinical manifestations and radiographic features of drug-resistant tuberculosis (TB) are identical to those of drug-susceptible disease.
Risk factors for MDR-TB

• Previous treatment for active TB, particularly if therapy was self-administered
• Previous TB treatment failure
• Acquiring TB in a region with known high rates of drug resistance
• Contact with a patient with drug-resistant TB
• Failure to respond to empiric therapy
• Receipt of fluoroquinolone therapy for treatment of another infection
• Poor absorption of anti-TB medications
Describe the components of an effective infection control program

- **Administrative controls:**
  - reduce risk of exposure via an effective Infection Control program (detect/treat)

- **Environmental controls:**
  - prevent spread and reduce concentration of droplet nuclei around a TB-infected person

- **Respiratory protection controls:**
  - further reduce risk of exposure to those who delivery care to the TB-infected
Please DON'T SPIT

SPITTING SPREADS DISEASE

HELP BANISH TUBERCULOSIS
CHEST X-RAY IS FREE – AND COMPEL Atom.

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Approaches to Reduce TB

• Enhanced detection methods of TB infection
  • Recognition, Isolation, Treatment

• Effective treatment programs
  • Active disease
    • Reduce transmissibility
    • Reduce risk of drug-resistance
  • Latent TB Infection
    • Reduce risk for individual illness and community burden of disease
Impact of culture v. smear screening of immigrants to the U.S.

Classification:
Class A: Pos. smear and abnl CXR
Class B1: Neg. smears with abnl CXR
Class B2: Neg. smears with CXR suggesting latent disease

A cumulative decline of 2231 reported TB cases among foreign-born persons within 1 y after arrival during implementation.

A total of 2195 smear-negative/culture-positive TB cases diagnosed overseas among immigrants and refugees bound for the United States during implementation.

Cases of reported TB among foreign-born persons within 1 y after arrival in the United States.
Cases of smear-negative/culture-positive TB diagnosed overseas among immigrants and refugees bound for the United States.*
Baseline for calculating the decline: the mean of annual number of reported TB cases among foreign-born persons within 1 y after arrival during 2002–2006.
Tuberculosis Cases by Directly Observed Therapy Utilization
Indiana, 2015

- 90.3% Total DOT
- 8.8% Partial DOT
- 0.9% Self-Administered

N=113

Kudos to Indiana! Over 90% DOT
TB Infectiousness

• Patients with Active pulmonary TB are no longer considered infectious if they meet all of these criteria:
  • Are on adequate therapy
  • Have had a significant clinical response to therapy, and
  • Have had 3 consecutive negative sputum smear results
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 arranged
- 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
Explain administrative, engineering controls, and respiratory protection

• How does a facility determine:
  • Level of risk for TB
  • What steps are needed to prepare?
  • How are cases of TB detected?
  • How does a facility and staff react when a suspected case presents?
TB Risk Assessment
Settings Expecting to Encounter TB Patients

• Collaborate with health department to review community TB profile, obtain epidemiologic data for risk assessment

• Review number of TB patients encountered

• Determine
  • HCWs to be included in TB testing and in RP program
  • Instances of unrecognized TB
  • Number of isolation rooms needed
  • Types of environmental controls needed
TB Risk Assessment

Settings Not Expecting to Encounter TB Patients

• Collaborate with health department to review community TB profile; obtain epidemiologic data for risk assessment

• Determine
  • If any HCWs need to be included in TB screening program
  • If unrecognized TB occurred in last 5 years
  • Types of controls in place, types needed
TB Risk Classifications

- **Low risk** – Persons with TB disease not expected to be encountered; exposure unlikely
- **Medium risk** – HCWs will or might be exposed to persons with TB disease
- **Potential ongoing transmission** – Temporary classification for any settings with evidence of person-to-person transmission of *M. tuberculosis*
## TB Risk Classifications

<table>
<thead>
<tr>
<th>Inpatient Settings</th>
<th>Low</th>
<th>Medium</th>
<th>Potential Ongoing Transmission</th>
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</thead>
<tbody>
<tr>
<td>&lt;200 beds</td>
<td>&lt;3 TB patients/yr</td>
<td>≥3 TB patients/yr</td>
<td>Evidence of ongoing transmission, regardless of setting</td>
</tr>
<tr>
<td>≥200 beds</td>
<td>&lt;6 TB patients/yr</td>
<td>≥6 TB patients/yr</td>
<td></td>
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</tbody>
</table>

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# TB Risk Classifications

<table>
<thead>
<tr>
<th>Outpatient Settings</th>
<th>Low</th>
<th>Medium</th>
<th>Potential Ongoing Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB treatment facilities, medical offices, ambulatory care settings</td>
<td>&lt;3 TB patients/yr</td>
<td>≥3 TB patients/yr</td>
<td>Evidence of ongoing transmission, regardless of setting</td>
</tr>
</tbody>
</table>
### TB Testing Frequency for HCWs

<table>
<thead>
<tr>
<th>Risk classification</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Baseline on hire; further testing not needed unless exposure occurs</td>
</tr>
<tr>
<td>Medium</td>
<td>Baseline, then annually</td>
</tr>
<tr>
<td>Potential ongoing transmission</td>
<td>Baseline, then every 8-10 wks until evidence of transmission has ceased</td>
</tr>
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</table>
# TB Testing Frequency for HCWs Who Transfer

<table>
<thead>
<tr>
<th>Situation</th>
<th>Risk Classification Change</th>
<th><strong>Baseline</strong></th>
<th><strong>Routine testing</strong></th>
<th><strong>After exposure</strong></th>
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</thead>
<tbody>
<tr>
<td>Low→Low</td>
<td>Yes</td>
<td>Yes</td>
<td>Every 12 months</td>
<td>As needed in investigation</td>
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<tr>
<td>Low→Med</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low or Med</td>
<td>Low or Med → Potential Ongoing Transmission</td>
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<td>Low or Med</td>
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<td></td>
</tr>
</tbody>
</table>

- Baseline: Yes, Yes, Yes
- Routine testing: No, Every 12 months, As needed in investigation
- After exposure: Yes, and if TST negative, 8–10 wks after last potential exposure to *M. tuberculosis*
Evaluating Environmental Controls

- Determine if recommended environmental controls are in place
- Review environmental control maintenance
- Evaluate performance of installed system
- Assess number and type of aerosol-generating procedures performed
- Determine if the number of airborne infection isolation (AII, or negative-pressure) rooms is adequate for the setting based on guidelines and the risk assessment
Suggested Components of Initial TB Training and Education for HCWs

- Clinical information
- Epidemiology of TB: local, U.S., global
- Recommended Infection Control practices
- TB and conditions of compromised immunity
- Role of public health in TB control
  - Communication
  - Hand-offs of care
Describe ways healthcare workers can protect themselves and others from infection with *Mycobacterium tuberculosis*
Respiratory Protection

General

• Third level in the IC hierarchy (Administrative, Environmental, Respiratory Protection)

• Should be used by persons
  • Entering rooms of suspected/confirmed TB patients
  • Around cough- or aerosol-producing procedures
  • In settings where administrative and environmental controls will not prevent the inhalation of infectious droplet nuclei
  • Some labs settings
Respiratory Protection Performance Criteria

- The following can be used for protection against *M. tuberculosis*
  - Nonpowered particulate filter respirators certified by CDC/NIOSH: including disposable respirators, or powered air-purifying respirators (PAPR) with high-efficiency filters
  - Respirators should fit different face sizes and features of HCWs
Respiratory Protection
Performance Criteria

• Respirators must be CDC/NIOSH approved

• Types of Respiratory Protection
  • Nonpowered air-purifying respirators
  • Powered air-purifying respirators (PAPRs)
  • Supplied-air respirators
Implementing a Respiratory Protection Program

- Assign responsibility
- Train HCWs annually
- Conduct fit testing of HCWs
  - During initial RP program training
  - Periodically thereafter
- Inspect and maintain respirators
- Evaluate program periodically
Cough- and Aerosol-Producing Procedures Requiring Use of RP

• Cough-producing procedures
  • Endotracheal intubation, suctioning, diagnostic sputum induction, aerosol treatments, bronchoscopy, laryngoscopy
  • Gastric aspiration and nasogastric intubation can induce cough in some patients

• Aerosol-producing procedures:
  • Irrigating TB abscesses, homogenizing or lyophilizing tissue, performing autopsies
Consult your State, regional and CDC resources!

http://www.in.gov/isdh/19662.htm
http://centerfortuberculosis.mayo.edu/
Questions
References
