Introduction to TB Nurse Case Management
Online
February 4, 11, 18 and 25, 2015

TB Medications Initiation Phase; Part 2
Module 4
Presented by Mary DaSilva, RN for Rachel Munoz, RN
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Mary DaSilva, RN has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity
Objectives

- Describe the monitoring process for adverse drug events associated with anti-TB drugs.
- Side effects and drug toxicities
- Recognize the most common adverse effects of TB therapy

Monitoring Process

- Ongoing process
- Begins with initial nurse assessment
- Obtain a thorough patient history
- Requires nurse-patient relationship
- Case management plan
- Patient education
- Toxicity assessment
  - Daily/B/W during DOT
  - Monthly
Baseline Monitoring

- Detect underlying problems
- Take a good medical and social history
- Blood work
  - CBC, LFT’s, Bun, Creatinine, Uric Acid, Hepatitis panel, Glucose, HIV (cd 4+ count),
- Visual Acuity (Snellen chart) — EMB, Rifabutin
- Ishihara (EMB)

Monitoring During Treatment/Monthly monitoring

- Clinical Evaluation Monthly at minimum-Identify adverse reactions, assess adherence, determine treatment efficacy
  - Use standard forms
  - Follow SDO’s, protocols
- CXR’s
- Laboratory
  - CDC- Not necessary every month for patients on first line drugs. (Be Careful)
  - Unless- abnormalities on baseline or clinical reason
  - Early then less frequently
- Sputa
- MD Evaluations
Side Effects

- Unpleasant, but mild
- No long lasting health effects
- Do not usually require changes in therapy

- Gas
- Bloating
- Mild Nausea/mild appetite shifts
- Discoloration of body fluids
- Irritability
- Difficulty sleeping
- Photosensitivity

Adverse Drug Reactions

- More Serious
- May be life threatening
- Require modification of dose/discontinuation of medications
- May require additional therapy and/or hospitalization

- Significant GI disturbances - vomiting
- Hepatotoxicity
- Dermatological and hypersensitivity reactions
- Vision changes, eye pain
- CNS toxicity
- Neurotoxicity
- Ototoxicity
- Musculoskeletal adverse effects
- Renal toxicity
First Line Drugs

- Isoniazid
- Rifampin (Rif)
  - Rifabutin
- Ethambutol (EMB)
- Pyrazinamide (PZA)
### Common Adverse Reactions to TB Drugs

<table>
<thead>
<tr>
<th>Caused by</th>
<th>Adverse Reaction</th>
<th>Signs and Symptoms</th>
<th>Significance of Reaction*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any drug</td>
<td>Allergic</td>
<td>- Skin rash</td>
<td>May be serious or minor</td>
</tr>
<tr>
<td>INH/PZA/RIF</td>
<td>Eye damage</td>
<td>- Blurred or changed vision - Changed color vision</td>
<td>Serious</td>
</tr>
<tr>
<td>INH/PZA/RIF</td>
<td>Hepatic toxicity</td>
<td>- Abdominal pain - Abnormal liver function test results - Dark urine - Fatigue - Fever for 3 or more days - Flu-like symptoms - Lack of appetite - Nausea - Vomiting - Yellowish skin or eyes</td>
<td>Serious</td>
</tr>
<tr>
<td>INH</td>
<td>Nervous system damage</td>
<td>- Dizziness; tingling or numbness around the mouth</td>
<td>Serious</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>- Tingling sensation in hands and feet</td>
<td>Serious</td>
<td></td>
</tr>
<tr>
<td>PZA</td>
<td>Stomach upset</td>
<td>- Stomach upset - Vomiting - Lack of appetite</td>
<td>May be serious or minor</td>
</tr>
<tr>
<td>Gout</td>
<td>Abnormal uric acid level**</td>
<td>- Joint aches</td>
<td>Serious</td>
</tr>
<tr>
<td>Rif</td>
<td>Bleeding problems</td>
<td>- Easy bruising - Slow blood clotting</td>
<td>Serious</td>
</tr>
<tr>
<td>Rif</td>
<td>Discoloration of body fluids</td>
<td>- Orange urine, sweat, or tears - Permanently stained soft contact lenses</td>
<td>Minor</td>
</tr>
<tr>
<td>Drug Interactions</td>
<td>- Interferes with certain medications such as birth control pills, birth control implants, and methadone treatment</td>
<td>May be serious or minor</td>
<td></td>
</tr>
</tbody>
</table>

* Patients should stop medications for serious adverse reactions and consult a clinician immediately. Patients can continue taking medication if they have minor adverse reactions. ** Asymptomatic elevated uric acid levels are expected with PZA treatment. Acute gouty arthritis, which is rare without preexisting gout, is a contraindication to PZA use.

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### Hepatitis

<table>
<thead>
<tr>
<th>Neurological</th>
<th>Renal</th>
<th>Ophthalmologic</th>
<th>Hematological (rare)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>Peripheral Neurotoxicity: Streptomycin</td>
<td>Vision Changes: Rifampin</td>
<td>Rifabutin</td>
</tr>
<tr>
<td>Rifampin</td>
<td>INH</td>
<td>Amikacin</td>
<td>Ethambutol</td>
</tr>
<tr>
<td>PZA</td>
<td>Ethionamide</td>
<td>Capreomycin</td>
<td>Rifabutin</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>Linezolid</td>
<td>Linezolid</td>
<td>PZA</td>
</tr>
<tr>
<td>PAS</td>
<td>Central Neurotoxicity: Rifampin</td>
<td>Uveitis: Linezolid</td>
<td>Linezolid</td>
</tr>
<tr>
<td>Levofloxacin (rare)</td>
<td>INH</td>
<td>Rifabutin</td>
<td>Rifabutin</td>
</tr>
<tr>
<td>Ethambutol (rare)</td>
<td>Ethionamide</td>
<td>Orange tears: Capreomycin (rare)</td>
<td></td>
</tr>
<tr>
<td>Fluoquinolones</td>
<td>Rifampin</td>
<td>Levofloxacin (rare)</td>
<td></td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Amikacin</td>
<td>Methotrexate (rare)</td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>Linezolid</td>
<td>PAS (rare)</td>
<td></td>
</tr>
</tbody>
</table>

*Revised 12-2010*
ADVERSE DRUG EVENTS - SYMPTOMS

HEMATOLOGIC: (all of these are rare)
- Low platelet count which impairs ability to bleed and may cause bleeding - stop drug. Rifampin, Rifabutin, vancomycin
- Leucopenia: SME, ERIE, ERT, PZP, CPZ, Carvacrol, Stop
- Low white blood count which limits ability to fight infections, especially bacterial infections. Rifampin especially in high doses. IV: Leucovorin, Rifampin, RIFIN, ERIE
- Anemia: Leucovorin, vancomycin, Rifampin, ERT, TPA, PZP, CPZ, Cotrimoxazole.

HEPATIC
Early signs: fatigue, rash, jaundice, nausea, vomiting
Later signs: swelling, abdominal pain, jaundice, dark urine, light stools, neurological problems
Laboratory evaluation: if symptoms (AST, ALT) and bilirubin, clotting studies (prothrombin time) and liver function. Medication must be stopped with AST/ALT above normal range present

GENERAL APPROACH
1. Hold TB med if AST + ALT >5 normal or symptomatic
2. Hold TB med if AST + ALT > 5 normal even if no symptoms
3. Hold TB med if T1 skin test increases. Do not wait and see other explanation

IMMUNE REACTIVITY
Rash: may be mild and medications continued without. (German measles) uncommon
Nausea: medication should be stopped and restarted only after side effect is gone and restart is done in hospital
Swelling of face, eyes, tongue, hands, mouth, do not restart
Breathing difficulty or wheezing: stop drug, do not restart
Drug fever: patient well except for fever, remove with stopping drug
Rifampin reaction: low platelets, rash, blisters, refractory, stop Rifampin
Drug induced rash does not to IV, vancomycin. Drug usually must be stopped

NEUROLOGIC TOXICITY: peripheral neuropathy: tingling, pain & numbness of hands & feet. More common in those with diabetes, scleroderma. HIV infected. Usually can be treated with change in dose or addition of vitamin B6. IM: Ethionamide.

Lisinopril, 5mg to 10mg, or ACE inhibitors, DIF
Central nervous: headache, steep diarrhea, loss of concentration, seizures, personality changes, memory loss. IV: Ethionamide, Cytosine, Levofloxacin, Lisinopril.

SEVERE HEMOLYTIC ANEMIA: Lisinopril is a mimairine sodium inhibitor (MAO) and cloxime with other drugs that cause a negative feedback release of norepinephrine or block its uptake. Cause exceeding CNS and peripheral sympathetic activity. May be fatal. Manifests as altered mental status, neurocirculatory activity and autonomic dysrhythmia

OPHTHALMOLIC
Visual toxicity: change in color vision. Change is visual acuity. Ethionamide, Rifampin, Lisinopril, Clarinex. Inflammation of eye (papilledema): pain, redness, tearing or vision. Rifampin

MUSCULOSKELETAL
Arthralgia: common with PZA, IV, Rifampin. Cloxime with other drugs that cause a negative feedback release of norepinephrine or block its uptake. May be due to electrolyte abnormalities. May occur with rifampin, amikacin, capreomycin, Gentamicin high ac in patients on PZA (with kidney disease). Tendinitis, tendinopathy, evaluate risk versus benefit of drug. Consider non-steroidal anti-inflammatories. May need to stop medication. Fluoroquinolones.

TECHNICAL<br>
Tender nodules: Usually noticeable in early. Fluoroquinolones: stop medication, stop exercise
REM
Knee, facial: patient will feel ill and may have decreased arm or leg movement. Strepotremycin, Amikacin, Capreomycin, Rifampin, Rifabutin

Consultation to healthcare providers at 1-800-TEX-LUNG, www.HeartlandNTBC.org. Produced by Heartland National TB Center with funds awarded by the Centers for Disease Control and Prevention (CDC). Adverse effects of taking TB remissions are to report hospital admissions or death also should be reported to the CDC through local public health authorities by calling (844) 864-6461.

TUBERCULOSIS MEDICATION

DRUG AND FOOD INTERACTIONS

Multiple significant interactions occur between TB medications and other medications. The absorption of many TB drugs is adversely affected by food and some medications

Consultation to healthcare providers at 1-800-TEX-LUNG
2303 S.E. Military Drive, San Antonio, TX 78223
www.HeartlandNTBC.org

Excellence Expertise Innovation Revised 12-31-10
**FOOD/DRUG INTERACTIONS**

**INH:** Take 1 hour before or 2 hours after meals. May take with small snack if needed. Take 1 hour before or 2 hours after antacids. Avoid alcohol. Supplement Vitamin B6 as needed (25-50 mg).

**Rifampin:** Take 1 hour before or 2 hours after meals. May take with small snack if needed. Take 1 hour before antacids. Avoid alcohol.

**Ethambutol:** May be taken with food.

**Moxifloxacin/Levofloxin:** Take 2 hours before or after aluminum magnesium or calcium containing antacids, iron, vitamins, sucralate, milk containing products and food supplements.

**PZA:** May be taken with food.

**Ethionamide:** Take with or after meals. Avoid alcohol. Supplement Vitamin B6 50-100 mg daily. Avoid alcohol.

**Amikacin:** Increase fluid intake. May be taken on a full or empty stomach.

**Streptomycin:** May affect the taste of food. Increase fluid intake.

**Capreomycin:** May need to increase intake of foods high in potassium, but assure normal renal function first. Increase fluid intake. May be taken on a full or empty stomach.

**Para-Aminosalicylic Acid (PAS):** Take with or immediately following meals. Increase fluid intake.

**Cycloserine:** Supplement Vitamin B6 as directed. Avoid alcohol.

**Linezolid:** May be taken with food. Supplement Vit B6 100 mg daily. Avoid food and drinks that contain tyramine. Do not use with drugs that promote release of serotonin or block its uptake (serotonin syndrome).

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**INH DRUG INTERACTIONS**

<table>
<thead>
<tr>
<th>Drug</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>
</tr>
<tr>
<td>Haldol</td>
<td>↑ haldol toxicity</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>↓ ketoconazole effect</td>
</tr>
<tr>
<td>Dilantin</td>
<td>↑ dilantin toxicity</td>
</tr>
<tr>
<td>Theophyllin</td>
<td>↑ theophyllin toxicity</td>
</tr>
<tr>
<td>Valproate</td>
<td>↑ hepatic and CNS toxicity</td>
</tr>
</tbody>
</table>
### RIFAMPIN DRUG INTERACTIONS

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Interaction</th>
<th>Example Drug</th>
<th>Interaction Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulants</td>
<td>↓ anticoagulants effect antidepressant</td>
<td>Diltiazem</td>
<td>↓ diltiazem effect</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>↓ effect</td>
<td>Fluconazole</td>
<td>↓ fluconazole effect</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>↓ beta blockade</td>
<td>Itraconazole</td>
<td>↓ itraconazole effect</td>
</tr>
<tr>
<td>Contraceptives</td>
<td>↓ contraceptive effect</td>
<td>Haloperidol</td>
<td>↓ haloperidol effect</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Marked ↓ steroid effect</td>
<td>Methadone</td>
<td>↓ methadone effect</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>↓ cyclosporine effect, ↑ Rifampin</td>
<td>Dilantin</td>
<td>↓ dilantin effect</td>
</tr>
<tr>
<td>Protease Inhibitors</td>
<td>Marked ↓ activity of PI, ↑ Rifampin</td>
<td>Verapamil</td>
<td>↓ verapamil effect</td>
</tr>
<tr>
<td>Delavirdine</td>
<td>Marked ↓ delavirdine effect</td>
<td>Tetracyclines</td>
<td>↓ tetracycline effect</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Slight ↓ efavirenz effect, ↓ Rifampin</td>
<td>Trimethoprim-Sulfa</td>
<td>Possible Rifampin toxicity</td>
</tr>
<tr>
<td>Digoxin</td>
<td>↓ digoxin effect</td>
<td>Chloramphenicol</td>
<td>↓ chloramphenicol effect</td>
</tr>
</tbody>
</table>

**Grapefruit Juice**

Grapefruit juice may interfere with your medications!

Some of the medications that should NOT be taken with grapefruit or grapefruit juice are:
- Voltarol® (diclofenac)
- Versed® (midazolam)
- Holcen® (triazolam)
- Budip® (buspirone)
- Tegetan® (carbamazepine)
- Ancefacin® (clonazepam)
- Zadef® (teratol)
- Propac® (ciproflaxacin)
- Celexa® (flurazepam)
- Viagra® (sildenafil)
- Lescol® (fluvastatin)
- Baycol® (cerivastatin)
- Lipitor® (atorvastatin)
- Pronestyl® (propranolol)
- Zocor® (simvastatin)
- Merisor® (lovastatin)
- Pravastatin® (pravastatin)
- Solar® (nadlopride)
- Norvasc® (amlodipine)
- Procardia® or Adalat® (nifedipine)

Your body may get more medicine than it is supposed to!

Some medicines that treat certain conditions, such as those listed below, may interact with grapefruit:
- HIV or AIDS
- Infections (sinus, fungal, ear, etc.)
- Birth control pills
- High cholesterol
- Anxiety
Gastrointestinal (GI) Upset

- **Underlying causes of GI symptoms**
  - Gastritis
  - Hepatitis
  - Biliary Disease
  - Pancreatitis
  - Peptic Ulcer Disease
  - IBS
  - C. Diff
  - Lactose intolerance
  - Acute renal failure-dialysis
  - GI TB, if early in course
  - Pregnancy

GI upset

- **Nausea/Vomiting/Diarrhea/Decreased Appetite**
  - Common within the first few weeks

**Intervention:**
- Change time of day medication given
- Take medication with meal- may slow absorption but better than no meds in patient
- Hydrate
- Antiemetic’s or antacids
  - Remembering the timing of antacids associated with certain meds, INH etc.
Hepatic Toxicity

- Liver injury can be caused by 3 of the First line drugs—INH, Rifampin and PZA
  - Abdominal pain, Nausea, vomiting, lack of appetite
  - Abnormal liver function test results
  - Dark urine
  - Fatigue
  - Fever for 3 or more days
  - Flu-like symptoms
  - Yellowish skin or eyes

- > 3x the upper limits of normal liver enzymes + symptoms = Significant liver toxicity

<table>
<thead>
<tr>
<th>AST and ALT Level</th>
<th>Level of Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST and ALT &lt; 5 times the upper limit of normal</td>
<td>MILD</td>
</tr>
<tr>
<td>AST or ALT 5-10 times the normal limit</td>
<td>MODERATE</td>
</tr>
<tr>
<td>AST or ALT &gt;10 times the normal limit</td>
<td>SEVERE</td>
</tr>
</tbody>
</table>

It is important that first-line drugs **NOT** be stopped without adequate justification!!!!

Proper management of serious adverse reactions often requires expert consultation.
Managing Hepatotoxicity

• Hold medications and repeat LFT’s immediately

➢ Continue therapy
  • ALT < 5x upper limit of normal and asymptomatic
  • 10-20% of patients on standard therapy have asymptomatic elevation in LFT’s

➢ Stop Therapy
  • ALT > 3 times upper limit of normal and symptoms
  • ALT > 5 times upper limit of normal and asymptomatic

Case Study

• 56 y/o male started on TB meds in prison
• Pt. has h/o Hep C with stage 4 cirrhosis in 2007
• 1 month after treatment AST 433, ALT 416, Alk Phos 110, Bili 0.6
• We rec’d pt. on a drug challenge of INH only and AST 96, ALT 96, Bili 0.2 asymptomatic
• Added Rifampin and EMB
• 3 days later AST 67, ALT 66, Alk phos 126, bili 0.5
• 1 week later we started on a B/W regimen of INH, Rifampin and dropped EMB
• 1 week after B/W started AST 103, ALT 111, AP 103, Bili 0.8
Case Study continued:

- Asymptomatic, admitted to some drinking
- 7 days later- AST-138, ALT-146 AP-82, bili-1.3- still asymptomatic
- 1 week later- AST-124, ALT-125, AP-85, bili-0.7
- Continued to monitor through Christmas
  LFT's declined, never normalized, pt. asymptomatic
- Medication continued

Case Study Continued

- Pt. seen 2 days after the New Year
  - AST-215, ALT-300, AP-100, Bili-1.0
  - Pt. admitted to binge drinking
- 5 days later AST-349, ALT-427, AP-102, Bili-0.7-Placed on liver friendly regimen of EMB, and Moxi- pt. continued asymptomatic
- 3 days later AST-453, ALT-569, AP102, Bili-0.7
- RX HELD
- Consulted Heartland= admit to TCID, drug challenge with EMB only until admission
- Upon admission to TCID(6 days later)-AST- 267, ALT-413, AP-118, Bili- 0.7
Case Study continued:

- TCID changed to Levo upon admission along with Rifabutin and EMB.
- Pt. developed severe joint pains.
- Pt. switched to Moxi
- One week later, LFT's increased again to 433, 360. Pt. switched back to Levo.
- Joint pains continued but manageable
- Pt's enzymes slowly decreased and final results AST - 53, ALT - 43, Bili 1.1

Rash/Hypersensitivity Reactions

- Check for other causes
  - Insect bites
  - Scabies
  - Bed bugs
  - Contact dermatitis- question regarding new soaps, lotions, perfumes, laundry detergents, etc.
  - Sunburn
  - Other medications
  - Viral or fungal (shingles)
Evaluate Rash

- Where is it?
- What does it look like?
- Does it itch?
- When did it start?
- Has it spread?
- What makes it better or worse?
- Have you had an insect bite?

Mild Rash/Itching

- All drugs used in TB disease can cause rash
- Common
- Often resolves after first several weeks of treatment
- Usually do not require stopping medication
- Treat with antihistamines (Benadryl), low dose prednisone
- May do LFT's if persist
Rash: Hypersensitive Reaction

- **Petechial Rash**
  - Thrombocytopenia (Rif)
    - Compare to baseline
    - Do platelet count
    - If low suspect hypersensitive
      - Reaction to Rifampin
    - Consult with MD/expert
    - Stop Rifampin- monitor platelets until normal
    - DO NOT RESTART RIFAMPIN

Case Study

- 58 y/o male hospitalized with fever, n/s, cough, fatigue, and 30 lb. wt. loss
- New HIV diagnosis and Hep B
- RIPE started
- 2 weeks later c/o slight itching, no rash – started on benadryl
- One month into TB treatment c/o white patches to mouth-(Thrush)= Diflucan-Bactrim-no ART
- 6 days after starting HIV prophylaxis meds- pt. c/o increased itching, slight rash and benadryl no longer helping
- RX HELD- topical steroid given, told to also hold Bactrim and Diflucan
Case Study continued…..

- 2 days later, rash better- *Drug challenge begun*
  - Rifampin started
- 3 days later- Rash improving
  - INH started
- Next day- Rash worsened
  - stopped INH and added EMB
- Next day- MD at HIV clinic called, patients rash worse but found out that pt. had restarted Bactrim a couple of days before.
  - Placed on prednisone
  - Continue Rifampin/EMB
  - STOP Bactrim
  - Placed on Diflucan and Dapsone
Case Study Continued….

- 5 days later- rash better
  - added MOXI
- Next day c/o fever and severe body aches
- RX HELD
- Next day- Fever resolved-rash mild
  - restarted on Rifampin, EMB and PZA
- 1+ weeks later, c/o of overwhelming fatigue past 24-48 hours, rash is tolerable- Labs wnl
- 3 days later- rash worsened with new area developing to arms and hands
- RX HELD
- Saw MD at HIV clinic on next day – started on Prednisone taper and restarted TB meds of RIF, EMB, and LEVO, NO PZA
Case Study Continued….

- 6 days later, rash worse
- RX HELD- also held Dapsone and prednisone
- 3 days later rash not improving- red, raised and vesicular
  - Prednisone restarted
- Rash improving, drying, slight itching
- 2 weeks after last RX HELD, began rechallenge- INH only
- 1 week later rash improved some with slight itching
  - Rifampin added
  - Prednisone continued
- Within the next week rash worsened
- RX HELD!
Case Study Conclusion….

- Heartland consulted
- Recommended admission
- Rx was not restarted at TCID for another 8 days, given prednisone and topical creams
- Restarted on challenge of INH, and Rifabutin and B6
- Rash resolved

Flushing Reactions

- “Feel a hot sensation”
- Isoniazid
- Can involve face and head- may start at chest
- Resolves within 2-3 hours after meds.
- May take antihistamines
- Continue medications
- Educate on Tyramine containing Foods
Neurotoxicity

- Peripheral Neuropathy - damage of the sensory nerves of the hands and feet
  - Tingling, prickling and burning sensation of balls of feet or tips of toes, may progress to fingers and hands
  - Sensory loss can occur: ankle reflexes lost; unsteady painful gait
  - Most common in Diabetes, alcoholism, uremia, HIV infection, pregnancy, malnutrition, hypothyroidism; seizure disorder
  - INH likely causative agent

- Skimp gray
- Nervous system is vital.
- Ammonium (in body fluids)
- Bacterial infection
- Chronic, non-specific
- Common
- Erythema
- Fever (most common)
- Gastrointestinal disturbance
- Headache
- Nausea
- Vomiting

- Malnutrition feet in event:
  - Edema and other skin changes
  - Edematous, red, puffy
  - Hamstring
  - Hypothyroidism
  - Parenteral feeding
  - Peripheral neuropathy is a common side effect of antipsychotic drugs
  - Poor nutrition
  - Poor nutrition can produce severe weight loss
  - Poor nutrition, hormones with minimal quantities of iron
Neurotoxicity

- Administer Vitamin B6 (pyridoxine) 50mg daily

- Increased symptoms can increase B6 to
  - 100-150mgs daily

- B6 in doses higher than 200mg can cause neuropathy

- Gabapentin

Central Nervous System Toxicity (CNS)

- Variety of mild effects can occur
  - Drowsiness, headaches, concentration, irritability, mood changes, insomnia
  - Caution patient to expect but generally abates after initial weeks of therapy
  - Continue treatment

- Response to treatment
  - Change timing of medication
  - Use analgesics- NOT Tylenol
  - Limit caffeine
  - Increase fluids
Drug Fever

- Causative agents- Rifampin, EMB, P.A.S., Streptomycin and rarely INH
- Fever in patients who has been on therapy for several weeks
- Most commonly seen with intermittent dosing
- Patient is usually showing microbiologic and radiographic improvements
- IRIS- (Immune reconstitution inflammatory syndrome)

Drug Fever Response

- Monitor fevers
- Stop all medications
- Drug challenge
- Consult if necessary
Ophthalmic Toxicity

- Ethambutol (EMB)- most common
  - Optic Neuropathy
    - Blurring, blind spots, distorted vision, decrease color vision and pain on eye movement
  - Uveitis- Rifabutin
    - Redness, eye pain, light sensitivity, blurred vision, floaters
    - (TB itself can cause Uveitis)
- Baseline
  - Visual Acuity- Snellen chart
  - Color discrimination- Ishihara
- Monthly Exam
  - EMB-Both
  - Rifabutin- Snellen Chart
  - Refer to ophthalmologist

Myalgia's/Arthralgia's

- Variety of medications can cause this
  - INH, PZA, Rifabutin, Fluroquinolones
- Acute swelling, erythema, warm to touch, evaluate for infection, gout, ruptured tendon
  - PZA may cause asymptomatic increase in uric acid, but rarely causes gout in patients unless patient has pre-existing gout.
- NSAIDS may often help in discomfort
- Usually not necessary to stop medications
Bedaquiline (Sirturo): the first new class of drugs to obtain FDA approval for TB in 40 years (for MDR use only)

### Second Line Drugs

#### Amikacin
- Rash
- Renal toxicity
- Ototoxicity
- Vestibular toxicity
- Local pain at injection site
- Electrolyte abnormalities (hypokalemia, hypomagnesemia)

#### Levofoxacin, Gatafloxacin, Moxifloxacin
- Rash
- GI Upset
- Hepatotoxicity (rare)
- Mild CNS toxicity
- Arthralgias, rare tendon rupture
- Photosensitivity
- EKG abnormalities

#### Capreomycin
- Rash
- Renal toxicity
- Ototoxicity
- Vestibular toxicity
- Local pain at injection site
- Electrolyte abnormalities (hypokalemia, hypomagnesemia)

#### Ethionamide
- Rash
- GI Upset, may be significant
- Hepatotoxicity
- Endocrine effects (gynecomastia, hair loss, acne, impotence, menstrual irregularity, reversible hypothyroidism)
- Peripheral neuropathy
Second Line Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rash</th>
<th>CNS toxicity - seizure, depression, suicidal ideation, psychosis</th>
<th>Peripheral neuropathy</th>
<th>Skin Changes (lichenoid eruptions, Steven Johnson Syndrome)</th>
<th>PAS (Para-Amino salicylate)</th>
<th>Rash</th>
<th>G.I. Upset may be significant</th>
<th>Hepatotoxicity</th>
<th>Reversible hypothyroidism</th>
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</thead>
<tbody>
<tr>
<td>Cycloserine</td>
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<tr>
<td>Clofazamine</td>
<td>Rash</td>
<td>G.I. Upset</td>
<td>Discoloration and dryness of skin</td>
<td>Photosensitivity</td>
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<tr>
<td>Linezolid</td>
<td>Rash</td>
<td>Myelosuppression</td>
<td>Nausea and Diarrhea</td>
<td>optic neuropathy</td>
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</table>

Auditory Toxicity

- No first line drugs have this effect
  - Amikacin, Capreomycin, Streptomycin

- Perform audiometry and Vestibular screening
  - Baseline
  - Repeat monthly
  - Identify pre-existing hearing loss
  - Refer for evaluation if any decrease from baseline
Vestibular Toxicity

- Vestibular toxicity monitoring
  - Baseline and monthly vestibular screen

VESTIBULAR TESTING PROTOCOL

1. QUESTIONS: (List details and record positive answers)
   a. How is your balance?
   b. Do you fall?
   c. Any dizziness?
   d. Are you nauseated? Faint, unsteady, all the time?

2. BALANCE
   Observe for normal balance, turning and/or falling

3. WALKING
   Observe for unsteadiness, weaving and/or staggering

4. EYE POINTING
   Patient is facing you, with both eyes closed.
   Have the patient point their fingers, then place their fingers below their eyes.
   Upright your positions, ask patient to walk both hands and return fingers to proof.

5. LATERAL INVOLUTION
   Patient sits on one side (for 20 seconds)
   Look for symptoms (tackling of eyes in side-to-side)
   Upright patient to one side, wait 30 seconds, look for symptoms.
   Try the other side.

6. ROMBERG
   Patient stands, arms at sides.
   Encourage patient with your arms, but do not touch.
   Tell the patient "I will let you go next".
   Have the patient close their eyes.
   Put right foot parallel.

7. DUETT-TOROSO WALKING
   Patient stands, side之道.
   Encourage patient with your arms, but do not touch.
   Tell the patient "I will let you go next".
   Observe for unsteadiness, falling, inability to balance.
   (a small degree of unsteadiness is acceptable)
Points to remember

- All medications have side effects
- Individual patients react differently
- Recognize adverse drug effects vs. side effects
- Assess appropriately and document
- Educate, Educate, Educate
- Baseline monitoring
- Intervene rapidly
  - Prevent further morbidity/mortality
  - Minimize treatment interruptions
  - Reduce opportunities for "medical mismanagement"
  - Avoid development of psychological intolerance
  - Support adherence and the therapeutic relationship
Check Your Meds by dugg simpson

The side effects?
Oh, I have pills
for those too.

Thank you!