TREATMENT OF TB DISEASE: IN THE CASE OF RESISTANCE

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Disclosures

- No financial affiliations with drug companies.
- Non-FDA approved uses of drugs will be discussed.
**First Line Drugs (New – 2002)**

- Isoniazid
- Rifampin
- Rifabutin
- Rifapentine
- Ethambutol
- Pyrazinamide

**Second Line Drugs (New – 2002)**

- Ethionamide
- Para-amino salicylic acid (PAS)
- Cycloserine
- Kanamycin
- Capreomycin
- Streptomycin
- Levofloxacin
Other Agents for TB

- Augmentin
- Clofazamine
- Carbapenems
  - Imipenem (Primaxin)
  - Meripenem (Merrem)
  - Ertapenem (?)
- Linezolid

First Versus Second Line

- Toxicity
- Tolerability
- Experience
- Efficacy
- Cost
Efficacy

• Bacteriocidal
  – Ability to kill
    • INH
    • Rifamycins
    • PZA
    • Aminoglycosides
      – STM, Amikacin, Kanamycin, CAP
    • EMB (in high doses)
    • Quinilones
    • Clofazamine (slowly)
    • Linezolid

Efficacy

• Bacteriostatic
  – Ability to inhibit the multiplication of the organism
    • EMB (low dose)
    • PAS
    • Ethionamide
    • Cycloserine
Efficacy Measures

- MIC
  - Minimal inhibitory concentration
  - Lowest concentration of drug that inhibits growth
- MBC
  - Minimal bacteriocidal concentration
    - Lowest concentration of drug that kills the organism
- CRITICAL CONCENTRATION
  - Lowest concentration that inhibited the growth of 99% of 100 different wild strains of TB.

Sensitivity

- Ability of a drug to kill or inhibit an organism at concentrations that are achievable in the plasma without toxicity
- Described in terms of MIC
## Resistance

- Increased need for higher plasma levels of drug to kill or inhibit
- Described in terms of increasing MIC

### MIC

<table>
<thead>
<tr>
<th>DRUG</th>
<th>S</th>
<th>MS</th>
<th>MR</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>&lt; 0.1</td>
<td>0.2 - 1.0</td>
<td>2.0</td>
<td>&gt; 4</td>
</tr>
<tr>
<td>RIF</td>
<td>&lt; 0.5</td>
<td>1.0 - 4.0</td>
<td>8.0</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>EMB</td>
<td>&lt; 2.0</td>
<td>4.0</td>
<td>8.0</td>
<td>&gt; 16</td>
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<tr>
<td>STM</td>
<td>&lt; 2.0</td>
<td>4.0</td>
<td>8.0</td>
<td>&gt; 16</td>
</tr>
</tbody>
</table>
Acquisition of Resistant TB

- Primary resistance
- Secondary resistance

Resistance

- Primary resistance
  - STM $1 \times 10^5$
  - INH $1 \times 10^6$
  - EMB $1 \times 10^6$
  - RIF $1 \times 10^8$
- Secondary resistance
  - Created during treatment
Secondary Resistance

• Non-compliance
• Non-compliance
• Inadequate treatment
  – Dose
  – Combination
  • Drug A kills bugs resistant to Drug B
  • While Drug B kills bugs resistant to Drug A
• Thick-walled cavities or poor penetration into site of ifx
• LOW SERUM DRUG LEVELS
  – Therapeutic drug levels

Genes Involved In TB Drug Resistance

- INH
  - inhA
  - katG
  - oxrR
  - ahpC
  - kasA
- RIF
  - rpoB
- EMB
  - embA
  - embB
  - embC
- PZA
  - pncA
- SM
  - rpsL
  - rrs
  - strA
- CAP
  - tlyA
- QUINALONES
  - gyr1
  - gyrB
Treatment of TB: In the Case of Resistance

**Resistance**

- Partial
  - INH, EMB, SM
- Total
  - RIF

**Epidemiology of Resistant TB**

<table>
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<tr>
<th>DRUG</th>
<th>% NEW</th>
<th>% RE-TX</th>
<th>% ALL</th>
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<tr>
<td>INH</td>
<td>8.2</td>
<td>21.5</td>
<td>9.1</td>
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<tr>
<td>RIF</td>
<td>3.5</td>
<td>9.0</td>
<td>3.9</td>
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<tr>
<td>PZA</td>
<td>5.0</td>
<td>17.6</td>
<td>5.8</td>
</tr>
<tr>
<td>EMB</td>
<td>2.3</td>
<td>3.8</td>
<td>2.4</td>
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</tbody>
</table>

Definitions

- **MDR** MULTI-DRUG RESISTANCE
  - Resistant to INH and RIF

- **XDR** EXTENSIVE DRUG RESISTANCE
  - Resistant to INH, RIF, a quinolone, at least one injectable (SM, KAN, AMK, CAP)

- **TDR** TOTAL DRUG RESISTANCE
  - Resistant to all standard TB drugs

TREATMENT OF MDR/XDR/TDR

- TREATMENT IS EXTENDED TO 24 MONTHS
  - AND AT LEAST 18 MONTHS POST CULTURE CONVERSION
- 6-MONTHS OF AN INJECTABLE POST CONVERSION
- TREAT WITH 4 TO 6 DRUGS TO WHICH PATIENT IS SENSITIVE
Fall is for black cats

TDR

- Patient is a 20 year old; Hispanic male; from Peru; entered US 4/2007.
- Patient claims in 9/07 developed fevers, productive cough and 10 pound weight loss.
- Patient hospitalized at a local Hospital in FL 10/13-11/27/2007 after he developed hemoptysis-told hospital staff coughing for 2 weeks. (Was placed in an Airborne Infection Isolation Room within 20 minutes of entering the ER)
- HIV (-)
- CXR on 10/13/2007—abnormal, bilateral infiltrates mostly in RUL and 4cm cavity in RUL.
TDR

- Patient denies a previous history of TB or being treated for TB in the past.
- Patient denies knowing anybody with TB
- Patient from Lima, Peru came to the US as a student to learn English (Was in a large high school in an English as second language classes from 1/07-5/07-3 mths before he claimed he had symptoms).
Treatment of TB: In the Case of Resistance

- Patient initially smear negative so bronchoscopy performed on 10/16/2007
- No endobronchial lesions, friable mucosa, no clear site of bleeding
- Bronch wash and brushing AFB (+)
- HD notified on 10/19/2007 by local Hospital

Hospital Specimens (Cultures done at Sekot Labs-Miami Lakes)
- AFB Bronch Brush RUL 10/16/2007 AFB + Moderate
- + AFB sputum smear 10/20/2007—Many AFB seen-Culture + Mod Growth 11/13/2007 "Genetic Probe Positive for MTC"—Reported 11/9/07-Test performed by Focus Technologies Cypress CA-Susceptibilities done by Sekot labs show resistance to first line meds reported 12/18/2007 from Sekot labs but sent by Focus Diagnostics in Cypress CA
- + AFB sputum smear 10/24/2007—Rare AFB seen-Culture pending
- + AFB sputum smear 10/25/2007—Many AFB seen-Culture + Light Growth 11/13/07
- + AFB sputum smear 10/26/2007—Rare AFB seen-Culture + <10 colonies 11/26/07
- + AFB sputum smear 10/28/2007—Many AFB seen-Culture + Mod Growth 11/26/07
- + AFB sputum smear 11/1/2007—Many AFB seen-Culture + Mod Growth 11/27/07
- + AFB sputum smear 11/2/2007—Mod AFB seen-Culture + Light Growth 11/27/07
- No AFB seen 11/5/2007-Culture + < 10 colonies 12/17/07
- Few AFB seen on smear 11/6/2007-Culture + Light Growth 11/27/07
- Many AFB seen on smear 11/7/2007-Culture + Mod Growth 11/27/07
- Few AFB seen on smear 11/12/2007-Culture + Light Growth 12/3/07
- Many AFB seen on smear 11/13/2007-Culture + Light Growth 12/3/07
- No AFB seen 11/19/2007-Culture pending

S H A R E  •  L E A R N  •  C U R E
TDR

- Initially Sputum AFB Smear (-)
- Given CXR and CT findings patient started 4-drug initial regimen RIPE on 10/13/2007.

TDR

- Discharged from Hospital 11/27 still smear + but decreased numbers and clinically responding.
- Waited because small children in house and wanted them to be evaluated and started on INH as well as assure the patient was less contagious.
Patient wants to fly home to Peru.

On 12/19, HD received information that patient was resistant to I/R/E/SM (PZA pending)

After discussions, a decision to admit patient to AGH made. Discussed with patient and family who agreed.

Patient admitted to Florida’s A.G. Holley State TB Hospital on 12/21/07

What Treatment Now?
WHAT TREATMENT NOW?

- A. KEEP HIM ON SAME REGIMEN (RIPE) PENDING CONFIRMATION LABS
- B. STOP ALL MEDS AND AWAIT CONFIRMATION LABS
- C. KEEP ON SAME REGIMEN AND ADD A QUINOLONE, ETHIONAMIDE AND PAS
- D. STOP ALL MEWDs AND START A QUINOLONE, STREPTOMYCIN AND PAS
- E. SHIP HIM HOME TO PERU AND LET THEM WORRY ABOUT IT

TDR

Upon AGH Admission Patient Started on:

- INH 900mg po BIW
- EMB 2.4gm po BIW
- PZA 1500mg po qD
- Rifabutin 300mg po qD
- Moxifloxacin 800mg po qD
- Cycloserine 250mg po qD
- Imipenem 1500mg IV q12 hrs
- Capreomycin 1gm IV TIW
- Vit B6 200mg po qD

Add at least 2 drugs that patient has not seen (usually at least an aminoglycoside and a Quinilone)
Rifabutin

• Trade Name: Mycobutin
• Derivative of rifampin
• Approved for prevention of MAC
• Trials for prevention of \( M. tb \) began in February of 1995
• Interferes with DNA synthesis
• Bactericidal or bacteriostatic

Rifabutin

• Kinetics
  - Widely distributed in body
    • lipophilic
    • crosses cell wall
  - Expected serum levels = 0.3 – 0.9 mcg/ml
    • Lung concentrations 5-10 times higher than serum levels
  - Half-life – 45 hours
  - Dose
    • 5 mg/kg/d or 300 mg po qd, BIW, or TIW
Rifabutin

- Discolors body fluids
- Cross-hypersensitivity with rifampin
- Cross-resistance with rifampin
  - ~5% sensitive when resistant to RIF
- Less hepatic effects than RIF
  - Useful in hepatitis patients
- Less potent enzyme inducer than RIF
  - Can use with most HIV PI

Rifabutin

- Adverse Drug Reactions:
  - Neutropenia – dose related
  - Hepatitis < 1%
  - Rash < 0.1%
  - Flu-like syndrome < 0.1%
  - Uveitis
    - 8% at higher doses, macrolides, Protease Inhibitors
### Quinilones

- **Ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin**
- **Bacteriocidal**
- **Broad spectrum**
- **MOA** - Interfere with bacterial DNA gyrase
- **Expected serum levels**
  - Oflox, levoflox 8-12 mcg/ml
  - Moxiflox 3 - 5 mcg/ml

<table>
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<tr>
<th>Quinilones</th>
<th>Doses</th>
<th>Expected Drug Levels</th>
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<tr>
<td></td>
<td>Ofloxacin 800 mg/day/ml</td>
<td>Ofloxacin 8 - 12 mcg</td>
</tr>
<tr>
<td></td>
<td>Levofloxacin 750 mg/day</td>
<td>Levofloxacin 8 - 12</td>
</tr>
<tr>
<td></td>
<td>Moxifloxacin 400 mg/day</td>
<td>Moxifloxacin 3 - 5</td>
</tr>
</tbody>
</table>
Quinilones

- ADR
  - Seizures, toxic psychosis, insomnia, tremor
  - Stevens-Johnson
  - Tendonitis/rupture
  - Cataracts, opacities
  - Pseudomembranous colitis
  - Premature closure of epiphiseal plates
  - Phototoxicity
  - Q-T prolongation

Quinilones

- Drug Interactions
  - Antacids
  - Zinc, iron salts
  - Cimetidine increases quinilone levels
  - Rbt + Moxi -> lower moxi levels
  - Ciprofloxacin +
    - Theophylline increases Theo levels
    - Anticoagulants increase bleeding
    - Phenytoin increases Phenytoin levels
Aminoglycosides

- Streptomycin, Amikacin, Kanamycin
  - Capreomycin (polypeptide abx)
- Bacteriocidal
- MOA
  - Inhibits protein synthesis
  - Does not penetrate cells or caseous material
    - Work extracellularly
  - Post antibiotic effect

Aminoglycosides

- Dose IM or IV
  - Child: 20-40 mg/kg/day
  - Adult: 15 mg/kg/day (max 1 gm/d)
    - 25-30 mg/kg/tiw (max 1.5 gm/d)
    - 750 mg for those > 60 years
    - TIW is all that is necessary
  - Adjust in renal disease, elderly
    - Better to reduce frequency than dose
  - Contraindicated in pregnancy
Aminoglycosides

• Drug Interactions
  — Loop diuretics
  — PCN/cephalosporins

• Monitor
  — Renal function
  — Hearing
  — Vestibular function
  — Peripheral pain, tingling, etc

Streptomycin

• ADR
  — 8th nerve damage
    • Ototoxicity, vestibular
      — ~16%
  — Nephrotoxicity
    • Least likely of the AMG, < 2% req dc
  — Numbness, tingling
  — Acute OBS, depression
**Kanamycin/Amikacin**

- Same as streptomycin
- No(?) cross-resistance with STM, CAP
- KAN cross-resistance with AMK
- Ototoxicity
  - 1.5% to 24%
- Nephrotoxicity
  - 3.4% to 8.7%

**Capreomycin**

- TN
  - Capastat
- Bactericidal peptide antibiotic
  - Similar to aminoglycosides
- Dose
  - 15 mg/kg/day
  - Maximum
    - 1 gm/day
    - IM or IV
- ADR
  - Same as aminoglycosides
    - nephrotoxicity ~20-36%
    - ototoxicity ~11%
Ethionamide (ETA)

- **Trade name:**
  - Trecator-SC
- **Bacteriostatic**
- **Related to INH**
  - Some cross-over resistance
  - INH-A gene -> low level resistance to INH and total resistance to ETA
- **Dose**
  - 250 mg 2 to 4 times a day with food
  - EXPECTED SERUM LEVELS 1-5 MCG/ML

Ethionamide

- **ADR**
  - GI Intolerance
  - Jaundice, hepatitis – 2%
  - Peripheral, optic neuritis – 1-2%
  - Psychosis, depression
  - Gynecomastia, impotence
  - Teratogenic in high doses
  - Endocrine disturbances
Para-Aminosalicylic Acid (PAS)

- **Bacteriostatic**
- **Dose**
  - 4 gm packet bid - tid
    - Sprinkled on soft food or in beverage
    - Adjust dose for renal insufficiency
  - EXPECTED SERUM LEVEL 10-60 MCG/ML @ 6HR
  - Keep in refrigerator
  - Discard if discolored
- Use caution in CHF, HTN

PAS

- **ADRs**
  - GI – n/v/diarrhea/abdominal pain
    - MAL ABSORPTION SYNDROME
  - Hypersensitivity reaction
    - Fever, rash, leukopenia, agranulocytosis
    - Thrombocytopenia, hepatitis, encephalopathy
  - Crystalluria
    - Encourage fluids
  - Hepatitis – more common in diabetics
- **DI**
  - VITAMIN B-12 DEPLETION, CONSIDER SUPPLEMENTATION
Cycloserine (CS)

- **Trade Name**
  - Seromycin
- **Bacteriostatic**
- **MOA**
  - Inhibits cell wall synthesis
- **Dose**
  - 250 mg – 1 gm daily, divided doses
  - Reduce dose in renal insufficiency
  - Expected serum levels 20 -30 mcg/ml

Cycloserine

- **ADR**
  - CNS
    - Convulsions
    - Tremor
    - Confusion
    - Somnolence
    - Psychosis
    - Aggression
    - Allergic dermatitis
- **Narrow therapeutic range**
  - Charcoal
  - Hemodialysis
  - Vitamin B6
- **Monitor**
  - Serum levels
  - Renal function
  - CNS side effects
Other Agents – 1

• Clofazamine
  – New availability issues
  – Distributed through National Hansen’s Disease Program
  – Individual patient Ind
  – FDA
    • Center for Drug Evaluation and Research
    • (301) 827-2127

Clofazamine

• TN
  – Lamprene

• MOA
  – Slow bactericidal effect
  – Binds to M. tb DNA to inhibit growth

• Dose
  – 200 mg po qd
  – Expected serum levels: 0.5 – 2.0 mcg at 2 hrs
Clofazamine

- ADR
  - Severe GI pain
  - Crystal deposits in gut, liver, gall bladder, etc.
  - Skin pigmentation
    - Also cornea and conjunctiva
  - Skin dryness and itching
  - Discolored sputum, sweat, feces, urine
- Excreted in breast milk

Carbipenems

- Imipenem, meripenem, ertipenem(?)
- IV only
- Once or twice daily dosing
- Generally combined with an AMG
- Use for at least 6 months post conversion
- Cross hypersensitivity with PCNs, cephalasporins
- Monitor renal function
**Carbapenems**

- ADR
  - Seizures
  - Nephrotoxicity
  - Rash

**LINEZOLID**

- Trade name: Zyvox
- Bactericidal
- MOA:
  - Inhibits bacterial protein synthesis

ADR:
- lactic acidosis
- myelosuppression
  - thrombocytopenia, leucopenia, pancytopenia
  - peripheral and optic neuropathy
    may be irreversible -> blindness
LINEZOLID

**Drug Interactions**
- Moderate MAOI activity results in many potential DI
  - Antidepressants
  - Decongestants (pseudoephedrine, phenylephrine)
  - Meperidine, Dilaudid, cyclobenzaprine (Flexeril), tramadol
  - \( \rightarrow \) serotonin syndrome
    - Agitation, confusion, hallucinations, shivering, tachycardia, hyper-reflexia, hypertensive crisis
- **Food interactions**
  - Serotonin, tyramine containing foods
    - Alcohol, aged cheese, pickles, sauerkraut, soy sauce, bananas, avocados, pickled fish or meats

**DOSE:**

?? 10 MG/KG/DAY OR 600 MG DAILY

Optimal dose has not been determined

Monitor:

- CBC weekly
- Peripheral and optic neuropathy (vision)
On 1/11/08 received following report from specimen of 10/20/07-confirmed by both Focus Diagnostics as well as FL State TB Lab Jax:

<table>
<thead>
<tr>
<th>Organism</th>
<th>MTB</th>
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<td>PZA 100</td>
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<td>R</td>
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<td>R (100%)</td>
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<tr>
<td>SM 1.0</td>
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<td>R</td>
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<td>SM 2.0</td>
<td>R</td>
<td>R</td>
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<tr>
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<td>R</td>
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<td>Ciprofloxacin 2</td>
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<td>R (12.5%)</td>
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<td>Pyrazinamide</td>
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<td>R</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Streptomycin</td>
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<tr>
<td>Pyrazinamide</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Ethambutol</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Rifampin</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Isoniazid</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>Streptomycin</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td></td>
</tr>
</tbody>
</table>

Treatment of TB: In the Case of Resistance

32
TDR

• What regimen would you place this patient on?

WHAT WOULD YOU DO NOW?

• A. STOP EVERYTHING AND PUT HIM ON AMK AND CLOFAZAMINE AND CYCLOSERINE
• B. KEEP HIM ON EVERYTHING ADD AMK, CLOFAZAMINE, AND LINEZOLID
• C. STOP EVERYTHING AND PUT HIM ON PZA, CYCLOSERINE AND LINEZOLID
• D. I HAVE NO IDEA
• E. SEND HIM BACK TO PERU
• F. NONE OF THE ABOVE
TDR-TB

Once susceptibilities returned the following medications were utilized:

- Linezolid 600mg po qD
- PAS 4 gms po (BID increased to TID after levels)
- Clofazamine 200mg po qD
- Cycloserine 250 alt 500mg qOD
- Moxifloxacin 800mg po qD
- Imipenim 1500mg IV BID and Capreomycin 1 gm IV TIW (for 6 m after culture (-))
- B6 200mg po qD

<table>
<thead>
<tr>
<th>TDR</th>
<th>Drug (crit conc)</th>
<th>2 Hr</th>
<th>6 Hr</th>
<th>Expected Peak (mcg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PAS 4gm TID (2.0-12%R, 6.0-S)</td>
<td>46.30</td>
<td>10-60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Linezolid 600mg qD (2.0 S)</td>
<td>2.6</td>
<td>10.15</td>
<td>12-26</td>
</tr>
<tr>
<td></td>
<td>CAP 1gm TIW (4.0-I, 10.0-S)</td>
<td>41.71</td>
<td>7.26</td>
<td>35-45</td>
</tr>
<tr>
<td></td>
<td>Clofaz 200mg qD (0.06 S)</td>
<td>0.62</td>
<td>0.83</td>
<td>0.5-2.0</td>
</tr>
<tr>
<td></td>
<td>Moxi 800mg qD (1.0 S)</td>
<td>2.45</td>
<td>4.25</td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>Cycloserine 250mg qD (30.0 S)</td>
<td>17.7</td>
<td>9.6</td>
<td>20-35</td>
</tr>
</tbody>
</table>
Treatment of TB: In the Case of Resistance

TDR

- Requires close monitoring for adverse reactions including:
  - CBC
  - metabolic panel
  - TFTs
  - renal and hepatic function
  - audiometry and vestibular function,
  - peripheral neuropathy
  - color and visual acuity
  - psychiatric

ADR

- Treatment of symptoms
  - Gout/joint/muscle pains
    - Allopurinol, colchicine, probenecid
    - NSAIDS
  - Insomnia
    - Hydroxyzine, Diphenhydramine, Trazodone
  - Peripheral neuropathy
    - B6
    - gabapentin
GI Intolerance

- Give at bedtime
- Give after meals
- Pre-medicate 30 minutes before TB meds with:
  - Metoclopramide 5 – 10 mg
  - Promethazine 25 mg
  - Hydroxyzine 25 – 50 mg
  - Lorazepam 0.5 – 1 mg
  - Ondansetron 4 – 8 mg

ADR

- Diarrhea
  - Immodium
  - Lomotil
  - TR of Opium

- Itching
  - Diphenhydramine
  - Hydroxyzine
Who should have TDM?

- Patients failing treatment
- Pts with possible toxic SE
- Pts with renal or hepatic dysfunction
- Drug interactions
- Compliance checks
TB DRUG LEVELS

- Pt on drug/dose for ~ 2 weeks
- Ideally done at the time and the way pt normally takes the drug
- Draw 2 levels
  - Peak level
    - 2 hrs post dose for most TB drugs
      - 3 Hrs for RBT
      - 6 hrs for PAS
  - Psuedo trough level
    - 6 hrs post dose
    - Serves as a check on 2 hr level

TB DRUG LEVELS

- Need ~ 1ML per drug level
- Use a red-top tube
- Spin, separate, freeze
- Ship frozen
- Results usually within 2 weeks
MIC Versus Concentration

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PK [ ]</th>
<th>MCG/ML MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>3 – 5</td>
<td>0.01 – 0.25</td>
</tr>
<tr>
<td>RIF</td>
<td>8 – 24</td>
<td>0.06 – 0.25</td>
</tr>
<tr>
<td>PZA</td>
<td>20 – 60</td>
<td>6.2 – 50</td>
</tr>
<tr>
<td>EMB</td>
<td>3 – 5</td>
<td>0.5 – 2.0</td>
</tr>
<tr>
<td>STM</td>
<td>35 – 45</td>
<td>0.25 – 2.5</td>
</tr>
<tr>
<td>CAP</td>
<td>35 – 45</td>
<td>1.25 – 2.5</td>
</tr>
<tr>
<td>OFLOX</td>
<td>8 – 10</td>
<td>0.25 – 2.0</td>
</tr>
</tbody>
</table>

HOW LONG WOULD YOU TREAT?
Treatment of TB: In the Case of Resistance

How Long Would You Treat Him?

- A. 1 YEAR
- B. 2 YEARS
- C. 1 YEAR AFTER CULTURE CONVERSION
- D. 18 MONTHS AFTER CULTURE CONVERSION
- E. 2 YEARS AFTER CULTURE CONVERSION

How Long Would You Treat Him?

Completed therapy on 7/3/09, 18 months after culture negative therapy
TDR-TB

- Patient smear and culture negative since 1/3/08
- Patient denies any adverse effects
- Patient has been “mostly” taking medications

Where to Get More Information

1-800-4TB-INFO