Tuberculosis Diagnosis and Treatment

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M. tuberculosis as Causative Agent for TB

In 1882, Robert Koch presented his discovery of the TB causing bacterium in 1882 (Koch also discovered anthrax and cholera bacteria.)

The Mycobacteria

Mycobacteria
- Numerous occurring zoonotically and in environment
- Named species increases daily!
- Most not a human or public health concern
  - Non-tuberculous mycobacteria (NTM)

Human pathogens
- M. tuberculosis Complex
  - M. tuberculosis, M. bovis, M. microti, M. canetti, M. africanum
  - New members - M. caprae, M. pinnipedii, M. mungi
- Most cause disease in humans
  - Respond as active TB if ill
  - M. leprae

Transmission of TB

- TB spreads from person to person through the air

Transmission of TB

- Airborne by droplet nuclei – 1–5 microns in diameter
- Can remain suspended for several hours
- Not transmitted by surface contact
TB: Airborne Transmission

TB bacteria becomes airborne

A person with active, pulmonary TB releases the TB bacteria into the air. Another person breathes in the air that contains the TB bacteria.

Probability of TB Transmission

- Transmission depends on the following factors:
  - Infectiousness of the person with TB
  - Environment in which the transmission occurs
  - Duration of the exposure to TB bacteria
  - Susceptibility of the exposed individual

Pathogenesis of TB

- Infection begins when the inhaled droplets reach the lungs
- Tubercle bacilli multiply
- A small number of tubercle bacilli may enter the bloodstream and spread throughout the body (lungs, kidneys, brain, bone)
- Within 2–10 weeks, the immune system produces a capsule that surrounds the tubercle bacilli

TB Invades/Infests the Lung

- Effective immune response
  - Infection limited to small area of lung
- Immune response insufficient
  - Active disease

Latent TB Infection vs. Active TB Disease

<table>
<thead>
<tr>
<th>Latent TB Infection (LTBI)</th>
<th>Active TB Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubercle bacilli in the body</td>
<td></td>
</tr>
<tr>
<td>Tuberculin skin test reaction usually positive</td>
<td></td>
</tr>
<tr>
<td>Chest x-ray usually normal</td>
<td>Chest x-ray usually abnormal</td>
</tr>
<tr>
<td>Sputum smears and cultures negative</td>
<td>Sputum smears and cultures may be positive</td>
</tr>
<tr>
<td>No symptoms</td>
<td>Symptoms such as cough, fever, weight loss</td>
</tr>
<tr>
<td>Not infectious</td>
<td>Often infectious before treatment</td>
</tr>
<tr>
<td>Not a case of TB</td>
<td>A case of TB</td>
</tr>
</tbody>
</table>

Sites of TB Disease

- Pulmonary TB (TB of the lungs)
  - 85% of cases
  - Potential for transmission – infectious until proven otherwise
- Extrapulmonary TB (outside the lungs)
  - Can occur anywhere in body
  - Portal of entry through lungs
  - Typical sites include larynx, lymph nodes, the pleura, brain, kidneys, bones, or joints
  - Usually not infectious – always rule out pulmonary!
- Respiratory sites of disease
Once infected with tubercle bacilli
- 90% chance of never developing the disease
- 10% life time chance that TB disease will develop
  - Half the risk within the first 2 years
  - Risk lower after the first 2 years
- Other personal health factors can influence risk
  - HIV infection – single highest risk for progression to active disease
  - 10% annual risk

**Relative Risk of Developing Active TB Disease**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>170 times</td>
</tr>
<tr>
<td>HIV infection</td>
<td>113 times</td>
</tr>
<tr>
<td>Recent infection</td>
<td>15 times</td>
</tr>
<tr>
<td>Certain Medical Conditions</td>
<td>3-16 times</td>
</tr>
</tbody>
</table>

**Diagnosis of Pulmonary TB**

(80-85% of TB Cases)

- **Chest x-ray**
  - Standard PA and lateral films; apical lordotic views may be helpful
  - Infiltrates, nodular densities, cavities, +/- hilar adenopathy
  - Abnormalities may be subtle or non-existent in immunocompromised patients
  - Previous x-rays for comparison may be useful
- **CT scans**
  - Often obtained
  - Nice to have but rarely critical to diagnosis
  - Expensive

**Diagnosis of Pulmonary TB**

- **Laboratory tests**
  - A continuum of testing
  - AFB smear – 24 hours
  - NAA – MTD – few days after smear
  - Culture – preliminary 7-14 days
    - Positive for an Nontuberculous mycobacteria does not rule out TB
    - ID of isolate – confirmation of *M.tb* or not
    - Antimicrobial susceptibility testing – 28 days
- **TST and IGRAs**
  - Positive supports but does not make diagnosis
  - Negative does not exclude TB as possible diagnosis

“The first rule of TB diagnosis: is to think TB....”
Diagnosis of Pulmonary TB

- Coughed sputum
  - Best specimen when available
  - Early AM best, supervise at least one collection
  - AFB smear best available tool for assessing infectiousness
  - Most likely to yield positive culture
  - Multiple specimens recommended to maximize chances for +AFB/culture

Yield of smear and culture from repeated sputum induction for the diagnosis of pulmonary tuberculosis

<table>
<thead>
<tr>
<th>Induced sputum (%) yield</th>
<th>specimen</th>
<th>one</th>
<th>two</th>
<th>three</th>
<th>four</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFB smear</td>
<td>64</td>
<td>81</td>
<td>91</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>AFB culture</td>
<td>70</td>
<td>91</td>
<td>99</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>


Laboratory Tests for \( M.\text{tb} \)

- AFB smear
  - Available in 24–48 hours
  - Simple test: requires skilled technologist to read
  - Not diagnostic for \( M.\text{tb} \). All AFB look alike
  - Used to assess infectiousness
  - Need for isolation, contact investigation
  - Monitor response to treatment
  - Decrease in AFB on smear correlates with effectiveness of treatment

Laboratory Tests for \( M.\text{tb} \)

- Culture and Identification of Isolate
  - "Gold standard" for TB diagnosis
  - Usually complete in 2–4 weeks
  - Not signed out as negative until 8 weeks
  - Traditional identification based on growth characteristics, biochemical tests
  - Preliminary ID by "probe" now standard
    - Requires isolate (2–4 weeks)
    - Tests DNA - can ID \( M.\text{tb} \) complex, \( M.\text{avium} \), +/- others
    - More rapid than chemicals, just as accurate
    - Cannot distinguish among \( M.\text{tb} \) complex species (\( M.\text{tb} \) vs. \( M.\text{bovis} \))

Laboratory Tests for \( M.\text{tb} \)

- Antimicrobial susceptibility testing
  - Requires isolate
  - 2–4 weeks after isolate available
  - IREZ +/- S testing standard
  - Second line drug testing only on request
  - 3–10% of VA TB isolates resistant to \( \geq 1 \) first line TB drug
  - Continue IREZ until susceptibility results available

Direct/rapid tests for TB

- Nucleic acid amplification – DCLS using MTD
- Results in 3–5 days
- Automatically done for positive smears
- TB Control must request on negative smears
- Cannot be on treatment for more than 7 days or within last 12 months
- Beware "the probe"
Other Diagnostic Tests

- **HAIN Test** - rapid molecular susceptibility testing for INH and rifampin
  - Requires authorization
  - Can be done from raw specimen

- **CDC molecular susceptibilities**
  - Requires authorization
  - Requires growing culture – i.e. preliminary culture report

Treatment of Tuberculosis

- **Overall goals**
  - Cure the individual patient
  - Minimize transmission within the community
  - Responsibility for successful treatment is assigned to public health department or private provider, not individual patient.
- Health department **ultimately responsible** for ensuring adequate, appropriate treatment.

Treatment of TB Disease

- **4 regimens approved for drug susceptible disease**
  - Recommendations for HIV–infected same with a few exceptions
  - Twice weekly options are not recommended for HIV+ patients with CD4+ cell counts less than 100

Antituberculosis Drugs Currently in Use in the United States

- **First–line Drugs**
  - Isoniazid
  - Rifampin
  - Rifapentine
  - Rifabutin*
  - Ethambutol
  - Pyrazinamide

- **Second–line Drugs**
  - Cycloserine
  - Ethionamide
  - Levofloxacin*
  - Moxifloxacin*
  - Gatifloxacin*
  - P-Aminosalicylic acid
  - Streptomycin
  - Amikacin/kanamycin*
  - Capreomycin

Ethambutol can be discontinued once susceptibility to INH and RIF demonstrated
- Must be on PZA
- Requires physician order
- PZA must be continued for full recommended 8 week course to qualify for short–course treatment
- Number of doses depends on prescribed regimen
- Dose count required
- DOT standard of care for all
- Never add a single drug to a failing regimen

Treatment Pearls
Drug Regimens for Culture–Positive TB with Drug Susceptible Organisms

Regimen 1
- Initial phase
  - INH/RIF/PZA/EMB
    - 7 d/wk for 56 doses (8 weeks)
    - Option – 5 d/wk for 40 doses (8 weeks)
- Continuation phase
  - INH/RIF
    - 7 d/wk for 126 doses (18 weeks)
    - 5 d/wk for 90 doses (18 weeks)
    - Twice weekly for 36 doses (18 weeks)*
  - INH/RPT
    - Once weekly for 18 doses (18 weeks)*

Regimen 2
- Initial phase
  - INH/RIF/PZA/EMB
    - 7 d/wk for 14 doses (2 weeks)
    - Then twice weekly for 12 doses (6 weeks)*
    - OR
    - 5 d/wk for 10 doses (2 weeks)
    - Then twice weekly for 12 doses (6 weeks)*
- Continuation phase
  - INH/RIF
    - Twice weekly for 36 doses (18 weeks)*
  - INH/RPT
    - Weekly for 18 doses*

Regimen 3
- Initial phase
  - INH/RIF/PZA/EMB
    - Three times weekly for 24 doses (8 weeks)
- Continuation phase
  - INH/RIF
    - Three times weekly for 54 doses (18 weeks)

Regimen 4
- Initial phase
  - INH/RIF/EMB
    - 7 d/wk for 56 doses (8 weeks)
    - OR
    - 5 d/wk for 40 doses (8 weeks)
- Continuation phase
  - INH/RIF
    - 7 d/wk for 217 doses (31 weeks)
    - 5 d/wk for 155 doses (31 weeks)
    - Twice weekly for 62 doses (31 weeks)*

Completion of Treatment
- Determination made more accurately by total number of doses taken, not time period
- Goal is to deliver the recommended specified number of doses in a maximum time frame
  - Important in cases of non-adherence, toxicity
  - 6 month regimen should be completed in 9 months
  - 9 month regimen should be completed in 12 months
- Non-standard treatment due to drug resistance or intolerance – longer, more complicated
  - Depends on missing drug or drugs

Management of Initial Phase Treatment Interruptions
- Management of lapses dependent on
  - Phase of treatment when lapse occurs
    - First 8 weeks – need for restart likely if prolonged
  - Duration of the lapse in treatment
  - Results of patient evaluation when treatment restarted
- Contact TB Control for assistance
TB Medications

Isoniazid

- Adverse Reactions and Side effects
  - Hepatitis
    - Loss of appetite
    - Tiredness, weakness
    - Stomach pain, nausea, vomiting
    - Yellow skin or dark colored urine
  - Can cause flushing with some fish or cheeses
  - Peripheral neuritis
  - Numbness or tingling in hands or feet
  - Arthralgias
  - Optic neuritis

- Preparation
  - 50 mg, 100 mg, and 300 mg tablets
  - Suspension (can cause diarrhea and cramping)
  - Only commercially prepared suspension
  - Must be kept at room temperature

- Administration tips
  - Can be cut or crushed
  - Mix with food just before administering
  - Do not take with large fatty meal
  - If upsets stomach, take with small amount of food
  - Avoid alcohol or OTC meds such as Tylenol or other pain relievers
  - No antacids within 1 hour

Rifampin

- Adverse Reactions and Side effects
  - Orange staining of body fluids – fast!
    - Will stain soft contact lens
  - Rash
  - GI upset, flu–like syndrome
  - Liver toxicity
    - Unusual tiredness or loss of appetite
    - Severe abdominal pain
    - Fever chills

- Preparation
  - 150 mg and 300 mg capsules

- Administration tips
  - Store at room temperature – humidity can affect
  - Powder from capsules can be mixed with liquid or soft food
  - Must be administered immediately after mixing
  - Be careful in opening capsules!

Ethambutol

- Preparation
  - 100 mg and 400 mg tablets

- Administration tips
  - Store at room temperature
  - Can be taken with food
  - Can be split or crushed and mixed – used immediately
**Ethambutol**

- **Adverse Reactions and Side effects**
  - Visual disturbances – vision changes, blurring, color blindness, trouble seeing, eye pain
  - Swelling of face
  - Rash, hives, trouble breathing
  - Numbness, pain or tingling of hands/feet
  - Joint pain
  - Fever chills
  - Nausea, vomiting, poor appetite, abdominal pain
  - Headaches, dizziness

**Pyrazinamide**

- **Preparation**
  - 500 mg tablets
- **Administration tips**
  - Store at room temperature
  - May be taken with food
  - Can be split or crushed
  - Use immediately following mixing with food

- **Adverse Reactions and Side effects**
  - Can cause rash after sun exposure – limit sun exposure
  - Gout-like symptoms (pain swelling in joints) and arthralgias
  - GI upset
  - Liver toxicity –
    - yellow skin/dark urine
    - nausea/vomiting
  - Skin rash, severe itching, hives

**Rifabutin**

- **Preparation**
  - 150 mg capsules
- **Administration tips**
  - Store at room temperature – humidity can affect
  - Powder from capsules can be mixed with liquids or small amount of food
  - Must be administered immediately after mixing
  - Be careful opening capsules!

- **Adverse reactions and side effects**
  - Rashes and skin discoloration
  - Uveitis and other eye toxicities
  - Liver toxicity similar to rifampin
  - Joint pains
  - Drug interactions

**Ethionamide**

- **Preparation**
  - Coated tablets – 250 mg
- **Administration tips**
  - Should be taken with food
  - Client should be on high-dose B6 (pyridoxine) while on drug
### Ethionamide

- **Adverse reactions and side effects**
  - GI upset and anorexia
  - Metallic taste
  - Hepatotoxicity
  - Endocrine effects – breast enlargement, hair loss, acne, impotence, menstrual issues
  - Neurotoxicity – may be worse if also on cycloserine

### Cycloserine

- **Preparation**
  - 250 mg capsules
- **Administration tips**
  - Best taken on empty stomach – decreases absorption
  - Avoid large amounts of fatty foods
  - Avoid alcohol
  - Must be on high-dose B6(pyridoxine) while on drug

### Linezolid (Zyvox)

- **Preparation**
  - Coated tablets – 250 mg, 500 mg, 750 mg
  - Solution for injection
  - Oral suspension
- **Administration tips**
  - Can be taken with food
  - Drink plenty of beverages
  - Avoid caffeinated foods and beverages
  - May cause sensitivity to sun
  - Do not take within 2 hours of antacids or multivitamins

### Levoquin
Levoquin

- Adverse reactions and toxicities
  - Nausea and bloating
  - Headache
  - Dizziness
  - Insomnia
  - Rare tendon rupture
  - Joint pain
  - Rashes, hives, blistering

Moxifloxacin (Avelox)

- Preparation
  - Tablets – 400 mg
  - Solution for IV injection

- Administration tips
  - Keep at room temperature
  - Can be taken with food, but not milk-based products
  - Do not take within 2 hours of antacids or vitamin supplements

Moxifloxacin (Avelox)

- Adverse reactions and toxicity
  - Nausea and diarrhea
  - Headache and dizziness
  - Rare tendon rupture
  - Rare hepatitis
  - Joint pains

Para-Aminosalicylate (PAS) – Paser

- Preparation
  - 4 gm packets

- Administration tips
  - Packets should be kept in refrigerator or freezer
  - Sprinkle over applesauce or yogurt or swirl in acidic juices (tomato, cranberry, apple, or orange)
  - Do not chew
  - May be taken with food
  - Do not use if packet expanded or granules discolored

Para-Aminosalicylate (PAS) – Paser

- Adverse reactions and toxicity
  - GI upset and diarrhea improve over time
  - Shells of granules may be seen in stool
  - Skin rash, severe itching
  - Nausea, vomiting
  - Unusual tiredness
  - Loss of appetite
  - Black stools or bleeding
  - Rare hepatotoxicity

Capreomycin – Streptomycin
Amikacin – Kanamycin

- Preparation
  - 1 gm vials for reconstitution
  - Vials of solution for injection

- Administration tips
  - IM or IV use
  - Options for longer term administration
Capreomycin – Streptomycin
Amikacin – Kanamycin

- Adverse reactions and toxicity
  - Kidney toxicity
  - Hearing loss
  - Risk increases with length and age of client
  - May not be reversible
  - Local pain at injection site
  - Electrolyte abnormalities

Treatment in Special Situations

Special Treatment Situations
Drug Resistant TB

- Established only by drug-susceptibility testing
- Treatment of TB caused by drug-resistant organisms should be done in close consultation with an expert
- DOT is mandatory for all patients with drug resistant disease

Special Treatment Situations
Definitions

- Primary Drug Resistance
  - Infected with TB which is already drug resistant
  - First susceptibility report will show resistance to one or more anti-TB drugs
- Secondary Drug Resistance
  - Drug resistance develops during treatment
  - Initial susceptibility report will show sensitive to primary anti-TB drugs
  - Later susceptibility report will show resistance to one or more anti-TB drugs
  - Causes
    - Noncompliance with medications
    - Subtherapeutic regimen – wrong dose
    - Low blood serum levels – lack of absorption
    - Laboratory errors
    - ????

Special Treatment Situations
Drug resistant TB

- Choice of drugs depends on resistance pattern
- May require second line drug(s)
  - Requires DOT
  - Requires > 26 weeks of treatment
  - Almost always requires daily therapy – 5 or 7 days/week
  - Monitoring for culture conversion, clinical improvement, side effects/toxicity critical

Special Treatment Situations
The importance of what’s missing

- INH only
  - can treat with rifampin, EMB and PZA for 6 months
  - Fluoroquinolone may help if extensive disease
- Ethambutol only
  - RIP for 2 months and IR for 4 months – 6 months total
- PZA only
  - RIE for 2 months and IR for 7 months – 9 months total
- Rifampin only
  - INH, EMB, fluoroquinolone and PZA for 1st 2 months
  - Total treatment 12 – 18 months
Treatment for HIV-positive patients same as for HIV-negative patients, except:

1) Once-weekly INH-rifapentine in continuation phase is contraindicated in HIV-positive patients
2) Twice-weekly INH-RIF or INH-rifabutin should not be used in patients with CD4+ T-lymphocyte counts less than 100/µL

Every effort should be made to use a rifamycin-based regimen for the entire course of therapy

Special Treatment Situations: Renal Insufficiency and End-Stage – Renal Disease

- Renal insufficiency complicates management of TB because some antituberculosis medications are cleared by the kidneys
- Dosage should not be decreased because peak serum concentrations may be too low; smaller doses may decrease drug efficacy

Special Treatment Situations Extrapulmonary TB

- Similar treatment regimen for pulmonary TB*
- 6- to 9-month regimens that include INH and RIF are effective
- Corticosteroids sometimes used as adjunctive therapy for patients with TB meningitis and pericarditis
- IF PZA cannot be used in the initial phase, continuation phase must be increased to ≥7 months

*Except for central nervous system (CNS) TB, including meningitis; length of therapy is 9-12 months

Special Treatment Situations Pregnancy

- Untreated TB represents greater hazard to a woman and her child than treatment of disease
- Treatment of pregnant woman with suspected TB should be started if probability of TB is moderate to high

Special Treatment Situations: Renal Insufficiency and End-Stage – Renal Disease

- Dosing interval of antituberculosis drugs should be increased
- Most drugs can be given 3 times weekly after hemodialysis; for some drugs, dose must be adjusted

Special Treatment Situations Pregnancy

- Initial phase treatment regimen should consist of INH, RIF, and EMB
- PZA not generally recommended for pregnant women in the United States
- SM should not be substituted for EMB because of possible teratogenic effects
Special Treatment Situations
Hepatic Disease

- May need to consider regimens with fewer hepatotoxic agents for patients with liver disease
- **Recommended regimens:**
  1. Treatment without PZA
     - Initial phase (2 months): INH, RIF, and EMB
     - Continuation phase (7 months): INH and RIF
  2. Treatment without INH
     - Initial phase (2 months): RIF, PZA, and EMB
     - Continuation phase (4 months): RIF, EMB, and PZA

Treatment Guidelines Online

- CDC Treatment of Tuberculosis Guidelines:
- New Core Curriculum on Tuberculosis: What the Clinician Should Know

Monitoring and Other Issues

- Periodic (minimum monthly) clinical evaluation to assess adherence and identify adverse reactions
- Bacteriologic monitoring
  - Sputum to assess early response until smear negative
  - After converted to smear negative, monthly sputum clusters (3) until culture negative
  - Obtain additional drug-susceptibility tests if patient remains culture-positive after 3 months of treatment
  - Also medical evaluation, possible drug serum levels

- Repeat chest x-rays generally not indicated
- Follow-up films may be needed:
  - At completion of initial treatment phase for patients with initial negative cultures to establish clinical diagnosis
  - At end of treatment to establish a new baseline
  - Individuals with extensive TB disease or who are HIV-infected

Special Treatment Situations
Hepatic Disease

- **Recommended regimens:** (continued)
  3. Regimens with only one potentially hepatotoxic drug
     - RIF should be retained
     - Duration of treatment is 12-18 months
  4. Regimens with no potentially hepatotoxic drugs
     - Duration of treatment is 18-24 months
Treatment Monitoring

- Repeat blood work if abnormalities at baseline or symptoms appear
  - Follow local district protocol
  - Lab monitoring changes for second line drugs
  - Varies with specific drugs used
- Visual acuity and color vision monthly if EMB used
- Hearing screening required for ototoxic drugs
  - Think injections

Types of Adverse Effects

- Side Effect – Uncomfortable but not dangerous effect of medications as properly administered
  - Most meds – nausea, other GI symptoms
    - usually can continue treatment – can be sign/symptom of hepatitis
  - Diarrhea less common but potentially important – can be marker for malabsorption, predict low blood/tissue drug levels
  - First line meds – non-specific itching
    - Itching, non-specific rashes common – can be initial sign of hepatitis
    - Hives, extensive maculo-papular, purpura rare – require D/C meds, contact HCP, consider ER

Types of Adverse Effects

- CNS/peripheral nervous system side effects
  - Irritability, sleepiness, insomnia common
  - Peripheral neuropathy – usually isoniazid; pyridoxine prevents
  - Optic neuritis – causes visual disturbances
    - Feared w/ ethambutol, can be seen w/ other meds
- Musculoskeletal
  - PZA can cause non-specific muscle and joint pain
  - PZA elevates uric acid – can induce gout
  - "Flu-like" symptoms – can occur w/ rifampin
  - more common twice weekly treatment
  - Report to case manager immediately

Common Adverse Reactions to Drug Treatment

<table>
<thead>
<tr>
<th>Caused by</th>
<th>Adverse Reaction</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any drug</td>
<td>Allergy</td>
<td>Skin rash</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Eye damage</td>
<td>Blurred or changed vision</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Changed color vision</td>
</tr>
<tr>
<td>Isoniazid, Pyrazinamide, or Rifampin</td>
<td>Hepatitis</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abnormal liver function test results</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lack of appetite</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nausea / Vomiting</td>
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<tr>
<td></td>
<td></td>
<td>Yellowish skin or eyes</td>
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<tr>
<td></td>
<td></td>
<td>Dark urine</td>
</tr>
</tbody>
</table>

Caused by | Adverse Reaction | Signs and Symptoms                  |
---------------|------------------|-------------------------------------|
Isoniazid     | Peripheral neuropathy | Tingling sensation in hands and feet |
Pyrazinamide  | Gastrointestinal intolerance | Upset stomach, vomiting, lack of appetite |
              | Arthralgia          | Joint aches                         |
              | Arthritis           | Gout (rare)                         |
Streptomycin  | Ear damage         | Balance problems                    |
              | Kidney damage      | Hearing loss                         |
              |                   | Ringing in the ears                  |
              |                   | Abnormal kidney function test results |
Common Adverse Reactions to Drug Treatment

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<th>Caused by</th>
<th>Adverse Reaction</th>
<th>Signs and Symptoms</th>
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</thead>
<tbody>
<tr>
<td>Rifamycins</td>
<td>Thrombocytopenia</td>
<td>Easy bruising</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>Gastrointestinal</td>
<td>Slow blood clotting</td>
</tr>
<tr>
<td>Rifapentine</td>
<td>intolerance</td>
<td>Upset stomach</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Drug interactions</td>
<td>Interferes with certain medications, such as</td>
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<tr>
<td></td>
<td></td>
<td>birth control pills, birth control implants,</td>
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<td></td>
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<td>and methadone treatment</td>
</tr>
</tbody>
</table>

Other TB Drug Effects

- Drug–drug interactions
  - May increase or decrease effective dose of either TB drug or other medication
  - Rifamycins
    - Rapid metabolism of methadone, warfarin, theophylline – may require increased doses
  - INH
    - May decrease concentrations of phenytoin, diazepam – require increased doses

When to Extend Continuation Phase of Treatment

- Treatment increased to 9 months total duration
  - from 2 drugs x 4 months to 2 drugs x 7 months
  - Recommended for patients with cavitary pulmonary disease and positive 2-month sputum culture
  - Extension may be considered if either factor is present
  - Initial phase did not include PZA

Miscellaneous Comments

- Difficulty swallowing pills
  - Patient may not tell you
  - Crushed pills, administered in small amt food ok
  - Make sure they will finish amount you use!
  - Teach how to swallow meds
    - Tablets SINK – TILT HEAD UP
    - Capsules FLOAT – TIL HEAD DOWN

Summary

- TB is treated with multiple drugs for a prolonged period of time
- Drug resistance generally extends treatment – length depends on missing drug(s)
- All anti–TB drugs have side effects and toxicities
- Second–line drug side effects are usually worse
- Regular monitoring for side effects and toxicities is critical!