Clinical Presentation & Diagnosis of Pulmonary Tuberculosis

Christopher Spitters, MD, MPH
PHSKC Tuberculosis Clinic
CITC Tuberculosis Intensive @ Seattle
June 26, 2019

Disclosures

- Financial ties: none
- Off-label uses: NAAT on non-respiratory specimens
Learning Objectives

• Recognize the most common pulmonary and systemic signs and symptoms of tuberculosis to more effectively diagnose tuberculosis disease.
• Initiate a comprehensive medical evaluation of a case presenting as potential tuberculosis to assess for disease.
• Initiate treatment based on radiologic findings, lab results, risk factors and symptoms to optimize clinical outcomes.
• Apply CDC’s national guidelines on rapid diagnosis of tuberculosis for clinical decisions to quickly analyze and treat patients when appropriate.

Missed TB Diagnoses
California, 2005-2011

Table 2. Counts and Prevalence of Potential Misdiagnoses for Various Potential Misdiagnosis Window

<table>
<thead>
<tr>
<th>Potential Misdiagnosis Window</th>
<th>TB Cases With Previous Visit and Respiratory Diagnosis</th>
<th>TB Cases With Previous Visit and No Respiratory Diagnosis</th>
<th>Potential Misdiagnosis Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-30</td>
<td>513</td>
<td>261</td>
<td>15.9%</td>
</tr>
<tr>
<td>5-60</td>
<td>714</td>
<td>426</td>
<td>22.2%</td>
</tr>
<tr>
<td>5-90</td>
<td>826</td>
<td>529</td>
<td>25.7%</td>
</tr>
<tr>
<td>5-120</td>
<td>880</td>
<td>609</td>
<td>27.3%</td>
</tr>
<tr>
<td>5-180</td>
<td>953</td>
<td>741</td>
<td>29.6%</td>
</tr>
<tr>
<td>5-270</td>
<td>1027</td>
<td>871</td>
<td>31.9%</td>
</tr>
<tr>
<td>5-360</td>
<td>1078</td>
<td>963</td>
<td>33.3%</td>
</tr>
</tbody>
</table>

Abbreviations: TB, tuberculosis.

* Proportion of TB patients of 3320 patients in the final sample having a previous visit with a respiratory diagnosis occurring in a given potential-misdiagnosis window.

Missed TB Diagnoses
California, 2005-2011

Table 2. Counts and Prevalence of Potential Misdiagnoses for Various Potential Misdiagnosis Windowa

<table>
<thead>
<tr>
<th>Potential Misdiagnosis Window</th>
<th>TB Cases With Previous Visit and Respiratory Diagnosis</th>
<th>TB Cases With No Respiratory Diagnosis</th>
<th>Potential Misdiagnosis Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>5–30</td>
<td>513</td>
<td>201</td>
<td>15.9%</td>
</tr>
<tr>
<td>5–60</td>
<td>714</td>
<td>426</td>
<td>22.2%</td>
</tr>
<tr>
<td>5–90</td>
<td>826</td>
<td>528</td>
<td>25.7%</td>
</tr>
<tr>
<td>5–120</td>
<td>880</td>
<td>609</td>
<td>27.3%</td>
</tr>
<tr>
<td>5–180</td>
<td>953</td>
<td>741</td>
<td>28.6%</td>
</tr>
<tr>
<td>5–270</td>
<td>1027</td>
<td>871</td>
<td>31.9%</td>
</tr>
<tr>
<td>5–360</td>
<td>1078</td>
<td>983</td>
<td>33.5%</td>
</tr>
</tbody>
</table>

Abbreviations: TB, tuberculosis.
aProportion of TB patients (of 3220 patients in the final sample) having a previous visit with a respiratory diagnosis occurring in a given potential-misdiagnosis window.

About ¼ of cases might have been diagnosed earlier when seen in the preceding 3 months.


Diagnostic Sequence

- Clinical syndrome
- Epidemiologic risk
- Physical exam findings
- Imaging
- Specimen collection
- Testing
- Results-->medical decision making
Clinical Evaluation

- History
  - Prior TB diagnosis/treatment
  - Epidemiologic risk
  - Predisposing medical conditions/therapies

- Exam
  - General, temperature, weight/BMI
  - Lymphadenopathy
  - Chest auscultation abnormalities
  - Abdominal distension or tenderness
  - Spine tenderness or deformity
  - Neurologic abnormalities

Clinical Presentation: Signs and symptoms

- Cough (dry/productive sputum) 75-80%
- Weight loss 45-75%
- Fatigue 60-70%
- Fever 50-60%
- Night Sweats 50-55%
- Hemoptysis 25-35%
- No symptoms 10-20%

Source: Barnes 1988, Miller 2000
### Accuracy of Symptom Check

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough (any)</td>
<td>93%</td>
<td>37%</td>
<td>21%</td>
<td>97%</td>
</tr>
<tr>
<td>Night sweats (24h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever (2wks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorexia (4wks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Good news: effective  
Bad news: inefficient


### Sites of Involvement

- Lungs
- Lymph Nodes
- Pleura
- Peritoneum
- Bones
- Brain
- Liver/Spleen
- Urinary tract
- Genitals
- Eyes
- Skin

**Clinical Presentation: Site of Disease**

CDC Reported TB Cases by Form of Disease United States, 2010

- Pulmonary (68%)
- Extrapulmonary (22%)
- Both (10%)
- Lymphatic (40%)
- Pleural (16%)
- Other (18%)
- Genitourinary (5%)
- Peritoneal (5%)
- Meningeal (6%)

**Imaging**

- CXR
- Neck CT
- Chest CT
- MRI brain
- MRI spine
- CT Abdomen/Pelvis
- Plus ultrasound for aspiration of LNs and effusions
Time course after exposure: Primary vs. postprimary

• Primary TB:
  – Progression of initial infection
  – time = weeks to months

• Postprimary TB
  – reactivation of latent/inactive TB
  – time = months to decades

General Patterns in Presentation of TB

<table>
<thead>
<tr>
<th>Primary/immunosuppressed</th>
<th>Reactivation/adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Adenopathy</td>
<td>• Pulmonary</td>
</tr>
<tr>
<td>• Effusions</td>
<td>• Reactivation type</td>
</tr>
<tr>
<td>• Dissemination</td>
<td>• Cavitation</td>
</tr>
<tr>
<td>• Extrapulmonary sites</td>
<td>• Less extrapulmonary</td>
</tr>
<tr>
<td>• Smear-negative more common</td>
<td>• Smear positive more common</td>
</tr>
<tr>
<td>• More IRIS</td>
<td>• Less IRIS</td>
</tr>
</tbody>
</table>
Differential Diagnosis

- Community acquired pneumonia
- Malignancy
- Septic emboli
- Lung abscess
- Non-TB mycobacteria
- Fungal infection (cocci, crypto, histo, blasto)
- Parasite (e.g., paragonimiasis)
- Sarcoidosis
- Rheumatologic disease (e.g., Wegener’s, RA)
- Other systemic infections (e.g., brucellosis, Q-fever, melioidosis, relapsing fever, etc.)

Case A

- 34 y/o Filipino male
- Cough, fever, sweats x 2 weeks
FQN Delays TB Diagnosis

- $t=0$; azithromycin
- $t=3$wks, moxifloxacin
- $t=6$wks; all better!
- $T=24$wks

Caution in Empiric Fluoroquinolone Use

- **Diagnostic Delays**
  - Fluoroquinolones add 12.9 days to time-to-diagnosis.
  - Impact greater for AFB smear-negative cases


- **Resistance**
  - Recent prior FQN use in 10% of sensitive but 30% of resistant cases
  - OR ~10 for >10 days use
  - Devasia, et al. Fluoroquinolone Resistance in Mycobacterium tuberculosis
### Specimen Collection

#### Airway
- Sputum x 3
- Induced sputum
- BAL
- Washings
- Gastric aspirate

#### Other
- Trans-bronchial bx
- Pleural fluid
- Pleural biopsy
- LN/abscess FNA
- LN excisional biopsy
- CT-guided needle biopsy
- Fluids
  - Pleura/peritoneum/pericardium
  - CSF
  - Joint
- Other tissues (peritoneum, gut, endometrium, etc.)

---

### Collection of Respiratory Specimens

- **Sputum Expectoration:**
  - 3 specimens (at least 8 hours apart)
  - 1 spot specimen (induce prn)
  - 2 consecutive first-morning specimens
- **Induction** (if unable to raise specimen)
- **Bronchoscopy**
- **Post-bronchoscopy sputum**
- **Gastric Aspiration**

ATS/IDSA/CDC 2017 Dx Guidelines: sputum→induction→bronchoscopy
Bronchoscopy Indications

• Unable to obtain specimen via induction or gastric aspirate
• Sputum smear/PCR negative but clinical suspicion of TB still high
• Sputum smear negative and MDR is a high concern
• Specimen needed for testing to address suspected non-TB conditions

Post-Bronchoscopy Sputum

• 57 sputum smear-negative or non-productive¹
  – 33% AFB smear-positive PBS
  – 7% PBS sole culture-positive specimen
• 56 culture-confirmed cases with negative sputum AFB smears or non-productive²
  – AFB smear sensitivity:
    • BAL 57%
    • PBS 77%
    • BAL + PBS 84%

Mycobacteriologic Examinations for TB

<table>
<thead>
<tr>
<th>Test</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFB stain</td>
<td>&lt;24 hours</td>
</tr>
<tr>
<td>Nucleic acid amplification</td>
<td>Hours-days</td>
</tr>
<tr>
<td>Molecular DST results</td>
<td>Days-weeks</td>
</tr>
<tr>
<td>AFB culture</td>
<td>2-6 weeks</td>
</tr>
<tr>
<td>Phenotypic DST results</td>
<td>4-8 weeks</td>
</tr>
<tr>
<td>DNA fingerprinting</td>
<td>Months</td>
</tr>
</tbody>
</table>

Specimen Testing

**Mycobacteriology**
- Acid-fast bacillus stain & culture
- TB nucleic acid amplification x 1-2
- *Unfixed* tissue specimens for PCR and culture!!

**Other (but TB-focused)**
- Cytology/histopathology
- Cell count and differential
- Protein, glucose, LDH
- Adenosine deaminase
- Interferon-gamma release assay (e.g., Quantiferon, T-Spot)

ATS/IDSA/CDC 2017 Dx Guidelines
Acid Fast Staining

• Preparation
  – Centrifugation to concentrate
  – NaOH, NaOCl wash to decontaminate
• Ziehl-Neelsen
  – Carbolfuchsin (red) → acid alcohol → methylene blue
• Flourescent
  – Auramine-Rhodamine

ATS/IDSA/CDC 2017 Dx Guidelines:
Specimen concentration preferred
Fluorescence microscopy preferred
AFB Smear Performance


Smear-Positive Pulmonary TB vs NTM?

- 27 y/o M, DM, from high incidence country
- Cough, sputum x3 months; night sweats, 5-kg weight loss

- 82 y/o US-born F, 41kg
- Chronic productive cough off and on for years
AFB smear-negative TB

- Up to 50% of TB cases are AFB smear-negative
- low bacillary load—usually but not always
- low infectiousness--usually
- negative smears do not exclude disease
- ...nor heavy bacillary load
- ...nor capacity to transmit

Smear-Negative TB

- 54 y/o male  
  High risk nation of origin  
  Cough, sputum x 2 weeks
- 35 y/o RA patient  
  High risk nation of origin  
  TNF alpha blockade
Nucleic acid amplification tests (NAAT)

- FDA-approved direct amplification tests
  - Gen-Probe/MTD and Xpert Mtb/RIF
- Use directly on specimens, result < 1 day
- Caution: in patients with
  - Current TB treatment > 7 days → false-negative
  - Prior TB treatment within past 12 months → false-positive

ATS/IDSA/CDC 2017 Dx Guidelines: Yes

---

Expert MTB-RIF
**Sensitivity of Xpert in Pulm TB Dx Low & High Burden Settings**

<table>
<thead>
<tr>
<th>TEST</th>
<th>SENS</th>
<th>SPEC</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xpert x 1</td>
<td>81.4%</td>
<td>98.7%</td>
<td>94.6%</td>
<td>99.7%</td>
</tr>
<tr>
<td>Smear pos</td>
<td>98.5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smear neg</td>
<td>54.8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xpert x 2</td>
<td>95.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smear pos</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smear neg</td>
<td>71.4%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- N = 992 (US, Brazil, S Africa)
- Sensitivity of AFB smear: 60%
- No difference between high and low prevalence settings

*Leutkerewy AF, et al. CID 2016*

**Caution with NAAT in Previously Treated Patients**

*Theron, et al. CID 2016*
- 45/321 (14%) positive were culture negative
- Recency of prior treatment
- Low DNA
- CXR not suggestive of TB

*Boyles, et al. IJTLT 2014*
- 4 false positive case reports
- 1, 2, 5 and 66 months after prior treatment
Laboratory Diagnosis: Approaches to Using NAAT

Patient with **smear-positive** specimen

- **MTB** ≥97%
- **NTM** <3%
- **NAAT Positive**

Patient with **smear-negative** specimen + high clinical suspicion

- **MTB** 1-8%
- **NTM** 92-99%
- **NAAT Negative**

### Positive NAAT

- **MTB** ≥97%
- **NTM** <3%

### Negative NAAT

- **MTB** 1-8%
- **NTM** 92-99%

- **2009 CDC Guidelines:** Test all AFB+/NAAT- specimens for inhibitors
- **2009 CDC Guidelines:** Probably not necessary if using Xpert, which tests for PCR inhibitors
Approach to the smear-positive patient when NAAT was not performed

- High clinical suspicion:
  - Isolation, empiric TB treatment, NAAT

- Low clinical suspicion:
  - Request NAAT (still consider possible isolation and empiric TB treatment unless NTM is very likely)

NAAT: Summary

- The test characteristics of NAAT are variable depending on the AFB smear results and clinical suspicion.
  - High suspicion → positive NAAT confirms TB
  - Low suspicion → Smear positive → negative NAAT supports NTM diagnosis
  - High suspicion → smear neg/NAAT neg, still can consider empiric therapy for TB.
  - Low suspicion → AFB smear is negative, don’t use NAAT because of ↑ false-positive
Case B

- 28 y/o Ethiopian woman
- Cough, dyspnea, fever, abdominal pain, blood in stools, headache, fatigue
- Sputum AFB smear- and NAAT-negative
- CXR normal
Case B—Miliary TB

- 28 y/o Ethiopian woman
- Cough, dyspnea, fever, abdominal pain, blood in stools, headache, fatigue
- Sputum AFB smear- and NAAT-negative
- BAL AFB smear neg/PCR neg
- TBBx
  - necrotizing granulomata
  - AFB smear-neg
  - TB PCR positive
- BAL and TBBx culture = MTB

AFB Culture

- Broth (faster, more expensive, complex)
  - Liberation of $^{14}$CO$_2$ (defunct)
  - Emission of fluorescence (MGIT)
- Plates (slower, less expensive, “simpler”)
  - Lowenstein-Jensen slant
  - 7H11 plates
- Identification of AFB growth
  - Phenotypic characteristics
  - Nucleic acid hybridization
  - DNA sequencing
  - HPLC

ATS/IDSA/CDC 2017 Dx Guidelines: Both broth and plates suggested
**AFB Culture Performance**


**Role of the 3rd Sputum Specimen**

<table>
<thead>
<tr>
<th>Specimen Number</th>
<th>Incremental Yield (of all culture positive)</th>
<th>Incremental Sensitivity (of all smear positive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>85.8%</td>
<td>53.8%</td>
</tr>
<tr>
<td>2</td>
<td>11.9%</td>
<td>11.1%</td>
</tr>
<tr>
<td>3</td>
<td>2.4%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>68.0%</td>
</tr>
</tbody>
</table>

Average yield of single early morning specimen: 86.4%
Average yield of single spot specimen: 73.9%

**AFB Culture Limitations**

- **False Positive** (up to 3% of total)
  - Laboratory cross contamination
  - Specimen mis-handling
- **False Negative**
  - Small inoculum
  - Delay in inoculation
  - Difficult-to-grow strain

---

**Approach to the smear-negative patient when the lab reports AFB growth**

<table>
<thead>
<tr>
<th>Level of clinical suspicion (especially based on epi risk factors and imaging)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
</tr>
<tr>
<td><strong>No Rx</strong></td>
</tr>
<tr>
<td>Isolate</td>
</tr>
<tr>
<td>Wait for Final ID</td>
</tr>
<tr>
<td>3. Risk of adverse effects</td>
</tr>
</tbody>
</table>

1. Repeat or additional imaging (e.g., CT)
2. Obtain tissue biopsy for culture and pathology

*Slide c/o M Narita*
Indications for Rapid Molecular Testing Resistance-Conferring Mutations

- Prior treatment for active TB
- Contact to known MDR case
- HIV infection
  
  **ATS/IDSA/CDC 2017 Dx Guidelines:**
  - 1 year in a country >20/100,000 TB Rate
  - 1 year in a country >2% MDR

- MDR Hotspot
  
  **ATA, IDSA, CDC. Diagnosis of TB in Adults and Children. Clin Infect Dis 2017;64(2):e31-e33**
Xpert MTB/RIF Test Performance

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smear pos. TB</td>
<td>95-98%</td>
<td>99%</td>
</tr>
<tr>
<td>Smear neg. TB</td>
<td>60-72%</td>
<td></td>
</tr>
<tr>
<td>Rifampin “R”</td>
<td>98-99%</td>
<td>99-100%</td>
</tr>
</tbody>
</table>


Molecular detection of drug resistance--CDC

Results for Molecular Detection of Drug Resistance (Sanger Sequencing, complete panel); Conventional Drug Susceptibility Test in progress.

<table>
<thead>
<tr>
<th>Location (region) examined</th>
<th>Result</th>
<th>Interpretation (based on in-house evaluation of 550 clinical isolates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rpoB (RDRQ)</td>
<td>Mutation: TCG&gt;TTG, Ser531Leu</td>
<td>Rifampin resistant; 100% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are RMP-R.</td>
</tr>
<tr>
<td>inhA (promoter)</td>
<td>No mutation</td>
<td></td>
</tr>
<tr>
<td>katG (sec315 codons)</td>
<td>Mutation: ACC&gt;ACC, Ser515Thr</td>
<td>Isolates resistant; 100% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are INH-R.</td>
</tr>
<tr>
<td>embB (MotF, MotG, MotJ)</td>
<td>Mutation: ATG&gt;GCT, Met30Val</td>
<td>Ethambutol resistance; 100% of isolates in our in-house evaluation of 550 clinical isolates with this mutation are EMR-R.</td>
</tr>
<tr>
<td>proA (promoter, coding region)</td>
<td>Mutation: A inserted after nt182, silent mutation: TCT&gt;TGT, Ser37Ser</td>
<td>Likely PZA resistant. The Ser37Ser mutation detected is a synonymous (silent) single-nucleotide polymorphism (SNP) and does not result in an amino acid change and is not considered clinically significant.</td>
</tr>
<tr>
<td>gyrA (GDRQ)</td>
<td>No mutation</td>
<td>Cannot rule out fluoroquinolone resistance: 80% of PZA-R isolates in our in-house evaluation of 550 clinical isolates have a mutation at this locus.</td>
</tr>
<tr>
<td>mls (1400 region)</td>
<td>No mutation</td>
<td>Cannot rule out resistance to injectable drugs (kanamycin, capreomycin, amikacin). In our in-house evaluation of 550 clinical isolates: * 91% of AMK-R isolates have a mutation in the mls locus; * 87% of KAN-R isolates have a mutation in either the mls locus or the 66A locus; * 58% of CAF-R isolates have a mutation in either the mls locus or the 66A locus.</td>
</tr>
<tr>
<td>ahp (promoter)</td>
<td>No mutation</td>
<td></td>
</tr>
<tr>
<td>rfa (gramicidin K)</td>
<td>No mutation</td>
<td></td>
</tr>
</tbody>
</table>
### BACTEC MGIT DST
WA PHL

**Sensitivity Report - 1st Line of Drugs**

<table>
<thead>
<tr>
<th>Drug (mg/day)</th>
<th>Result</th>
<th>Performed by</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOXIT Pyrazinamide (PZA) 10</td>
<td>RESISTANT</td>
<td>CAL</td>
<td>7/2/2015</td>
</tr>
<tr>
<td>MOXIT Streptomycin (Sm) 1.0</td>
<td>RESISTANT</td>
<td>CAL</td>
<td>7/6/2015</td>
</tr>
<tr>
<td>MOXIT Isoniazid (INH) 0.1</td>
<td>RESISTANT</td>
<td>CAL</td>
<td>7/6/2015</td>
</tr>
<tr>
<td>MOXIT Rifampicin (RFP) 1.0</td>
<td>RESISTANT</td>
<td>CAL</td>
<td>7/6/2015</td>
</tr>
<tr>
<td>MOXIT Ethambutol (EM) 5.0</td>
<td>Sensitive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: Drug resistance to be confirmed by TB-10 Plate method. Performed at CDC*

### WA PHL Plate DST Results

**Sensitivity Report - 2nd Line of Drugs**

<table>
<thead>
<tr>
<th>Drug (mcg/mL)</th>
<th>Result</th>
<th>Percent Resistance</th>
<th>Colonies at 10^3</th>
<th>Colonies at 10^5</th>
<th>Performed by</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth Control</td>
<td>Satisfactory</td>
<td>0</td>
<td>200</td>
<td>100</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Isoniazid 0.2</td>
<td>Resistant</td>
<td>100</td>
<td>200</td>
<td>100</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Isoniazid 1.0</td>
<td>Resistant</td>
<td>100</td>
<td>200</td>
<td>100</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Ethambutol 1.0</td>
<td>Resistant</td>
<td>100</td>
<td>200</td>
<td>100</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Streptomycin 2.0</td>
<td>Resistant</td>
<td>100</td>
<td>200</td>
<td>100</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Streptomycin 10.0</td>
<td>Resistant</td>
<td>100</td>
<td>200</td>
<td>100</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Ethionamide 5.0</td>
<td>Sensitive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Ethambutol 5.0</td>
<td>Resistant</td>
<td>100</td>
<td>200</td>
<td>100</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Ethambutol 10.0</td>
<td>Sensitive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>p-Aminosalicylic Acid 2.0</td>
<td>Sensitive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Amikacin 4.0</td>
<td>Sensitive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
<tr>
<td>Ofloxacin 4.0</td>
<td>Sensitive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CAL</td>
<td>6/23/2015</td>
</tr>
</tbody>
</table>
CDC Plates DST Results

Culture-negative TB Diagnostic Criteria

- Compatible clinical and radiographic syndrome
- AFB cultures negative
  - 10-15% pulmonary
  - 30-40% extrapulmonary
- Clinical/radiographic improvement on therapy
- Other causes reasonably excluded
- Positive TST-or-IGRA helpful but not required
**Culture-negative TB Diagnostic Criteria**

- Compatible clinical and radiographic syndrome
- AFB cultures negative
  - 10-15% pulmonary
  - 30-40% extrapulmonary
- Clinical/radiographic improvement on therapy
- Other causes reasonably excluded
- Positive TST-or-IGRA helpful but not required

ATS/CDC/IDSA 2016 Rx Guidelines

"Patients who have negative cultures but who still are presumed to have pulmonary tuberculosis should have thorough clinical and radiographic follow-up after 2 months of therapy. If there is clinical or radiographic improvement and no other etiology is identified, treatment should be continued."

**Summary**

- Cough, sputum, fever, night sweats or weight loss highly sensitive but very non-specific
- Diagnosis: epi/med background+clinical findings→imaging→mycobacteriology+accessory tests→medical decision making
- 3 respiratory specimens for AFB smear/culture.
- NAAT (e.g., Xpert, PCR) on 1-2 specimens.
- Collect specimens from additional suspected sites
- Avoid FQN use for CAP in patients with a reasonable likelihood of TB.
Questions/Comments

christopher.spitters@kingcounty.gov