Disclosure / Disclaimer

- No financial conflicts of interest
- No mention of off-label use of FDA-approved medications
OBJECTIVES:
• Describe the components of an effective infection control program
• Explain administrative, engineering controls, and respiratory protection
• Explain how drug-resistant TB disease develops
Case 1. Elderly patient with chronic cough and weight loss

HOPI

- 74 year-old, African American female
- Seen at Emergency Room with complaints of shortness of breath and progressive weakness
- Increasing shortness of breath over the last 4 days
- Associated with fevers, chills, cough, with purulent sputum
- Family noted history of cough and weight loss over last several months
CXR

Admission

8 months prior to admission
CT Scan: Extensive air-space disease left apical, post cavitary
Hospital Course

- Admitted to floor – Community Acquired Pneumonia
- Treated: ampicillin/sulbactam/azithromycin
- Respiratory failure → Intubated 24 hours later
- Blood and routine sputum cultures negative.
- 5/5 respiratory specimens “Heavy AFB Positive”

• Family History
  – Patient’s mother died productive cough and weight loss
Infectiousness

**Transmission** = conveyance of disease from one person to another (an event)

**Infectiousness** = the characteristic of the disease that concerns the ease with which it is transmitted (a capacity)
Case 1: Transmission Questions

- Is she infectious?
- Who has she infected?
- Where and how was she infected?
TB is an Airborne Contagion

Work / School

Household / Residential

Leisure / Recreation
Transmission of TB

- Transmission is **airborne** from patients with **active** pulmonary TB
- **Vehicle:** droplet nucleus (coughing, talking, sneezing); size (1-5 μm)
- **Quantity** of organisms; high with cavitary disease
- **Environment:** spread is enhanced by crowded, poorly ventilated conditions
- Bottom line: duration of exposure and concentration of organisms in the air
• Update in 2005 and replaced the 1994 *Mycobacterium tuberculosis* infection control (IC) guidelines

• Purpose: Promote vigilance and expertise needed to avert another TB resurgence
Guideline includes:

- **Broadens the scope of health-care settings**
  - Further reduce threat to health-care workers (HCWs)
  - Expand guidelines to nontraditional settings

- **Redefines TB risk assessment**
  - Simplify procedures for assessing risk

- **Changes TB testing frequency for HCWs**

- **Defines “airborne infection isolation” (AII)**

- **Summarizes respiratory fit testing**

- **Expands information on engineering controls**
Fundamentals of Infection Control

- **Administrative controls**: reduce risk of exposure via effective Infection Control program
- **Environmental controls**: prevent spread and reduce concentration of droplet nuclei
- **Respiratory protection**: further reduce risk of exposure
- **Hierarchy of Infection Control**
Really important levels of control

Administrative
Without, TB control fails

Environmental
Personal respiratory protection
NOT the 1st level of control, training is critical
What is the most important risk for transmission of *Mycobacterium tuberculosis* in health-care settings?

*Unrecognized contagious TB patients*
Think TB!

Positive Skin Test
Weight Loss
Nausea
Chills
Malaise
Fever
Night Sweats
Fatigue
Difficult Breathing
Cough
Shortness of Breath
Abnormal X-Ray
Significant Skin Test
Failure to Thrive
Anorexia
Chest Pains
Loss of Appetite
Exposure to Tuberculosis
Coughing up blood

Recognition, prevent, report and respond to tuberculosis. Early diagnosis and treatment reduce spread. Contact your Health Department or physician for more information.
Case 2: Possible TB in the Hospital

• 32 y/o male from China seen for “possible TB”
• Placed in airborne infection isolation isolation room
• TB evaluation
  • Mild dry cough x 3 weeks
  • TST placed, at 48 hours = 0 mm
  • CXR done same day
Criteria for Initiating Airborne Infection Isolation(AII) Precautions

- Patient has signs or symptoms of infectious TB disease
  
or
- Whenever patient has documented culture-positive pulmonary TB disease and is still infectious

AII: Airborne Infection Isolation
Case 2

- Two negative AFB sputum smears
- The patient improved within 48 hours of starting levofloxacin for CAP...
- Patient released from isolation

- **After release, a specimen grew** *M. tuberculosis*

CAP: Community Acquired Pneumonia
*M.tb*: *Mycobacterium tuberculosis*
Consensus statement on the use of Cepheid Xpert MTB/RIF® assay in making decisions to discontinue airborne infection isolation in healthcare settings

April 2016

http://www.tbcontrollers.org/resources/airborne-infection-isolation/#.WD7mTE0VCpo
**STEP 1.**
Collect sputum* for AFB smear microscopy, AFB culture, and Xpert

- **Positive Xpert result:**
  - *M. tb* complex detected
  - TB likely
  - Stop Xpert testing and continue A.I.I.

- **Negative Xpert result:**
  - *M. tb* complex not detected
  - Infectious TB not excluded
  - Continue A.I.I.

- **Invalid Xpert result**

**STEP 2.**
Collect second sputum specimen at least 8 hours after first specimen for AFB smear microscopy, AFB culture, and Xpert

- **Positive Xpert result:**
  - *M. tb* complex detected
  - TB likely
  - Stop Xpert testing and continue A.I.I.

- **Negative Xpert result:**
  - *M. tb* complex not detected
  - Infectious TB not likely
  - Make the decision to discontinue A.I.I. in conjunction with clinical data****

- **Invalid Xpert result**
  - Continue A.I.I. and use AFB smear results with Xpert result and clinical judgment to make decision to discontinue A.I.I.

---

*First morning specimen preferred to maximize diagnostic yield of AFB sputum smear, culture, and Xpert.
**Most laboratories/protocols will automatically retake leftover sample if an initial invalid (failed) result is obtained; in such cases, a reported invalid result reflects repeat testing of a single specimen.
***If this result is negative following an initial invalid result in Step 1 and infectious TB still is clinically suspected, a repeat test (repeat Step 2) using a new specimen, if available, is recommended in order to improve sensitivity. Alternatively, the clinician may use the single negative Xpert result from Step 2 with smear results and clinical information to make the decision to discontinue or maintain A.I.I.
****Note: This process does not rule out tuberculosis with 100% certainty. Refer to Appendix IIB Application of AFB Sputum Microscopy to Negative Xpert Results to assist in diagnostic evaluation.
NTM: nontuberculous mycobacteria
TST, smears and contagiousness

• 20% of patients with TB who have no immunosuppression will have a negative TST
• ~50% of patients with non-cavitary TB are sputum smear negative
• 5-10% of patients with cavitary TB are smear negative
• TB with positive smears is more contagious than is smear negative TB, but…BOTH are contagious

TST: tuberculin skin test
Clinical Pearl

• *M. tuberculosis* is a laboratory diagnosis

• TB treatment is a clinical decision
Case 3 – Active TB or LTBI?

**HOPI**

- 28 year old Chinese female, 32 week pregnant
- Presented to Emergency Room with hemoptysis
- C/O cough X 2 days, associated with mild shortness of breath
- No fever, chills, night sweat, appetite loss, fatigue, or weight loss
- Denies any history contact with known active tuberculosis
- History BCG vaccine as a child in China
- History of positive TST, no latent TB infection therapy
• CXR:
  • Mild asymmetric patchy opacity in the left upper lobe

CT scan
• NO pulmonary embolus
• Extensive diffuse nodular air-space disease with peripheral distribution
Hospital course

- Admitted for Community Acquired Pneumonia and
- “Rule out TB” - in Negative Air Isolation
- Azithromycin and ceftriaxone
• PPD 17mm
• Interferon gamma release assay (QuantiFERON-TB Gold®)
  • Positive

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Smear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum day 1</td>
<td>Negative</td>
</tr>
<tr>
<td>Sputum day 2</td>
<td>Negative</td>
</tr>
<tr>
<td>Sputum day 3</td>
<td>Negative</td>
</tr>
<tr>
<td>BAL day 4</td>
<td>Negative</td>
</tr>
</tbody>
</table>

• Discharge home on INH for Latent TB Treatment
• Follow up at Ben Franklin TB Clinic
• Nucleic acid amplification test:
  • Positive

<table>
<thead>
<tr>
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<th>Smear</th>
<th>Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum day 1</td>
<td>Negative</td>
<td>M. tb</td>
</tr>
<tr>
<td>Sputum day 2</td>
<td>Negative</td>
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</tr>
<tr>
<td>Sputum day 3</td>
<td>Negative</td>
<td>M. tb</td>
</tr>
<tr>
<td>BAL day 4</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Sputum day 9*</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

• Drug susceptibility:  
  Resistant to Rifampin, Isoniazid, and Streptomycin
What are the risk factors for drug resistant TB?

How does drug resistant TB develop?
Transmission of Drug-Resistant TB

- Transmitted same way as drug-susceptible TB

- Drug resistance is divided into two types:
  1. **Primary resistance** - initially infected with resistant organisms
  2. **Secondary resistance** - develops during TB therapy
     a) Non-adherence to therapy
     b) Inappropriate therapy
     c) Decrease drug concentration – malabsorption, rapid metabolizer

Slide courtesy of Dr. Mase
Rates of Spontaneous Resistance in *M. tuberculosis*

- Isoniazid: 1 in $10^6$
- Rifampin: 1 in $10^8$
- Ethambutol: 1 in $10^6$
- Streptomycin: 1 in $10^5$
- INH & RIF: 1 in $10^{14}$

Number of organisms in a TB cavity = $10^9$-$10^{11}$

Slide courtesy of Dr. Mase
Spontaneous mutations develop as bacilli proliferate to $>10^8$.
Drug-resistant mutants in large bacterial population

Mono-therapy: INH-resistant bacteria proliferate

INH

Slide courtesy of Dr. Mase
Drug-resistant mutants in **large** bacterial population

Mono-therapy: INH
INH-resistant bacteria proliferate

Slide courtesy of Dr. Mase
Drug-resistant mutants in **large** bacterial population

Multi-drug therapy: No bacteria resistant to all 3 drugs

Mono-therapy: INH-resistant bacteria proliferate

INH

RIF

PZA

INH

Slide courtesy of Dr. Mase
Spontaneous mutations develop as bacilli proliferate to \(>10^8\)

INH resistant bacteria multiply to large numbers

INH mono-resistant mutants killed, RIF-resistant mutants proliferate \(\rightarrow\) MDR TB
Which is NOT associated with Risk of Drug Resistant TB?

1. U.S. residents who travel to high risk areas
2. Exposure to patient on TB therapy
3. Prior treatment for TB
4. Treatment failure
5. Relapse in a patient not on DOT
Case 4: Stepping Out

- 22 y/o student from Russia
- Seen by private MD for chest pain, fatigue
- History of prior treatment for TB
- Sputum smear is positive for AFB
- Started on TB treatment
- Culture positive for *M. tuberculosis*
Can she attend class with a N95 mask?

1. Yes
2. No
3. After proper fit testing
Protect the innocent

• Young children
• Immunocompromised
• Uninfected
• Non-exposed
Criteria for Discontinuing AII

When infectious TB is unlikely and either

1) Another diagnosis is made that explains the clinical syndrome
   or
2) Patient has three consecutive negative AFB sputum smear results*

* Exception: MDR-TB
Criteria for Discharge

• What do you need to know?
  • About the patient
  • About the home setting
  • About visitors
Case 4: Long-term care

• 82 year old female with some dementia
  • cough x 2 weeks
  • 10 lb. weight loss

• No insurance

• Sputum AFB smear positive
• *M. tb* PCR positive
Discontinue isolation?

Discharge back to nursing home?
When can this patient be discharged and return to her facility?

1. Minimal TB symptoms
2. Three (3) negative smears
3. Tolerating TB medications
4. All of the above
5. ???
### AIRBORNE PRECAUTIONS

**PRIVATE ROOM, NEGATIVE AIRFLOW**

<table>
<thead>
<tr>
<th>HANDS</th>
<th>Clean thoroughly with alcohol handrub or with soap and water upon entering and leaving the room.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASK</td>
<td>An <strong>N95</strong> (particulate filter) respirator must be worn when entering the room and must fit snugly around the nose and face.</td>
</tr>
<tr>
<td>ROOM</td>
<td>Private room with negative air flow. <strong>Door must remain closed.</strong></td>
</tr>
<tr>
<td>PATIENT TRANSPORT</td>
<td>Place procedure mask on patient.</td>
</tr>
<tr>
<td>VISITORS</td>
<td>Please report to Nurse's Station before entering the room</td>
</tr>
</tbody>
</table>

**Questions?**

Call Department of Clinical Epidemiology: University Hospital James 293-8556; University Hospital East: 257-2037. (June 2006)
Case 5  Non-adherence with therapy

- 41 y/o with HIV infection presents with fever, chills and productive cough
- Hospitalized 2 weeks for smear-positive pulmonary TB
- Not cooperative with DOT in hospital
- Lives with HIV-infected partner
Discontinue isolation?
Discharge home?
Home Infection Control

- Discharge from the hospital should not take place until a plan that includes DOT has been approved.
- Patients can be at home while infectious if there is no risk of exposing uninfected persons who are at high risk for progressing to TB disease (e.g., young children, HIV-infected persons).
- Until the patient is deemed noninfectious, he or she should not have uninfected visitors.

*Connecticut Advisory Committee for the Elimination of Tuberculosis, 2008*
## TB precautions in the home

<table>
<thead>
<tr>
<th>Setting</th>
<th>Administrative controls</th>
<th>Environmental controls</th>
<th>Respiratory protection</th>
</tr>
</thead>
</table>
| **Home health care** | • Train patients about meds, cough etiquette  
• Screen visitors  
• Postpone travel until noninfectious | • Ventilate the home                      | • When transporting patients in an enclosed vehicle |
Collaboration with Public Health

- Reporting cases
- Coordinating discharge planning
- Facilitate continuity of care
- Review of policies and procedures
- Home evaluation
- Community investigations
Health care setting

- Risk Classifications:
  - Low
  - Medium
  - Potential for ongoing transmission
## Risk Classifications for Hospitals

<table>
<thead>
<tr>
<th>Inpatient settings</th>
<th>Low</th>
<th>Medium</th>
<th>Potential Ongoing Transmission</th>
</tr>
</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>
</tr>
</tbody>
</table>
## Risk Classifications for Outpatient Settings

<table>
<thead>
<tr>
<th>Outpatient settings</th>
<th>Low</th>
<th>Medium</th>
<th>Potential Ongoing Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>medical offices, ambulatory care settings,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB treatment facilities</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>
## Risk Classifications for Other Health-Care Settings

<table>
<thead>
<tr>
<th>Nontraditional facility-based settings</th>
<th>Low</th>
<th>Medium</th>
<th>Potential Ongoing Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMS, LTCFs, medical settings in correctional facilities, outreach care</td>
<td>Only LTBI; system for detection of persons with TB symptoms</td>
<td>Settings where persons with TB disease are treated</td>
<td>Evidence of ongoing transmission, regardless of setting</td>
</tr>
</tbody>
</table>
Example of Risk Classification (1)

- A 100 bed hospital in a small city
- Two TB patients admitted in the previous year – one directly to AII, one after 2 days on a medical ward
- Contact investigation in exposed employees found no evidence of transmission

*Risk Classification:*

Low
Example of Risk Classification (2)

- Big city hospital admits 30 TB patients/ year
- TB test conversion rate of 1.0%; 3/20 (15%) respiratory therapists (RTs) converted
- Problem evaluation:
  - The three who converted spent time where induced sputum specimens collected
  - Ventilation in this area inadequate

**Risk Classification:**

1. Potential ongoing transmission for RTs
2. Rest of facility: medium
Example of Risk Classification (3)

- A home healthcare agency that serves a clientele w/ TB rates higher than community
- No patients with TB in past year
- 125 workers; 1/3 are foreign-born
  - provide nursing, PT, basic home care
  - at baseline two-step testing, 4 TST+; 2 TST+ on second-step; no cases

*Risk Classification:*

Low
## TB Screening Frequency

<table>
<thead>
<tr>
<th>RISK CLASSIFICATION</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Baseline; then further screening not necessary 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 weeks until transmission interrupted</td>
</tr>
</tbody>
</table>
Question 1

25 year old patient admitted to the hospital with cough x 1 month. CXR with right upper lobe cavitary lesion. Sputum AFB smear positive, *Mycobacterium tuberculosis* PCR positive.

When can you discontinue isolation in this patient?

A. Clinical improvement
B. Three negative AFB sputum smears
C. Tolerating TB medications
D. All of the above

D. All of the above. Criteria for discontinuing isolation should be a case by case basis based. All three of these criteria should be met: Show clinical improvement, have converted their sputum smear, and tolerating TB medication. Other factors such as suspicion for drug resistance, type of employment, etc may also need to be considered.
Question 2
Development of drug resistant TB
(please check all that apply)

A. Prior history of TB
B. Non-adherence with TB medication
C. Chronic nausea, vomiting, and diarrhea in patient taking TB medication
D. Travel to or immigration from high risk areas
E. All of the above
Summary

Keys to good infection control

- Think TB!
- Isolate
- Start 4 drugs (active agents)
- Patient education
- Directly Observed Therapy
- Discharge planning
- Respiratory protection
- Contact Investigation
Thank you!

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