Scenario #1

While in your outpatient clinic, you evaluate a 58 yo woman w/6 weeks of productive cough, night sweats, and 10 lb weight loss. She has a 50 py tobacco hx and rheumatoid arthritis (RA). She takes methotrexate and intermittent steroid bursts for her RA. Her mother died of lung cancer at age 63. Though a lifelong NH resident, your pt did spend 1 year in Lima, Peru, volunteering on a hospital’s pulmonary ward a few years ago. While awaiting basic labs, sputum sample, and chest xray, what precautions are indicated?

A. None – she has no TB risk factors
B. She should don a surgical mask and be moved to a room equipped for All (airborne infection isolation)
C. She should be transferred to the nearest ED to rule out tuberculosis
D. She should stay in the current (non-AI) examining room providing she dons a surgical mask
E. She should stay in the current (non-AI) examining room providing she dons a PAPR (powered air purifying respirator)

Scenario #2

You are paged by a Radiology technician regarding a 70 yo man w/lung cancer and recently confirmed pulmonary TB, admitted w/right frontal headaches x 2 weeks. The pt is on All precautions awaiting a brain MRI to evaluate metastases from the lung cancer. The technician is concerned that there is no negative pressure room in Radiology, and inquires as to what precautions should be taken to prevent TB transmission. You recommend:

A. The MRI should be scheduled when it can be performed without prolonged waiting. The pt wears a surgical mask while outside of his room. HCPs in Radiology wear respiratory protection (N95 or PAPR). No HEPA filtration is indicated given the short duration of the scan.
B. The MRI should be scheduled when it can be performed without prolonged waiting. The pt wears a surgical mask when not in AI; HCPs in Radiology wear N95/PAPR. A HEPA filter should be used through the end of the study + another 30 minutes prior to the room being cleaned.
C. The pt should not have the MRI as the risks of nosocomial TB transmission outweigh the benefits of performing the scan.

Scenario #3

67 yo man is admitted following head trauma. He is otherwise healthy; has lived his whole life in Vermont. CXR done during trauma work-up shows incidental finding of RUL tree-in-bud nodular opacities. Upon ROS, he reports frequent colds w/associated cough in past year. The patient is placed on All precautions. How should he be managed?

A. Discontinue AI with no further testing
B. Perform AFB smear microscopy on sputum daily for three days; discontinue AI if all smears are negative
C. Test 1 sputum sample with Xpert MTB/RIF; discontinue AI if negative
D. Test 2 sputum samples with Xpert MTB/RIF; discontinue AI if both negative
E. Treat empirically for TB; discontinue AI after 2 weeks of effective therapy

Scenario #4

Would your decision change if, instead of being a lifelong Vermont resident, he’d just moved from Haiti?

A. Discontinue AI with no further testing
B. Perform AFB smear microscopy on sputum daily for three days; discontinue AI if all smears are negative
C. Test 1 sputum sample with Xpert MTB/RIF; discontinue AI if negative
D. Test 2 sputum samples with Xpert MTB/RIF; discontinue AI if both negative
E. Treat empirically for TB; discontinue AI after 2 weeks of effective therapy
TB Transmission

- Airborne route
- Droplet nuclei can remain suspended in air for prolonged time
  - Can be transmitted distances > 1 m
- Smear+ sputum contains $10^6-10^7$ AFB/mL
- Smear- sputum contains $<10^3$ AFB/mL
- Transmission affected by:
  - Patient infectiousness
  - Environmental conditions
  - Duration of exposure

Patient Characteristics That Increase TB Infectiousness

- Active cough >3 weeks
- Failing to cover cough
- TB disease of respiratory tract, lungs, larynx
- Previous inadequate TB treatment
- AFB smear positive sputum
- Cavitation on chest xray
- Cough-inducing or aerosol-generating procedures

Environmental Factors Increasing Risk for TB Transmission

- Exposure in small, enclosed spaces
- Inadequate ventilation
- Recirculating air containing infectious droplets
- Inadequate cleaning/disinfection of equipment
- Improper specimen-handling procedures

Risks for Healthcare–Associated TB Transmission and/or Exposure

- High TB prevalence in:
  - Health-care setting
  - Community
- Patient population served
- Environmental factors
- Effectiveness of infection control measures

HCW Risk Factors for TB Transmission and/or Exposure

- Treating high-risk patients
- Exposed unknowingly to an infectious pt w/TB
- Performing aerosol-generating procedures
  - Bronchoscopy
  - Endotracheal intubation or succioning
  - Open abscess I+D
  - Autopsy
  - Sputum induction
  - Aerosol medication treatments (ie nebulizers)

Unprotected Healthcare-Associated TB Exposure

- 30 cumulative minutes in an enclosed space when HCP is without RP or the infectious pt without surgical mask
  - or -
- Shorter but > intense exposure (ie unprotected participation in aerosolizing procedure)
- Infectious pt = person w/productive cough, and sputum testing + for MTB
Preventing HCW TB Exposure

- Biggest transmission risk to HCWs is pt w/unrecognized infectious TB disease
  - Early recognition is key!
  - Evaluate for symptoms/signs of TB disease
  - Ask about previously treated TB
- Promptly initiate AII precautions
  - If pt has symptoms or signs of TB disease or
  - If pt has not yet completed anti-TB treatment and has documented infectious TB disease
  - Surgical mask for pt
  - Separate pt from immunocompromised pts

Fundamentals of TB Infection Control

- Administrative controls
  - Reduce risk of exposure via effective infection control program
- Environmental controls
  - Prevent spread, reduce concentration of droplet nuclei
- Respiratory protection controls
  - Further reduce risk of exposure in special areas and circumstances

AII Precautions for Settings Expecting to Encounter TB Patients

<table>
<thead>
<tr>
<th>Setting</th>
<th>Administrative Controls</th>
<th>Environmental Controls</th>
<th>Respiratory Protection Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient rooms</td>
<td>Written AII policies</td>
<td>≥1 inpatient AII room</td>
<td>For anyone entering room of patient with suspected/confirmed infectious TB</td>
</tr>
<tr>
<td></td>
<td>Persons with suspected/confirmed TB placed in AII room</td>
<td>Air cleaning to increase air changes/ hour (ACH)</td>
<td></td>
</tr>
</tbody>
</table>

All in the Inpatient Setting: Environmental Aspects

- Airflow in All rooms should be ≥6 ACH, preferably ≥12
- Adjust or modify the ventilation system w/UVGI or HEPA filtration if needed
- Check room for negative pressure daily when in use
- Keep doors closed as much as possible
- Maintain adequate number of All rooms
- Group All rooms together

All in the Inpatient Setting: The Patient’s Room

- All rooms are single-patient, private bathroom
- Control environmental factors including entry of HCWs/visitors to minimize M. tuberculosis transmission
- HCWs who enter wear at least N95 disposable respirators
- Visitors to All rooms offered RP w/education
Inpatient Setting All: Accessing the Facility Outside the Patient’s Room

- Diagnose and treat the pt in the All room as much as feasible
- Ensure patient adheres to All precautions
- Schedule procedures when a minimum number of HCWs and other patients are present
- Provide a surgical or procedure mask during transport, in waiting areas, and when others are present
- In diagnostic/treatment areas where negative pressure rooms are not available:
  - Use HEPA filters
  - Allow to run for 30 minutes after pt leaves room prior to usual cleaning procedures

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All in Various Healthcare Settings

For All guidelines in specific clinical and non-traditional healthcare settings, see:


All Precautions: Triage Settings Not Expecting to Encounter TB Patients

<table>
<thead>
<tr>
<th>Setting</th>
<th>Administrative Controls</th>
<th>Environmental Controls</th>
<th>Respiratory Protection Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triage only</td>
<td>Written plan for triage</td>
<td>Separate holding area</td>
<td>As needed for patients attending ED</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>As needed for unrecognized TB patients</td>
</tr>
</tbody>
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All Precautions for Inpatient Settings: Emergency Department/Medical Office/Ambulatory-Care Setting

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<th>Environmental Controls</th>
<th>Respiratory Protection Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promptly detect, evaluate, and separate patients with suspected or confirmed TB.</td>
<td>24 All room for settings with high volume of suspected or confirmed TB patients, or effectively vented room + air cleaning</td>
<td>At least N95 RP for anyone entering All rooms of persons with suspected or confirmed infectious TB</td>
</tr>
</tbody>
</table>
Scenario #2
You are paged by a Radiology technician regarding a 70 yo man w/lung cancer and recently confirmed pulmonary TB, admitted w/right frontal headaches x 2 weeks. The pt is on All precautions awaiting a brain MRI to evaluate metastases from the lung cancer. The technician is concerned that there is no negative pressure room in Radiology, and inquires as to what precautions should be taken to prevent TB transmission. You recommend:
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All Precautions for Inpatient Settings: Surgical Suites or Operating Rooms (OR)

<table>
<thead>
<tr>
<th>Administrative Controls</th>
<th>Environmental Controls</th>
<th>Respiratory Protection Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpone non-urgent procedures on suspected/confirmed TB patients until known to be non-infectious. Do procedure at end of day and during low traffic times.</td>
<td>OR anteroom should be either positive pressure relative to both OR and corridor, or negative relative to both OR and corridor. If no anteroom, keep OR door closed, minimize traffic. Provide sterile field while preventing contamination with M. tuberculosis.</td>
<td>Use RP with a valveless filtering facepiece, e.g., N95 disposable.</td>
</tr>
</tbody>
</table>

Discontinuing All Precautions
- Infectious TB is unlikely and another diagnosis is made that explains the syndrome
- 3 consecutive negative AFB sputum smears collected in 8- to 24-hour intervals (one should be an early morning specimen)
- If pt is found to have TB, starts on and is adherent to adequate treatment regimen for ≥2 weeks and
- Demonstrates clinical improvement
- Has 3 consecutive negative AFB sputum smears collected in 8- to 24-hour intervals (one should be an early morning specimen)

Discharge to Home
- Patient w/suspected TB can be discharged home without 3 negative sputa if:
  - Follow-up plan has been made with local TB program
  - Patient is on standard treatment and directly observed therapy (DOT) is arranged
  - No person in home <4 years old or immunocompromised
  - All in household previously exposed
  - Patient willing to stay home until sputum results as negative
  - Do not discharge if high-risk persons will be exposed

Drug-Resistant TB Disease
- Transmission from MDR TB patients may be extensive
- Consider All precautions for MDR TB patients until hospital discharge or culture conversion
Sputum Microscopy to Discontinue All

• 3 negative sputum smears for AFB previously required to discontinue All
• 3 samples collected 8-24 hours apart
• At least 1 early morning sample
• Good quality
• May need RT to induce sputum

Role of Sputum AFB Microscopy in All Discontinuation

• Sputum AFB smear positivity is marker of infectiousness
• Historical data demonstrated low risk of transmission from pts w/smear negative, culture positive TB
• Among TB contacts, 30-50% convert PPDs if source pt is smear (+) vs ~5% if source is smear (-)
• Studies show sensitivity of smears to diagnose TB are ~50-60%
• Some studies suggest sensitivity as low as 35% in HIV+ pts

Practical Limitations w/Sputum Microscopy Use to Discontinue All

• Long duration of hospitalization
• High costs
• Limited number of All rooms
• Adverse effects to pt remaining in isolation:
  – In systematic review, pts were seen less by HCPs
  – Had 8-fold increase in adverse effects
  – Have negative perspective of their care
  – Had delay in getting proper procedures performed

Sputum Microscopy for All Discontinuation

• Pts suspected of pulmonary TB spend several days in All awaiting sputum AFB microscopy collection and results
  – Patient can’t produce sputum
  – Sputum cup not at bedside
  – Specimen rejected by lab – poor quality

Enter Xpert MTB/RIF

• Automated, real-time nucleic acid amplification-based test
• Uses disposable cartridge in GeneXpert Instrument System – GeneXpert can be used to evaluate multiple other diseases
• Easy to use
• 100 mins to dx TB and rifampin susceptibility
• 92% sensitivity overall
• 99% specificity

Sputum Sample and Processing in Xpert

• Quality sample induced or expectorated sputum
• FDA-approved on raw or concentrated sputum sediment only
• Pts must have received no or <3 days anti-TB therapy
• 3 good quality specimens >8 hrs apart
• At least one must be early morning sample
• Still need to send AFB smear/culture
  – Identification
  – Antimicrobial susceptibility testing
  – Genotyping
  – Tracking response to treatment
**Possible Xpert MTB/RIF Results**

1. *Mycobacterium tuberculosis* not detected
2. *Mycobacterium tuberculosis* detected
   - Rifampin resistance detected
3. *Mycobacterium tuberculosis* detected
   - Rifampin resistance not detected
4. *Mycobacterium tuberculosis* detected
   - Rifampin resistance indeterminate

- Failure of assay
- 2.2% of results in a large validation study

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**Interpreting AFB Smear Microscopy and Xpert**

**Table 1. Interpretation of Rapidly Available Diagnostic Tests for Active Pulmonary Tuberculosis Disease When Mycobacterial Culture Is Pending**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFB smear microscopy</td>
<td>+</td>
</tr>
<tr>
<td>NAAT</td>
<td>–</td>
</tr>
</tbody>
</table>

**Interpretation**
- **TB**: Probable
- **TB**: Possible
- **TB**: Unlikely

---

**Sensitivity/Specificity of Xpert vs AFB Microscopy**

- In study of 139 patients suspected of TB disease (10 w/culture positive TB), Xpert was equivalent to 3 AFB smears
  - 89% sensitivity
  - 99% specificity
- Among 207 pts suspected of TB disease admitted on All precautions:
  - One Xpert detected 5 of 6 culture-confirmed cases
  - Second Xpert detected 6th
  - Sensitivity was same as 3 AFB smear series (93%)
  - Specificity 99.8% Xpert vs 98.9% 3 AFB smear series

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**Xpert vs AFB as TB Diagnostic Tool in Low Prevalence Setting**

**Table 2. Sensitivity of Xpert MTB/RIF Assay Versus 3 AFB Smears for Identification of US Case-Defined Tuberculosis Cases**

<table>
<thead>
<tr>
<th>Group</th>
<th>Xpert Positive</th>
<th>Xpert Negative</th>
<th>AFB Positive</th>
<th>AFB Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFB smear positive</td>
<td>99.7% (95.8%)</td>
<td>0.3% (0.1%)</td>
<td>100% (95.8%)</td>
<td>0.3% (0.1%)</td>
</tr>
<tr>
<td>AFB smear negative</td>
<td>99.7% (95.8%)</td>
<td>0.3% (0.1%)</td>
<td>0.3% (0.1%)</td>
<td>99.7% (95.8%)</td>
</tr>
</tbody>
</table>

**What Extra is Gained with Xpert vs AFB Microscopy?**

- **AFB Smear + Disease**
  - 1 negative Xpert predicted absence of TB disease with negative predictive value = 99.7%
  - 2 negative Xpert assays NPV = 100%

- **AFB Smear+ or - Disease**
  - 1 negative Xpert NPV = 97.6%
Xpert to Discontinue All Precautions

- Feb 2015 – FDA approved use of either 1 or 2 Xpert tests to discontinue All
- Xpert package insert: “An Xpert MTB/RIF Assay result of “MTB NOT DETECTED” from either one or two sputum specimens is highly predictive of the absence of M. tuberculosis complex bacilli on serial fluorescent acid-fast sputum smears from patients with suspected active pulmonary tuberculosis and can be used as an aid in the decision of whether continued airborne infection isolation (AII) is warranted in patients with suspected pulmonary tuberculosis.”

Xpert Limitations: Xpert is Not Sole Diagnostic in Pulmonary TB

- Pt w/ negative sputum Xpert may have positive AFB culture, but is not infectious enough to maintain AII
- AFB culture is required
  - Still gold standard
  - More sensitive than Xpert
  - “Xpert negative or AFB smear-negative sputum may contain viable organisms and represent infectious tuberculosis”
  - Needed for drug susceptibility testing

Xpert Use in Pulmonary TB: Limitations

- FDA approval is for Xpert MTB/RIF assay only
- Hospitals using other NAATs should validate test before making decision to d/c pt from AII
- Use of Xpert to d/c AII only applies to pts in healthcare facilities
- Research used for FDA approval was based on studies of pts ≥18 years of age
- Interpretation of Xpert results must be made in conjunction w/clinical and radiographic data
Xpert for All Discontinuation: Decreased Length of Stay and Costs

- In various studies, Xpert has decreased time spent in All precautions by 17-47 hrs \(^1\)\(^3\)
- Median laboratory processing time for smear microscopy was 2.5 x Xpert\(^2\)
- 48% reduction in All bed usage/yr\(^1\)
- Saved avg of $2,278/admission, $533,520/yr\(^2\)

Scenario #3

67 y/o man is admitted following head trauma. He is otherwise healthy; has lived his whole life in Vermont. XDR done during trauma work-up shows incidental finding of RUL tree-in-bud nodular opacities. Upon ROS, he reports frequent colds w/associated cough in past year. The patient is placed on All precautions. How should he be managed?

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E. Treat empirically for TB; discontinue All after 2 weeks of effective therapy

Scenario #4

How about the same gentleman though born, raised, and recently moved from Haiti?

A. Discontinue All with no further testing
B. Perform AFB smear microscopy on sputum daily for three days; discontinue All if all smears are negative
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References