Treatment of Tuberculosis Disease

Objectives

- Review treatment guidelines
- Monitoring during therapy
- Adverse effects
- HIV, pregnancy, renal failure

Treatment Guidelines
Tenets of Therapy

- 6 months minimum treatment
- Multidrug therapy
- Directly observed therapy (DOT)

Current Drugs Available

First Line Drugs
- Isoniazid
- Rifampin
- Rifapentine
- Rifabutin*
- Ethambutol
- Pyrazinamide

Second Line Drugs
- Cycloserine
- Ethionamide
- Levofloxacin*
- Moxifloxacin*
- Gatifloxacin*
- p-Aminosalicylic acid
- Streptomycin
- Amikacin/kanamycin*
- Capreomycin
Treatment Algorithm

Treatment Related Risk Factors for Early Relapse of TB

- Evaluation of 113 cases of relapsed Tb when matched with case controls
  - Non-cavitary Tb, relapse rate: 1.1%
  - Cavitary Tb relapse rates:
    - Thrice weekly Rx: 7.8%
    - Daily Rx: 3.3%
    - Extended thrice weekly: 0.5%
    - Extended daily 0.4%
    - Extending either intensive phase or both was beneficial

Chang, Am J Respir Crit Care Med. 2004; 170: 124-30
Monitoring During Drug Therapy

Monitoring

- Baseline Testing
  - SPUTUM!!!
  - HIV Testing
  - Liver Enzymes
  - Creatinine
  - Platelet Count
  - Visual Testing if on Ethambutol

Follow-up monitoring

- Repeat sputum stains and cultures monthly until negative
- Repeat liver enzymes in high risk patients
- Consider repeat platelet and creatinine in patients with baseline abnormalities
- Toxicity screening
Adverse Events

- Isoniazid (INH)
  - Asymptomatic transaminitis (10%-20%)
  - Hepatitis

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TABLE 10. Clinical hepatitis in persons taking isoniazid and rifampin

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of studies</th>
<th>Patients</th>
<th>Clinical Hepatitis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>6</td>
<td>38,237</td>
<td>0.6</td>
</tr>
<tr>
<td>INH plus other drugs but not Rif</td>
<td>19</td>
<td>2,053</td>
<td>1.6</td>
</tr>
<tr>
<td>INH plus Rif</td>
<td>19</td>
<td>6,165</td>
<td>2.7</td>
</tr>
<tr>
<td>Rif plus other drugs but not INH</td>
<td>5</td>
<td>1,364</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Definition of abbreviations: INH = isoniazid; Rif = rifampin.
### Adverse Events

**Isoniazid (INH)**
- Asymptomatic transaminitis (10%-20%)
- Hepatitis (0.6%-2.7%)
- Peripheral neuropathy (0.2%)
- Lupus-like syndrome (1%)
- Hypersensitivity reaction (rare)
- Diarrhea (with liquid formulation)

**Rifampin**
- Pruritic rash (6%)
- GI upset
- Myalgias (0.5%)
- Hepatitis
- Orange discoloration of body fluids (100%)

**Pyrazinamide**
- Hepatotoxicity (1%?)
- GI upset (common)
- Arthralgia (40%)
- Gouty arthritis (in predisposed patients)
- Photosensitivity dermatitis
Adverse Events

- Ethambutol (EMB)
  - Retrobulbar neuritis
  - Peripheral neuropathy (rare)
  - Rash (<0.7%)

Special Situations

- Active TB in HIV
  - Same as HIV negative except...
  - If CD4+ <100/ul
    - Daily or 3x/week therapy in continuation phase
  - Immune reconstitution syndrome
    - May delay initiation of anti-retroviral therapy for few weeks
  - DRUG INTERACTIONS!
Active TB in Pregnancy

- Risk of untreated TB usually outweighs risk of therapy
  - INH
  - Rifampin
  - Ethambutol
  - (Pyrazinamide)
- 9 months of therapy if no PZA
- Pyridoxine supplementation

Active TB in Renal Failure

<table>
<thead>
<tr>
<th>Drug</th>
<th>Change in frequency (per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>No change, 15 mg once daily, or 30 mg twice weekly</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Yes, 15 mg once daily, or 30 mg twice weekly</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Yes, 15-30 mg/kg once daily, or 30 mg twice weekly</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Yes, 15-30 mg/kg once daily, or 30 mg twice weekly</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Yes, 15-30 mg/kg once daily, or 30 mg twice weekly</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>Yes, 15-30 mg/kg once daily, or 30 mg twice weekly</td>
</tr>
</tbody>
</table>

Active TB in Severe Liver Disease

- Treatment without INH
  - Rifampin, PZA, EMB for 6 months
- Treatment without PZA
  - INH, Rifampin, EMB for 9 months
- Treatment with only one hepatotoxic agent
  - Rifampin plus 2 second line drugs for 12-18 months
- Treatment with no hepatotoxic agents
  - 4 drug therapy (which?) for up to 2 years
Multidrug Resistant TB

Extensive-drug Resistant TB

- Call an expert

More Information

- www.cdc.gov
- “Treatment of Tuberculosis” MMWR, vol 52, June 2003