Treatment Module
Comprehensive TB Clinical Course

Connie A. Haley, MD MPH
Southeast National TB Center
University of Florida
Division of Infectious Diseases and Global Medicine
General Principles of Chemotherapy for TB Disease

1. Reduce the bacillary population rapidly, thereby decreasing severity of disease, preventing death and halting transmission of MTB

2. Eradicate persisting bacilli in order to prevent relapse after completion of therapy

3. Prevent acquisition of drug resistance during therapy through use of multidrug therapy
General Principles of Chemotherapy for TB Disease

• Existence of mutant bacilli with *innate resistance* to antibiotic action that occur at constant low rates

• Slow or intermittent growth of mycobacterium permits the persistence of viable organisms despite prolonged antibiotic treatment, because only actively replicating organisms are killed by antibiotics

• Combination therapy required for “durable” cure
Treatment of Active Tuberculosis

• Initial treatment aimed at
  - Extracellular organisms
  - Sterilize sputum
  - Reduce infectivity

• Secondary treatment aimed at
  - Eradicating persisting organism from
    • Macrophage
    • Granulomas
Treatment of Active Tuberculosis

Site of activity of TB drugs

<table>
<thead>
<tr>
<th>DRUG</th>
<th>EXTRACELLULAR</th>
<th>MACROPHAGE</th>
<th>GRANULOCYTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>++</td>
<td>+</td>
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<tr>
<td>RIF</td>
<td>++</td>
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<tr>
<td>PZA</td>
<td>++</td>
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<tr>
<td>EMB</td>
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<td>STM</td>
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Major Goals of Tuberculosis Treatment

• Provide safest, most effective therapy in the shortest period of time
• Minimize drug toxicity
• Maximize the likelihood of treatment completion
Factors Influencing TB Treatment Outcomes

- **Patient**: age, comorbid conditions, immune status, nutritional status, ETOH use
- **Radiographic features**: extent of disease, cavities on CXR
- **Microbiology**: baseline colony count, culture positivity at 2-3 months
- **Pharmacokinetic**: drug absorption
- **Regimen**: number of active drugs, duration of therapy
- **Programmatic**: case management, adherence support, DOT
Patient-Centered Care

“Providing care that is respectful of and responsive to individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions.”

---The Institute of Medicine, 2001
Case Management

1. Educate patients about TB, its treatment, including possible side effects
2. Discuss expected outcomes, specifically the ability to **cure** the patient of the disease
3. Review methods of supervision and assessing response to therapy
4. Discuss infectiousness and infection control measures using terminology appropriate to age, culture, language, reading level of the patient
Develop Treatment and Monitoring Plan

Plan should include:

• Description of treatment regimen
• Methods for assessing/ensuring adherence
• Monitoring methods for treatment response and adverse events
### Enablers/Incentives for Adherence

**Table 4. Possible Components of a Multifaceted, Patient-Centered Treatment Strategy**

<table>
<thead>
<tr>
<th>Enablers</th>
<th>Incentives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventions to assist the patient in completing therapy [130]</td>
<td>Interventions to motivate the patient, tailored to individual patient wishes and needs and, thus, meaningful to the patient [130]</td>
</tr>
<tr>
<td>Transportation vouchers [30]</td>
<td>Food stamps or snacks and meals [30]</td>
</tr>
<tr>
<td>Clinic personnel who speak the languages of the populations served [428]</td>
<td>Assistance in finding or provision of housing [429]</td>
</tr>
<tr>
<td>Reminder systems and follow-up of missed appointments [28]</td>
<td>Clothing or other personal products [30]</td>
</tr>
<tr>
<td>Social service assistance (referrals for substance abuse treatment and counseling, housing, and other services) [429]</td>
<td>Books [428]</td>
</tr>
<tr>
<td>Outreach workers (bilingual/bicultural as needed; can provide many services related to maintaining patient adherence, including provision of directly observed therapy, follow-up on missed appointments, monthly monitoring, transportation, sputum collection, social service assistance, and educational reinforcement) [429]</td>
<td>Stipends [30]</td>
</tr>
<tr>
<td>Integration of care for tuberculosis with care for other conditions [428]</td>
<td>Patient contract [30]</td>
</tr>
</tbody>
</table>
Directly Observed Therapy (DOT)

- Preferred management strategy for all patients
  - Health-care worker watches patient swallow each dose
  - Can reduce acquired drug resistance, treatment failure, and relapse
  - Allows for early recognition of adverse drug reactions, treatment complications
Initiating TB Treatment
Deciding to Initiate Treatment

• Decision to start TB therapy is based on clinical, radiographic, laboratory, patient and public health factors

• Clinical judgement and index of suspicion play a critical role

• Empiric therapy with a 4-drug regimen is initiated:
  ➢ In patients with high likelihood of having TB
  ➢ In seriously-ill patients with a clinical presentation suspicious for TB
<table>
<thead>
<tr>
<th>Patient</th>
<th>Elevated concern for adverse treatment events (eg, severe liver disease, pregnancy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 2 years</td>
<td>No TB exposure risk</td>
</tr>
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<tr>
<th>Laboratory / Radiographic</th>
<th>Radiographic imaging not consistent with TB</th>
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<tr>
<td>Risk for progression/dissemination (eg, HIV, TNF alpha inhibitor)</td>
<td>Evidence of Mtbi infection (ie, positive TST or IGRA)</td>
</tr>
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<td>Age &lt; 2 years</td>
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<table>
<thead>
<tr>
<th>Clinical Status / Suspicion</th>
<th>AFB smear positive, Rapid molecular test negative</th>
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</thead>
<tbody>
<tr>
<td>Life-threatening disease</td>
<td>AFB smear positive, Rapid molecular test negative</td>
</tr>
<tr>
<td>Symptoms typical for TB</td>
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<tr>
<th>Public Health</th>
<th>Favors Treatment Initiation</th>
<th>Favors Delayed or No Treatment</th>
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<tr>
<td>Concern for loss to follow-up</td>
<td>High transmission risk (eg, congregate setting, corrections)</td>
<td>Low transmission risk</td>
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**Figure 1.** Factors to be considered in deciding to initiate treatment empirically for active tuberculosis (TB) (prior to microbiologic confirmation). Abbreviations: AFB, acid-fast bacilli; HIV, human immunodeficiency virus; IGRA, interferon-γ release assay; Mtb, *Mycobacterium tuberculosis*; TNF, tumor necrosis factor; TST, tuberculin skin test.
Case 1—Mr. P

- February: 36 yo Peruvian male presents to ER with cough, fever and hemoptysis
- Former smoker
- No ETOH use
- HIV negative
- Treated for pneumonia with levofloxacin with initial improvement in symptoms
Case 1—Mr. P

• April: Continues to complain of “chest tightness,” cough, sore throat
• Seen in Urgent Care
• Given Z-pak (azithromycin)
• Symptoms improved initially
Case 1—Mr. P

- May: Presents to ER c/o
  - Hemoptysis
  - Cough
  - Fever
- CXR worsening upper lobe infiltrate, now with cavitary lesion
- Placed in isolation
- Sputum smear AFB+
- TST+

Would you start on TB treatment? Why or why not?
### Deciding to Initiate Treatment

- **Decision to start TB therapy based on clinical, radiographic, laboratory, patient and public health factors**

- **Clinical judgement and index of suspicion play a critical role**

- **Empiric therapy with a 4-drug regimen is initiated:**
  - In patients with high likelihood of having TB
  - In seriously ill patients with a disorder suspicious for TB

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### Treatment of Drug-Susceptible Tuberculosis

** Clin Infect Dis. 2016 Oct 1;63(7):853-67 **

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Case 2—Mr. T

• 63 yo African-American gentleman
• Presents with 4 months of feeling poorly, 25-30 lb weight loss, failure to thrive, cough, increasing dyspnea on exertion
• BMI: 18
• Recently complaining of nausea/vomiting
• Daily ETOH use: 2 x 40 oz
• Long-term smoker
Heterogeneous consolidation in posterior and anterior segments of both UL as well superior segment of the LLL. Lateral aspect of consolidation in LUL is confluent with a full area of cavitation. Several other smaller probable cavities are noted more medially in LUL. This pattern may represent pneumonia although malignancy should be considered most highly. There are calcifications in the mediastinum at the level of the left paraspinal region and the azygos node. These probably represent calcifications in lymph nodes. There is no pleural effusion.
Case 2—Mr. T

- Placed in airborne precautions
- Sputum smear positive for AFB
- TST 0 mm induration
- Quantiferon negative
- HIV negative
- Would you start TB treatment?
- Why or why not?
### Deciding to Initiate Treatment

Decision to start TB therapy based on clinical, radiographic, laboratory, patient and public health factors.

- Clinical judgement and index of suspicion play a critical role.
- Empiric therapy with a 4-drug regimen is initiated:
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Case 3—Mr. W

- 28 yo African-American gentleman presents with 2 weeks of cough, fever
- Treated for pneumonia with azithromycin
- Without a stable living situation
Case 3—Mr. W

• Presents to ER two months later with similar complaints: cough, right flank pain, 10 lbs. weight loss

• History of incarceration for 30 days—3 years ago

• Undocumented history of positive TST while incarcerated, untreated for LTBI
Case 3—Mr. W

- Placed in isolation
- AFB smear x 3 negative
- Undergoes bronchoscopy; AFB smear negative
- HIV negative
- Would you order additional tests?
- Would you start on TB treatment?
- Why or why not?
Deciding to Initiate Treatment

- Decision to start TB therapy based on clinical, radiographic, laboratory, patient and public health factors
- Clinical judgement and index of suspicion play a critical role
- Empiric therapy with a 4-drug regimen is initiated:
  - In patients with high likelihood of having TB
  - In seriously ill patients with a disorder suspicious for TB

Treatment of Drug-Susceptible Tuberculosis

- Clinically stable
- Symptoms not typical for TB
- Alternative diagnosis

- Concern for loss to follow-up
- High transmission risk (eg, congregate setting, corrections)
- Favors Treatment Initiation

- Elevated concern for adverse treatment events (eg, severe liver disease, pregnancy)
- No TB exposure risk
- Radiographic imaging not consistent with TB
- AFB smear positive, Rapid molecular test negative
- AFB smear negative, Rapid molecular test negative

- Risk for progression/dissemination (eg, HIV, TNF alpha inhibitor)
- Age < 2 years
- TB exposure risk (eg, contact, born in higher TB incidence country)
- Radiographic imaging consistent with TB
- Evidence of Mtb infection (ie, positive TST or IGRA)
- Extended time to microbiologic confirmation (eg, Rapid molecular test not available)
- Pathologic findings consistent with TB
- AFB smear positive, Rapid molecular test positive
- AFB smear negative, Rapid molecular test positive

- Life-threatening disease
- Symptoms typical for TB
- Alternative diagnosis less likely
- Favors Delayed or No Treatment

- Clinically stable
- Symptoms not typical for TB
- Alternative diagnosis

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- Low transmission risk

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Case 3—Mr. W

Pathology from bronchoscopy:
• Granulomatous pneumonitis accompanied by necrotic cellular debris (caseation)
• Acid Fast Bacterial Stain: Positive for Acid Fast Bacilli

AFB cultures became positive for AFB at three weeks
• Identified as TB one week later
• (NAAT not done...but could have made diagnosis sooner)
Case 4--Mrs. S

- 54 yo lady with diabetes, presents with 2-day history of fever, cough, worsening shortness of breath
- Placed in airborne isolation due to remote history of positive TST
Case 4—Mrs. S

• She is improving on antibiotics
• One AFB sputum smear is negative and the TB PCR (NAAT) on that specimen is also negative
### Deciding to Initiate Treatment

- **Decision to start TB therapy** based on clinical, radiographic, laboratory, patient and public health factors.
- **Clinical judgement** and index of suspicion play a critical role.
- **Empiric therapy** with a 4-drug regimen is initiated:
  - In patients with high likelihood of having TB
  - In seriously ill patients with a disorder suspicious for TB

### Treatment of Drug-Susceptible Tuberculosis

#### Factors to be considered in deciding to initiate treatment empirically for active tuberculosis (TB) (prior to microbiologic confirmation):

- **Risk for progression/dissemination** (eg, HIV, TNF alpha inhibitor)
- **Age < 2 years**
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- **Radiographic imaging consistent with TB**
- **Evidence of Mtb infection** (ie, positive TST or IGRA)
- **Extended time to microbiologic confirmation** (eg, Rapid molecular test not available)
- **Pathologic findings consistent with TB**
  - AFB smear positive, rapid molecular test positive
  - AFB smear negative, rapid molecular test positive
- **Life-threatening disease**
  - Symptoms typical for TB
  - Alternative diagnosis less likely
- **Concern for loss to follow-up**
  - High transmission risk (eg, congregate setting, corrections)

- **Elevated concern for adverse treatment events** (eg, severe liver disease, pregnancy)
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- **AFB smear positive, rapid molecular test negative**
- **AFB smear negative, rapid molecular test negative**
- **Clinically stable**
- **Symptoms not typical for TB**
- **Alternative diagnosis**

#### Elevated concern for adverse treatment events

- **Low transmission risk**

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If Clinical Suspicion for Active TB is Low:

Defer treatment until additional data obtained

**OR**

*If patient has a positive TST or IGRA,* Consider starting 4-drug combination chemotherapy and if after two months of therapy:
- cultures remain negative
- no clinical improvement
- no change/improvement in x-ray

**THEN**

Stop therapy and consider patient as having completed treatment for LTBI (2 mos RIF/PZA)

“No Loose Solution”
TB Treatment: Drugs and Regimens
Current Anti-TB Drugs

11 drugs FDA-approved for treatment of TB

Isoniazid (INH)  Streptomycin (SM)
Rifampin (RIF)  Cycloserine
Pyrazinamide (PZA)  Capreomycin
Ethambutol (EMB)  $\rho$-Aminosalicylic acid
Rifapentine (RPT)  Ethionamide
  Bedaquiline
Current Anti-TB Drugs (cont.)

• Four first-line drugs considered standard treatment:
  - Isoniazid (INH)
  - Rifampin (RIF)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)

• Rifabutin and rifapentine also considered first-line drugs in some circumstances

• Streptomycin (SM) formerly first-line drug, but now less useful owing to increased SM resistance

• Fluoroquinolones (levofloxacin, moxifloxacin) can be substituted for first-line in the US if resistance, toxicity
Isoniazid (INH)

- Daily dose: 5 mg/kg → typically 300 mg
- Intermittent dose: 15 mg/kg → 900 mg
- INH absorption decreases when combined with glucose or lactose

**INH DRUG INTERACTIONS**

<table>
<thead>
<tr>
<th>Drug Interactions</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemics</td>
<td>Monitor glucose, may cause hyperglycemia</td>
</tr>
<tr>
<td>Tylenol</td>
<td>↑hepatotoxicity</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>↑anticoagulant effect</td>
</tr>
<tr>
<td>Valium (&amp;others)</td>
<td>↑valium toxicity</td>
</tr>
<tr>
<td>Carbamazepines</td>
<td>↑toxicity of both</td>
</tr>
<tr>
<td>Disulfiram (Antabuse)</td>
<td>Psychotic episodes</td>
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<tr>
<td>Haldol</td>
<td>↑haldol toxicity</td>
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<tr>
<td>Ketoconazole</td>
<td>↓ketoconazole effect</td>
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<tr>
<td>Dilantin</td>
<td>↑dilantin toxicity</td>
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<tr>
<td>Theophyllin</td>
<td>↑theophyllin toxicity</td>
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<tr>
<td>Valproate</td>
<td>↑hepatic and CNS toxicity</td>
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</table>
Isoniazid (INH)

- Side effects: GI intolerance, hepatitis, peripheral neuropathy
- To prevent peripheral neuropathy, give vitamin B6 25 mg daily to:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevention</th>
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<tbody>
<tr>
<td>HIV +</td>
<td>Diabetics</td>
</tr>
<tr>
<td>ETOH Abuse</td>
<td>Chronic Renal Failure</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Advanced Age</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>Breastfeeding Infants</td>
</tr>
</tbody>
</table>

- Give 100 mg B6 to patients to treat neuropathy
Rifampin (RIF)

• Daily dose: 10 mg/kg → typically 600 mg
• Intermittent dose: 10 mg/kg → 600 mg
• Side effects: red-orange urine, GI intolerance, hepatitis, flu-like syndrome

<table>
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<th>RIFAMPIN DRUG INTERACTIONS</th>
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<tr>
<td>Anticoagulants</td>
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<tr>
<td>Antidepressants</td>
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<tr>
<td>Beta-Blockers</td>
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<td>Contraceptives</td>
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<td>Corticosteroids</td>
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<td>Cyclosporine</td>
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<td>Protease Inhibitors</td>
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<tr>
<td>Trimethoprim-sulfamethoxazole</td>
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<td>Chloramphenicol</td>
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Ethambutol (EMB)

- Dosing based on weight

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<tr>
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<th>40–55</th>
<th>56–75</th>
<th>76–90</th>
</tr>
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<tbody>
<tr>
<td>Daily (mg/kg)</td>
<td>800 mg (14.5–20.0)</td>
<td>1200 mg (16.0–21.4)</td>
<td>1600 mg (17.8–21.1)</td>
</tr>
<tr>
<td>Thrice weekly (mg/kg)</td>
<td>1200 mg (21.8–30.0)</td>
<td>2000 mg (26.7–35.7)</td>
<td>2400 mg (26.7–31.6)</td>
</tr>
<tr>
<td>Twice weekly (mg/kg)</td>
<td>2000 mg (36.4–60.0)</td>
<td>2800 mg (37.3–50.0)</td>
<td>4000 mg (44.4–52.6)</td>
</tr>
</tbody>
</table>

* With normal renal function.
* Based on estimated lean body weight. Optimal doses for obese patients are not established.
* Numbers in parentheses are the calculated mg/kg doses for patients at the highest and lowest body weights in the weight band.

- Side effects: optic neuritis
Pyrazinamide (PZA)

- Dosing based on weight:

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<td>Daily (mg/kg)</td>
<td>1000 mg (18.2–25.0)</td>
<td>1500 mg (20.0–26.8)</td>
<td>2000 mg (22.2–26.3)</td>
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<td>Thrice weekly (mg/kg)</td>
<td>1500 mg (27.3–37.5)</td>
<td>2500 mg (33.3–44.6)</td>
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- Side effects: mild anorexia and nausea, dose-related hepatitis, polyarthralgias, hyperuricemia
- May be taken with food
Fluoroquinolones

- Daily dose: 400 mg moxifloxacin (MFX) or 500-1000 mg levofloxacin (LFX)
- Side effects:
  - GI upset
  - Tendonitis, tendon rupture
    - Mild-stop exercise, consider NSAIDS; rupture-stop drug
  - QT prolongation with other QTc prolonging drugs
  - CNS: headache, insomnia, confusion
- Take 2 hours before or after aluminum, magnesium or calcium containing antacids, iron, sucralfate, milk containing products and food supplements
TB Disease Treatment Regimens

• Four regimens recommended for treatment of drug-susceptible TB, with different options for number of doses and for length of continuation phase

• Initial phase: standard four drugs (INH, RIF, PZA, EMB) for 2 months

• Continuation phase: typically INH/RIF for an additional 4 months; 7 months for some patients
TB Disease Treatment Regimens (cont.)

• When to use 7-month continuation phase:
  - Disease is cavitary and sputum culture is positive at end of initial phase;
  - Initial phase excluded PZA

• Treatment also extended for:
  - Bone and joint TB (6-9 months total)
  - CNS TB (12 months)
Table 2. Drug Regimens for Microbiologically Confirmed Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Druga</th>
<th>Intensive Phase</th>
<th>Continuation Phase</th>
<th>Range of Total Doses</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>INH</td>
<td>7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)</td>
<td>INH RIF</td>
<td>7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)</td>
<td>182–130</td>
</tr>
<tr>
<td>2</td>
<td>INH</td>
<td>7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)</td>
<td>INH RIF</td>
<td>3 times weekly for 54 doses (18 wk)</td>
<td>110–94</td>
</tr>
<tr>
<td>3</td>
<td>INH</td>
<td>3 times weekly for 24 doses (8 wk)</td>
<td>INH RIF</td>
<td>3 times weekly for 54 doses (18 wk)</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>INH</td>
<td>7 d/wk for 14 doses then twice weekly for 12 dosesb</td>
<td>INH RIF</td>
<td>Twice weekly for 36 doses (18 wk)</td>
<td>62</td>
</tr>
</tbody>
</table>

Abbreviations: DOT, directly observed therapy; EMB, ethambutol; HIV, human immunodeficiency virus; INH, isoniazid; PZA, pyrazinamide; RIF, rifampin.

a Other combinations may be appropriate in certain circumstances; additional details are provided in the section “Recommended Treatment Regimens.”

b When DOT is used, drugs may be given 5 days per week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice. DOT should be used when drugs are administered <7 days per week.

c Based on expert opinion, patients with cavitary on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31-week) continuation phase.

d Pyridoxine (vitamin B6), 25–50 mg/day, is given with INH to all persons at risk of neuropathy (e.g., pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

e See [426]. Alternatively, some US tuberculosis control programs have administered intensive-phase regimens 5 days per week for 15 doses (3 weeks), then twice weekly for 12 doses.
Regimen 1 for Treatment of Pulmonary, Drug-Susceptible TB
6-Month Standard Regimen for Most Patients

Initial phase
INH, RIF, PZA, EMB daily (7 or 5 days/week) for 8 weeks

4-month continuation phase
INH, RIF daily (7 or 5 days/week) for 18 weeks
Regimen 2 for Treatment of Pulmonary, Drug-Susceptible TB

6-Month Standard Regimen for Most Patients

Initial phase
INH, RIF, PZA, EMB daily (7 or 5 days/week) for 8 weeks

4-month continuation phase
INH, RIF three times weekly for 18 weeks

*Only consider when more frequent DOT during continuation phase is difficult to achieve
Regimen 3 for Treatment of Pulmonary, Drug-Susceptible TB
6-Month Intermittent Dosing Options

Initial phase
INH, RIF, PZA, EMB intermittently (3 days/week) for 8 weeks

4-month continuation phase
INH, RIF intermittently (3 days/week) for 18 weeks

*Only consider in HIV-negative patients and also those at low risk of relapse i.e. noncavitary, pansusceptible, smear negative when daily DOT unavailable or unable to tolerate daily medications
Regimen 4 for Treatment of Pulmonary, Drug-Susceptible TB
6-Month Daily + Intermittent Dosing Options

Initial phase
INH, RIF, PZA, EMB daily (7 or 5 days/week) for 2 weeks, then 2 days/week for 6 weeks

4-month continuation phase options
INH, RIF intermittently (2 days/week) for 18 weeks

*The Denver Regimen: only consider in HIV-negative, and those also at low risk of relapse i.e. noncavitary, pansusceptible, smear negative
Other regimens

Once weekly continuation phase with INH 900 mg plus Rifapentine 600 mg:

• Less active than standard RIF-base treatment
• Relapse seen in: cavitation, underweight, sputum culture positivity at end of intensive phase
• ONLY recommended in the uncommon situation where more than once-weekly DOT is difficult to achieve in HIV-negative without cavitation on x-ray
Other regimens

If PZA cannot be used either due to intolerance, pregnancy, or resistance (*M. bovis*):

- Initial phase: INH, RIF, EMB for two months
- Continuation phase: INH, RIF given daily or thrice weekly for 7 months
Fluoroquinolones

Occasionally used:
• In place of INH throughout treatment when it cannot be used due to intolerance or resistance
• In place of EMB in intensive phase when it cannot be used
• No data to support substituting fluoroquinolone for RIF or PZA and still maintaining 6-month treatment duration
• Duration: 6 months or longer
TB Treatment: Monitoring Therapy
Evaluating Response to Treatment

Assess patient’s response to treatment using three methods:

- Clinical evaluation, bacteriological examination, CXR

<table>
<thead>
<tr>
<th>Activity</th>
<th>Baseline</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>End of Treatment Visit</th>
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</thead>
<tbody>
<tr>
<td>MICROBIOLOGY</td>
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<tr>
<td>Sputum smears and culture¹</td>
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<td>Drug susceptibility testing²</td>
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<td>Chest radiograph or other imaging³</td>
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<td>CLINICAL ASSESSMENT</td>
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<td>Weight⁴</td>
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<td>Symptom and adherence review⁵</td>
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<td>Vision assessment⁶</td>
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<tr>
<td>LABORATORY TESTING</td>
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<tr>
<td>AST, ALT, bilirubin, alkaline phosphate⁷</td>
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<td>Platelet count⁸</td>
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<td>Creatinine⁹</td>
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<td>HIV⁹</td>
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<tr>
<td>Hepatitis B and C screen¹⁰</td>
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<tr>
<td>Diabetes Screen¹¹</td>
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</tr>
</tbody>
</table>
Evaluating Response to Treatment

Conduct clinical evaluations at least monthly

- Monitor adherence and improvement in TB symptoms
- Monitor weight monthly
- After 2 months of therapy, if symptoms do not resolve, re-evaluate for: potential drug-resistance, non adherence to drug regimen, malabsorption
Evaluating Response to Treatment

Bacteriological examination

• If cultures do not convert to negative after 3 months of therapy, evaluate patient for drug resistance or adherence issues; after 4 months, consider treatment failed.

Chest radiograph

• Patients with initially *negative* cultures should have CXR after 2 months of treatment and at completion of therapy.

References

Evaluating Response to Treatment

• Patients with cavitation on CXR and positive cultures at two months are more likely to relapse so the continuation phase is extended to 7 months (9 months total)

• Extension of treatment to 9 months in pulmonary TB can be considered:
  - Cavitation on CXR
  - Positive cultures at two months
  - Diabetic
  - HIV +
  - Malnourished
  - Smoker
  - Having extensive disease on CXR
Patient Monitoring

Establish rapport with patient and emphasize:
- Benefits of treatment
- Importance of adherence to treatment regimen
- Possible adverse side effects of regimen
- Establishment of optimal follow-up plan
# Patient Monitoring--Baseline

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>AST, ALT, bilirubin, alkaline phosphatase</td>
</tr>
<tr>
<td></td>
<td>Platelet count</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
</tr>
<tr>
<td>Patients at risk for hepatitis B or C</td>
<td>Conduct serologic tests</td>
</tr>
<tr>
<td>(e.g., injection drug user, born in Asia or</td>
<td></td>
</tr>
<tr>
<td>Africa, HIV infected)</td>
<td></td>
</tr>
<tr>
<td>Patients at risk for diabetes</td>
<td>Fasting glucose or HbA1c</td>
</tr>
<tr>
<td>(age&gt;45 yo, BMI&gt;25, first-degree relative</td>
<td></td>
</tr>
<tr>
<td>with DM, race/ethnicity of African American,</td>
<td></td>
</tr>
<tr>
<td>Asian, Hispanic, American Indian/Alaska</td>
<td></td>
</tr>
<tr>
<td>Native, or Hawaiian Native/Pacific Islander)</td>
<td></td>
</tr>
<tr>
<td>Patients who are taking EMB</td>
<td>Test visual acuity (Snellen chart) and color vision</td>
</tr>
<tr>
<td></td>
<td>(Ishihara)</td>
</tr>
<tr>
<td>HIV-infected patients</td>
<td>Obtain CD4+ lymphocyte count</td>
</tr>
</tbody>
</table>
# Patient Monitoring—During Treatment

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| All patients | Repeat at least monthly clinical evaluations to  
| | • Identify possible adverse reactions to medications  
| | • Assess adherence  
| |  
| Those with: abnormal baseline LFTS, symptoms of hepatotoxicity, ETOH consumption, other hepatotoxic drugs, viral hepatitis or history of liver disease, HIV | Monthly AST, ALT, Bilirubin, Alkaline phosphatase  
| |  
| Patients who are taking EMB | • Question monthly regarding visual disturbances  
| | • Repeat monthly testing for visual acuity (Snellen chart) and color vision (Ishihara)  
| |  
| Extrapulmonary TB | • Depends on site and ease with which specimens can be obtained  

Treatment Interruptions

• Treatment interruptions are common
• Restart or continue therapy based on when interruption occurred and duration of interruption
• Bacteriologic status of patient (i.e. smear/culture positive) prior to and after the interruption are also important considerations
Table 6. Management of Treatment Intermittences

<table>
<thead>
<tr>
<th>Time Point of Interruption</th>
<th>Details of Interruption</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>During intensive phase</td>
<td>Lapse is &lt;14 d in duration</td>
<td>Continue treatment to complete planned total number of doses (as long as all doses are completed within 3 mo)</td>
</tr>
<tr>
<td>During intensive phase</td>
<td>Lapse is ≥14 d in duration</td>
<td>Restart treatment from the beginning</td>
</tr>
<tr>
<td>During continuation phase</td>
<td>Received ≥80% of doses and sputum was AFB smear negative on initial testing</td>
<td>Further therapy may not be necessary</td>
</tr>
<tr>
<td>During continuation phase</td>
<td>Received ≥80% of doses and sputum was AFB smear positive on initial testing</td>
<td>Continue therapy until all doses are completed</td>
</tr>
<tr>
<td>During continuation phase</td>
<td>Received &lt;80% of doses and accumulative lapse is &lt;3 mo in duration</td>
<td>Continue therapy until all doses are completed (full course), unless consecutive lapse is &gt;2 mo</td>
</tr>
<tr>
<td></td>
<td>Received &lt;80% of doses and lapse is ≥3 mo in duration</td>
<td>If treatment cannot be completed within recommended time frame for regimen, restart therapy from the beginning (ie, restart intensive phase, to be followed by continuation phase)</td>
</tr>
<tr>
<td></td>
<td>Received &lt;80% of doses and lapse is ≥3 mo in duration</td>
<td>Restart therapy from the beginning, new intensive and continuation phases (ie, restart intensive phase, to be followed by continuation phase)</td>
</tr>
</tbody>
</table>

Abbreviation: AFB, acid-fast bacilli.

a According to expert opinion, patients who are lost to follow-up (on treatment) and brought back to therapy, with interim treatment interruption, should have sputum resent for AFB smear, culture, and drug susceptibility testing.

b The recommended time frame for regimen, in tuberculosis control programs in the United States and in several European countries, is to administer all of the specified number of doses for the intensive phase within 3 months and those for the 4-month continuation phase within 6 months, so that the 6-month regimen is completed within 9 months.
Treatment Interruption During Initial Phase

The earlier the break and the longer the duration, the greater the need to start from the beginning:

- If lapse $\geq 14$ days, restart treatment
- If lapse $< 14$ days, continue treatment to completion as long as all doses are completed within 3 months
Treatment Interruption During Continuation Phase

• If patient received ≥80% of doses and:

  - Sputum smear was negative on initial testing, further therapy *may not* be needed
  
  - Sputum smear was positive on initial test, continue therapy until all doses are completed
Treatment Interruption During Continuation Phase

• Obtain sputum smear and culture
• If patient received <80% of doses, and lapse is:
  - <3 months long, continue therapy, to complete in 6 months
  - >3 months long, restart therapy from beginning of initial phase
Treatment Interruption During Continuation Phase

• If culture is positive, restart treatment from the beginning

• If culture is negative, could treat as having culture-negative TB with 4 months of INH/RIF, as long as had drug susceptible organism and was treated originally with RIF/INH/PZA
Treatment Completion

• Defined as ingesting prescribed number of doses within specified time:
  - Initial phase: completed in 3 months
  - Continuation phase: completed in 6 months

• Duration depends on drugs used, isolate’s susceptibility, and patient’s response to drugs

• Most patients can be treated with 6-mo or 9-mo therapy; 6 mo is used for most patients
TB Treatment: Culture-negative TB
Case 5—Mr. F

- 60 yo gentleman, a recent immigrant from the Philippines presents for evaluation
- Denies cough, fever, chills, sweats
- Positive TST at 10 mm
- HIV negative
Case 5—Mr. F

- Sputum smears negative x 3
- 4 drug therapy started
- Due to concern for being a clinical case, patient kept on home isolation until he had received 5 days of therapy
Case 5—Mr. F

• Cultures finalized as negative at 8 weeks
• Repeat CXR performed after 2 months of therapy and found to be improved
• TB medications continued to complete 4 months of total therapy
Culture-Negative Pulmonary TB

• Failure to isolate TB bacilli from person with clinical evidence does not exclude TB
• Up to 15% of cases in US are culture negative
• At minimum, TB suspects should have 3 specimens for smear and culture
Treating Culture-Negative Pulmonary TB

• Start patient on four-drug TB therapy if high clinical suspicion for TB
• If cultures are negative, clinical and radiographic follow-up after two months of therapy is indicated
Treating Culture-Negative Pulmonary TB

If patients exhibit either a clinical response or significant improvement in their CXR, and no other etiology has been identified, continue therapy for 4-6 months:

• RIF/INH/EMB/PZA x 2 mos, then RIF/INH x 2 mos or

• RIF/INH/EMB/PZA x 4 months
  - If concern for drug resistance
If negative cultures, TST or IGRA+ and no clinical or radiographic changes after 2 months of treatment:

Treat for latent TB infection (LTBI):
1. Complete 2-months of 4 drugs
2. Continue treatment with rifampin for 4 months
3. Continue isoniazid for 9 months
4. Give 12 weekly doses of INH/RPT by DOT
TB Treatment: Special Situations
Case 6—Mrs. R

- 29 yo female originally from El Salvador
- Presents for obstetrics care around 20 weeks into her pregnancy
- Asymptomatic, IGRA positive
- CXR: a 1.9 cm nodule in the right mid lung with adjacent fibrotic linear density
- Sputum smears AFB negative x 3
- Sputum cultures positive for TB
- What is the next step?
Pregnant and Breastfeeding Women

• TB drugs cross the placenta but do not appear to be teratogenic

• Initial regimen should consist of INH, RIF, and EMB
  - PZA not contraindicated, but detailed data on teratogenicity not available
  - If PZA not used, duration of therapy is 9 months

• Breast-feeding not contraindicated for women being treated for TB disease

• Vitamin $B_6$ supplementation (25-50 mg/day) is recommended if taking INH and breastfeeding
  - Baby may need INH if exposed to infectious mom
  - Baby should receive B6 supplement if mom taking INH
Case 7—Mr. V

• 58 yo Filipino gentleman with ESRD, on dialysis MWF
• As part of kidney transplant evaluation, he has a TST which is positive
• CXR is abnormal
• Sputum smears x 3 negative
• What is the next step?
Renal Insufficiency

• Patients with renal insufficiency or ESRD are immunocompromised

• They have worse clinical outcomes than those without renal failure

• In general, the doses of the anti-TB medications should not be reduced but rather the interval should be increased
Dosing of TB Medications in Renal Failure

• INH and Rifampin are metabolized by the liver so conventional dosing is used
• PZA is also metabolized by the liver but active metabolites are excreted by the kidney and requires interval modification
• EMB is 80% metabolized by the kidney and also needs an increase in the dosing interval
### Table 12. Dosing Recommendations for Adult Patients With Reduced Renal Function

<table>
<thead>
<tr>
<th>Drug</th>
<th>Change in Frequency?</th>
<th>Recommended Dose and Frequency for Patients With Creatinine Clearance &lt;30 mL/min, or Patients Receiving Hemodialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>No</td>
<td>300 mg once daily, or 900 mg 3 times/wk</td>
</tr>
<tr>
<td>Rifampin</td>
<td>No</td>
<td>600 mg once daily, or 600 mg 3 times/wk</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Yes</td>
<td>25–35 mg/kg/dose 3 times/wk (not daily)</td>
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<tr>
<td>Ethambutol</td>
<td>Yes</td>
<td>20–25 mg/kg/dose 3 times/wk (not daily)</td>
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<tr>
<td>Levofloxacin</td>
<td>Yes</td>
<td>750–1000 mg/dose 3 times/wk (not daily)</td>
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<td>Moxifloxacin</td>
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<td>400 mg once daily</td>
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<td>Cycloserine</td>
<td>Yes</td>
<td>250 mg once daily, or 500 mg/dose 3 times/wk&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>Ethionamide</td>
<td>No</td>
<td>250–500 mg/dose daily</td>
</tr>
<tr>
<td>Para-amino salicylic acid</td>
<td>No</td>
<td>4 g/dose twice daily</td>
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<td>Streptomycin</td>
<td>Yes</td>
<td>15 mg/kg/dose 2-3 times/wk (not daily)</td>
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<tr>
<td>Capreomycin</td>
<td>Yes</td>
<td>15 mg/kg/dose 2-3 times/wk (not daily)</td>
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<td>Kanamycin</td>
<td>Yes</td>
<td>15 mg/kg/dose 2-3 times/wk (not daily)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Yes</td>
<td>15 mg/kg/dose 2-3 times/wk (not daily)</td>
</tr>
</tbody>
</table>

- Standard doses are given unless there is intolerance.
- The medications should be given after hemodialysis on the day of hemodialysis.
- Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.
- Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing using serum concentration monitoring.
- In patients with 30–50 mL/min creatinine clearance, standard doses are used by experts, but measurement of serum concentrations 2 and 6 hours after timed administration can be used to assist with optimizing drug dosages.

*Including adult patients receiving hemodialysis.*

*The appropriateness of 250-mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity.*
TB Treatment in Renal Failure

• Administer all medications post dialysis
• For patients with 30-50 ml/min CrCl use standard doses of medications
• May need to consider checking drug levels in these patients
Case 8—Mrs. P

- 54 yo African-American female presents with 3 months of cough
- CXR obtained
- Sputum smears 4+ AFB positive
- TB PCR positive
Case 8—Mrs. P

• On methadone
• Current ETOH use/abuse
• Active Hepatitis C with baseline elevated LFTS:
  AST: 65
  ALT: 48
• What therapy to start?
TB Treatment in Hepatic Disease

Drug-induced hepatitis increased in patients with:

• Prior advance liver disease, liver transplant, hepatitis C infection, abnormal baseline LFTS

• Consider treatment regimens with fewer hepatotoxic agents:
  - In patients with advanced liver disease
  - Those with ALT > 3 times ULN at baseline

• Try to retain INH/RIF
Alternative Regimens in Hepatic Disease

Treatment without PZA:
• INH/RIF/EMB for two months, followed by 7 months INH/RIF

Treatment without INH:
• RIF/PZA/EMB with or without a fluoroquinolone for 6 months

Treatment without INH/PZA:
• RIF/EMB with a fluoroquinolone, injectable agent or cycloserine for 12-18 months
Alternative Regimens in Hepatic Disease

For patients with severe, unstable liver disease:

• EMB, fluoroquinolone, cycloserine and second-line injectable for 18-24 months
Monitoring of Treatment in Hepatic Disease

- Consider checking LFTS/bilirubin every few weeks for the first 2-3 months of treatment.
- Consider stopping medications if ALT 3X ULN in asymptomatic patients with severe liver disease (cirrhosis, encephalopathy).
Case 9—Mr. A

- 94 yo Filipino gentleman presents to local ER with the following: “generalized malaise, weakness, fatigue, decreased appetite, abdominal pain, and intermittent back pain”
- Abdominal pain started approximately two weeks earlier after a “fall”
- Denies fever, chills
- Son accompanies patient in ER, helps with translation
- Patient described as “cachectic” in appearance
Case 9—Mr. A

• Past Medical History: Stroke, Diabetes, HTN
• Diagnosed with: pneumonia
Case 9—Mr. A

• Treated for pneumonia with antibiotics
• Discharged to follow-up with his primary care doctor
• Unfortunately, started to feel poorly again
• Findings on chest x-ray were unchanged
• Finally referred to see a pulmonologist
Case 9—Mr. A

• Unable to produce sputum
• 5/10/13: underwent bronchoscopy
• AFB smear negative
• 6/18/13: 1 of 3 specimens became AFB positive (grew one colony)
• 8/13: Started on TB therapy
The Challenge of Diagnosing TB in an Older Adult

• Often complain about nonspecific symptoms:
  - Chronic fatigue/weakness
  - Cognitive impairment
  - Anorexia/weight loss
  - Persistent low-grade fever
  - Changes in activities of daily living

• Symptom duration may be greater in the elderly

• May be confused with age-related illnesses:
  - Malignancy
  - Diabetes mellitus
  - Malnutrition

# Adverse Drug Effects

## Table 3: Adjusted Hazard of All, or Specific, Side Effects in Association with Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Any Serious*</th>
<th>Rash/Fever†</th>
<th>Hepatitis‡</th>
<th>GI Upset§</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Female sex (versus male)</td>
<td>2.5</td>
<td>1.3 to 4.7</td>
<td>1.9</td>
<td>0.7 to 4.8</td>
</tr>
<tr>
<td>Age, yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–59 (versus &lt; 35)</td>
<td>1.7</td>
<td>0.8 to 3.8</td>
<td>1.0</td>
<td>0.3 to 3.1</td>
</tr>
<tr>
<td>60+ (versus &lt; 35)</td>
<td>2.9</td>
<td>1.3 to 6.3</td>
<td>1.3</td>
<td>0.4 to 4.1</td>
</tr>
<tr>
<td>From Asia (versus all others)</td>
<td>2.5</td>
<td>1.3 to 5.0</td>
<td>2.8</td>
<td>1.1 to 7.5</td>
</tr>
<tr>
<td>Method of detection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>passive (versus active)</td>
<td>2.5</td>
<td>0.9 to 6.6</td>
<td>2.3</td>
<td>0.6 to 8.3</td>
</tr>
<tr>
<td>Smear positive (versus smear negative)</td>
<td>1.3</td>
<td>0.7 to 2.6</td>
<td>1.0</td>
<td>0.4 to 2.7</td>
</tr>
<tr>
<td>Drug resistant (versus pansensitive)</td>
<td>1.8</td>
<td>0.8 to 4.3</td>
<td>1.0</td>
<td>0.2 to 4.5</td>
</tr>
<tr>
<td>Abnormal baseline LFTs (versus normal)</td>
<td>1.6</td>
<td>0.6 to 4.2</td>
<td>2.3</td>
<td>0.6 to 8.0</td>
</tr>
<tr>
<td>HIV-positive (versus negative or NA)</td>
<td>3.8</td>
<td>1.05 to 13.4</td>
<td>5.1</td>
<td>1.02 to 27</td>
</tr>
</tbody>
</table>

**Definition of abbreviations:** CI = confidence interval; GI = gastrointestinal; HIV = human immunodeficiency virus; HR = hazard ratio; LFT = liver function test; NA = not available.

*Boldface entries indicate statistically significant associations.*

- Any serious side effects.
- † Occurrence of rash or drug fever.
- ‡ Hepatitis defined as transaminases greater than three times the upper limit of normal with symptoms, or five times the upper limit of normal in the absence of symptoms.
- § Severe GI intolerance: sufficient to cause discontinuation of some or all medications and/or hospitalization.
- †† Insufficient numbers, so estimates unstable.
- †‡ Before anti-TB therapy the liver transaminases were above the upper limit of normal.
Hepatotoxicity

• Incidence of INH-associated hepatotoxicity increases with age:
  - risk of liver damage at age < 35: 0.3%
  - risk of liver damage at age > 50: 2.3%
• Severity of hepatitis also increases with age, higher mortality in patients older than 50
• Consider avoiding PZA in patients >75 years old
• Need to monitor for drug interactions
Case 9—Mr. A

- 8/14 Started on RIPE
- Four weeks into therapy:
  - AST 400
  - ALT 580
- All medications held until LFTS normalized
- Isolate fully drug susceptible
- Restarted sequentially on:
  - rifampin/ethambutol, INH
- Tolerated remainder of therapy
- Passed-away in mid-July due to “natural causes”
TB Treatment: Extrapulmonary TB
Lymphatic TB

• Lymphatic TB in non-immunosuppressed patients is associated with female sex, foreign-birth, and Asian/Pacific Islanders

• Unlike pulmonary disease with 20-25% false negative PPD, PPD is positive in over 90%
Lymphatic TB Treatment

• A 6-month regimen is recommended:
  - 2 months of INH/RIF/EMB/PZA followed by
  - 4 months of INH/RIF

• Although the disease is pauci-bacillary, the development of nodes during therapy or at the end of therapy is common

• Usually there is no evidence of bacteriological relapse

• No role for steroids except perhaps in unusual circumstances of IRIS with HIV co-infection
Clinical Manifestations of TB Pleuritis

• Usually presents as an acute illness
• Associated with non-productive cough and pleuritis chest pain
• Effusion is usually unilateral and can be of any size

• 20% will have concomitant parenchymal disease on CXR
• Up to 80% may have concomitant parenchymal disease on CT
• Rarely, pleural TB can present with pleural-based nodules and thickening
Treatment of TB Pleuritis

• A 6-month regimen is recommended:
  - 2 months of INH/RIF/EMB/PZA followed by
  - 4 months of INH/RIF

• No evidence to support routine use of steroids
Bone and Joint TB

• Bone and joint disease due to TB affects all ages but the greatest risk appears to be in those >age 65y

• Prior to the HIV era, bone and joint disease accounted for about 9% of all extra-pulmonary disease in the US

• Spinal TB or Pott’s is the most common followed by hip and then knee
Bone and Joint TB

• Diagnosis is ideally made with isolation of the organism from the affected area
• The diagnosis is supported by
  - Monoarticular disease
  - Cold abscesses
  - Positive PPD
  - Epidemiological risks
  - Chest x-ray with findings consistent with TB
1. Place on volunteer's arm.
2. Inject intradermally (wheat).
3. Read induration 2-3 days after test applied.
4. Must be read by nurse/physician.
5. Record results as (number) mm. induration.

4/28/04
Treatment of Bone and Joint Disease

• Same therapy as for other forms
• Several studies have shown that six to nine month regimens containing RIF are as effective as 18 month regimens without RIF
• 9 months is favored because it is hard to assess response
• Myelopathy with or without functional impairment responds medically
Role of Surgery

• The role of surgery comes up most often with the treatment of Pott’s disease (spine)

• A randomized trial of the Medical Research Council comparing surgical debridement with multi-drug regimens found no benefit to surgery

• Instances where surgery should be considered:
  - poor response to chemotherapy
  - relief of cord compression when persistent neurologic deficit
  - instability of the spine
TB Pericarditis

- Very rare in the US
- Most common cause of pericarditis in Africa, Asia
- Typical signs/symptoms of pericarditis
- Treatment: 6 months of therapy
TB Pericarditis

• Corticosteroids previously universally recommended
• Recent data does not find statistically significant benefit in terms of mortality or constrictive pericarditis
• Adjunctive steroids no longer routinely recommended in treatment of pericarditis
• Selective use of steroids may be considered in patients at highest risk for inflammatory complications
TB Meningitis

• Historically, it has been a disease of mostly young children, however, HIV and other forms of immune suppression have led to an increase in older age groups

• Without therapy, thought to be uniformly fatal
Treatment for TB Meningitis

• Initial phase: INH/RIF/PZA/EMB for 2 months
• Continuation phase: INH/RIF for 7-10 months
• Optimal duration not defined
• Adjunctive corticosteroid therapy conveys mortality benefit:
  - dexamethasone taper over 6-8 weeks
Miliary TB

- Disseminated TB
- 1-2 mm nodules
- TST likely to be false negative
Miliary TB Treatment

• Standard daily 6-month regimen
Treatment Response

• Among patients with drug-susceptible pulmonary TB, even with extensive lung cavitation, 90-9% will be culture negative after three months with a RIF/INH containing regimen

• Clinical improvement: reduced fever, reduced cough and weight gain

• Paradoxical reaction
Resources

- 2016: Treatment of Drug-Susceptible TB. Clinical Infect Dis
  http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full
- Self Study Modules on Tuberculosis (CDC),
  http://www.cdc.gov/tb/education/ssmodules/default.htm
- Medical Management of Tuberculosis: An Online Presentation
  http://www.currytbcenter.ucsf.edu/products/view/medical-management-tuberculosis-online-presentation
- Tuberculosis medication drug and food interactions pocket card,
  http://www.heartlandntb.org/assets/products/tuberculosis_medication_drug_and_food_interactions.pdf
- CDC Training - Report of Verified Case of Tuberculosis
Resources

- Tuberculosis adverse drug events pocket cards http://www.heartlandntbc.org/assets/products/tuberculosis_adverse_drug_events.pdf
Resources

• Asking the Right Questions: A Visual Guide to TB Case Management for Nurses,
  http://www.currytbcenter.ucsf.edu/products/view/asking-right-questions-visual-guide-tuberculosis-case-management-nurses

• Case Studies in TB - Nurse Case Management Training Tools

• Client/Patient Management Algorithms and Short Clinical Guides,
  http://www.heartlandntb.org/products/
  - Administration of Amikacin Injection
  - Administration of Capreomycin Injection
  - Administration of Streptomycin Injection
Resources

• Fact sheets:
  - TB 101 for Health Care Workers
  - Diagnosis of Tuberculosis Disease
    http://www.cdc.gov/tb/publications/factsheets/testing/diagnosis.htm
  - General Considerations for Treatment of TB Disease
  - TB can be treated
  - TB in pregnancy
  - Bovine Tuberculosis in Humans,