

**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



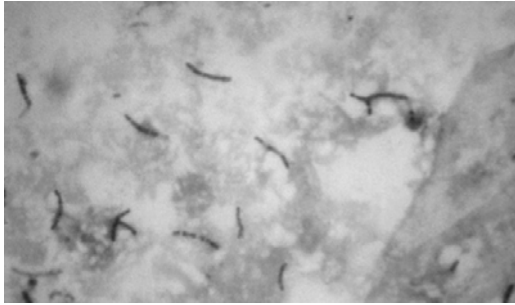


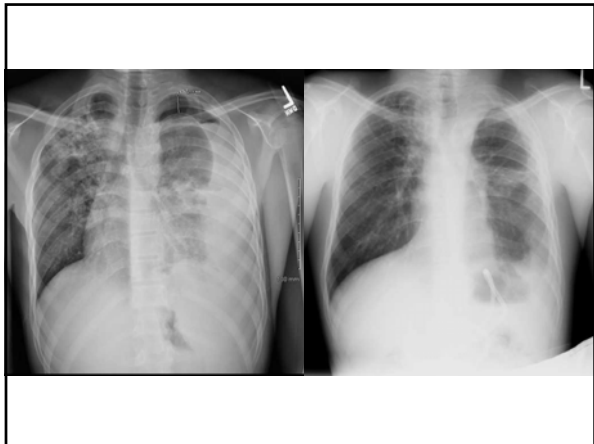
Image compliments of Tennessee Dept. of Health Tuberculosis Guidelines and Recommendations

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

Advantages

- Ensure adequate levels
- Potentially decrease risk of resistance
- Avoid delays in clearance of bacteria

Disadvantages

- Cost
- Not routinely necessary for clearance
- Wide therapeutic window for 1st line drugs

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
