Case Studies:
Therapeutic Drug Monitoring

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Case 1

- 17 yo man with “2 weeks” of cough
- Weight 48kg
- Admitted 3/09
- Father with TB 7 yr ago
Case 1, cont’d

- Started on I/R/E/Z via DOT
- 3 months into treatment
  - Remained smear positive
  - Weight down to 40 kg (BMI = 14)
- Added moxifloxacin, amikacin
- Started on enteral tube feeds

Case 1, cont’d

- Isoniazid & Rifampin both subtherapeutic
- Isoniazid increased to 900 mg / d to achieve therapeutic level
- Rifampin increased to 900 mg / d to achieve therapeutic level
- Cleared sputum, gained weight
- Completed 12 months total
Case 2

- 38 yo man with cough and hemoptysis
- Panlobar cavitary TB
- Started on I / R / E / Z
- Drug-susceptible TB
- Remained smear + > 2 mos of DOT

Case 2, cont’d

- Isoniazid & rifampin subtherapeutic
- Required INH 600, RIF 900 / d to achieve therapeutic levels
- Cleared sputum at approx 3 mos tx
Case 3

- 43 yo man with massive TB adenitis
- Started on I / R / E / Z / moxi
- Drug-susceptible disease; E / moxi stopped
- @2 mos- increasing adenopathy
- @3 mos- new intracranial tuberculomas
- @5 mos- subtherapeutic INH / RIF
  – Req’d INH 600 / RIF 900 to be therapeutic

Case 3, cont’d

- SLOW improvement in adenopathy
- Now at 9 mos tx; planning 12+ mos

CDC Guidelines* for Therapeutic Drug Monitoring (TDM)

- Slow response to DOT
- HIV
- Malabsorption
- Renal insufficiency
- MDR TB

* “Treatment of Tuberculosis.” MMWR, 2003
Therapeutic Drug Monitoring

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>• Ensure adequate levels</td>
<td>• Cost</td>
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<td>• Potentially decrease risk of resistance</td>
<td>• Not routinely necessary for clearance</td>
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<tr>
<td>• Avoid delays in clearance of bacteria</td>
<td>• Wide therapeutic window for 1st line drugs</td>
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Common Features in our Cases

• No identified risk factors for low therapeutic levels
• Slow clinical response led to testing
• All required longer treatment due to delayed clearance
• ? Role of stage / burden of disease

Areas for Research

• Correlation between drug levels and outcomes for 1st-line drugs
• Role of TDM in TB treatment
• Factors that predict subtherapeutic levels
• Markers of metabolism of TB drugs