

# Recognizing and Responding to Adverse TB Drug Events Part II March 12, 2008

Jamey "Todd" Braun, RN, BSN, MPH  
TB Nurse Consultant  
New Mexico Department of Health  
Tuberculosis/Refugee Health Program



## Overview

DRUGS*	TOXICITIES	INFORMATION
INH Rifampin/Rifabutin PZA EMB (Fluoroquinolones: LV, MX, GT) (Aminoglycosides: AK, KN, SM)  *Treatment of TB Disease	GI Disturbances Hepatotoxicity Immune Reactions Ophthalmic Toxicity CNS/Neurotoxicity Ototoxicity Musculoskeletal Renal Toxicity	Drugs Involved Monitoring Assessment Response



## Guidelines TB Disease

- Centers for Disease Control and Prevention. Treatment of Tuberculosis: American Thoracic Society, CDC and Infectious Diseases Society of America. MMWR 2003; 52 (No. RR-11)
- Francis J. Curry National Tuberculosis Center and California Department of Health Services, 2004. Drug-Resistant Tuberculosis: A Survival Guide for Clinicians.
- Hepatotoxicity of Antituberculosis Therapy: AJRCCM, 2006; 174: 935-952



## Guidelines LTBI

- Centers for Disease Control and Prevention. Targeted Tuberculin Skin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000; 49 (No. RR-6).
- Pediatric Tuberculosis Collaborative Group. Targeted Tuberculin Skin Testing and Treatment of Latent Tuberculosis Infection in Children and Adolescents. Pediatrics 2004; 114: 1175-1201.



## Adverse Drug Events Gastrointestinal Upset

- Drugs: PZA, rifabutin, fluoroquinolones, (ethionamide, PAS, clofazimine)
  - Any drug
- Common in first few weeks of therapy
  - Nausea and vomiting are most common
  - Abdominal cramps
  - Gas
  - Diarrhea
  - Anorexia



## Adverse Drug Events Gastrointestinal Upset

- Intervention
  - Evaluate for other causes of GI symptoms, particularly hepatotoxicity
    - Hold medications
    - Repeat LFT's
  - Give a light snack before medications
  - Ask patient which medication is causing the GI upset
    - Separate from other drugs by several hours or give at bedtime
  - Space medications out during the day to lessen pill burden given as a single dose



## Adverse Drug Events Gastrointestinal Upset

- Administer antiemetics or antacids
  - Phenergan, Reglan, Zofran
  - Antacids cannot be given within 2 hours of fluoroquinolones
- Eliminate or minimize alcohol consumption
- Minimize use of NSAID's
- Diagnose and treat gastritis, acid reflux, *H. pylori* infections
  - Sucralfate (Carafate) cannot be given within 2 hours of fluoroquinolones
- Encourage hydration
- If outpatient interventions fail, hospitalization should be pursued

## Adverse Drug Events Hepatotoxicity

- Drugs:
  - INH
    - Most likely to cause hepatitis (?)
    - Hepatotoxicity appears to be increased when used with rifampin
  - Rifampin/Rifabutin
  - PZA
  - Fluoroquinolones
  - (Ethionamide)
  - (PAS)

## Adverse Drug Events Hepatotoxicity

- Risk factors
  - Chronic alcohol consumption
  - Viral hepatitis
  - Pre-existing liver disease
  - Pregnant/3 months post-partum
  - Other hepatotoxic medications
  - Previous ALT/AST or bilirubin abnormal
  - HIV-infected, particularly if on HAART therapy
  - Age > 35 years (?)

## Adverse Drug Events Hepatotoxicity

- Other hepatotoxic drugs
  - Tylenol
  - Alcohol
  - Tetracycline, erythromycin, others
  - Dilantin
  - Valproate
  - Cholesterol lowering medications
  - Antifungal drugs
  - Glucose lowering drugs
  - Valium

# Adverse Drug Events Hepatotoxicity

- Pretreatment evaluation
  - Physical examination: liver tenderness, hepatosplenomegaly, jaundice, caput medusa, spider angiomas, ascites, edema
  - Consider screening for viral hepatitis
    - HIV-infected
    - IV drug users
    - Patients from endemic areas of the world
    - Sexual or household contacts
    - Occupational exposure to infected blood
    - Undiagnosed liver disease
    - Chronic hemodialysis patients



# Adverse Drug Events Hepatotoxicity

- Laboratory monitoring
  - Baseline transaminases: all adults
  - Periodic laboratory monitoring
    - Severe, preexisting liver disease: PT/INR
    - Baseline transaminases > 3 X ULN
      - Repeat ALT, bilirubin
      - Screen for other possible causes of hepatitis
    - Liver risk factors
      - ALT (AST, bilirubin, alk. phos.) q 2-4 weeks
    - Age over 35 (?)
      - ALT (AST, bilirubin, alk. phos.) q 4-8 weeks



## Adverse Drug Events Hepatotoxicity

- Clinical monitoring
  - Face-to-face, monthly, clinical assessments
  - EARLY signs and symptoms are non-specific
    - Fatigue
    - Poor appetite
    - Taste alteration
    - Nausea
    - Abdominal discomfort
    - Bloating
    - Minimal rash

## Adverse Drug Events Hepatotoxicity

- LATER signs and symptoms
  - Vomiting
  - Abdominal pain
  - Jaundice
  - Change in color of urine and stool
  - Changes in behavior, memory loss

## Adverse Drug Events Hepatotoxicity

- If hepatitis suspected, hold medications and repeat LFT's immediately
  - Continue therapy
    - ALT < 5 times upper limit of normal and asymptomatic
      - 20% of patients on standard therapy have asymptomatic elevation of transaminases
  - Hold therapy
    - ALT > 3 times upper limit of normal and symptomatic
    - ALT > 5 times upper limit of normal and asymptomatic
    - Disproportionate increases in bilirubin and/or alk. phos.
  - Evaluate for viral hepatitis, biliary disease and exposure to other hepatotoxins (alcohol, hepatotoxic drugs)

## Adverse Drug Events Hepatotoxicity

- Consider a “liver friendly regimen”
  - Likely to be a delay of greater than 2-3 weeks in restarting therapy while waiting for LFT's to normalize
  - Patient would not tolerate well an interruption in therapy
    - Early in treatment course
    - Clinically ill
    - AFB smear positive
  - EMB, fluoroquinolone, aminoglycoside

# Adverse Drug Events Hepatotoxicity

- Restarting therapy
  - When ALT < 2 times upper limit of normal
    - One hepatotoxic drug plus EMB
      - Usually rifampin
        - » Least hepatotoxic
        - » Most active drug
    - Monitor ALT for 3-7 days
      - Stop therapy if symptoms recur or ALT increases
    - If initial drugs are tolerated, add second hepatotoxic drug (INH) and monitor carefully, as above
      - If symptoms recur or ALT increases, stop last drug added

# Adverse Drug Events Hepatotoxicity

- If INH, RIF and EMB tolerated, evaluate need for PZA ... usually not needed
  - May supplement with fluoroquinolone if extensive disease
  - Continue EMB until drug susceptibility results completed
  - Extend therapy (9 months total) if PZA not given for full 8 weeks
- Some patients may tolerate only one hepatotoxic drug (ex: cirrhosis)
  - Adjust duration of regimen and include second-line drugs, as needed
    - RIF, EMB, fluoroquinolone X 12-18 months
    - INH, EMB and fluoroquinolone X 12-18 months, plus possible aminoglycoside for first 2 months
- Rarely, patients tolerate none of the first-line hepatotoxic drugs (ex: encephalopathic disease)
  - Treat as MDR-TB: EMB, aminoglycoside, fluoroquinolone, + second-line oral drug X 18-24 months

## Adverse Drug Events Hepatotoxicity

- Increased risk of hepatotoxicity seen in contacts of MDR-TB treated with ...
  - PZA/levofloxacin
  - PZA/EMB
- LFT's q 2-4 weeks until stable, then monthly
- EMB/levofloxacin may be preferred regimen

## Adverse Drug Events Hepatotoxicity

- Case study
  - 38 yo male diagnosed with PTB during incarceration
  - 3/13: started standard RIPE regimen
    - Baseline laboratory values: ALT 42, AST 63
  - 4/15: changed to BIW dosing; EMB discontinued when susceptibility results showed isolate to be susceptible to INH/RIF
  - 6/4: F/U laboratory values: ALT 304, AST 97
    - Asymptomatic for hepatitis

## Adverse Drug Events Hepatotoxicity

- What is the appropriate response?
  - Hold TB medications!
  - ALT  $\geq$  5X upper limit of normal in asymptomatic patient or  $\geq$  3X upper limit of normal in patient with signs/symptoms consistent with hepatitis
- When can therapy be safely restarted?
  - Once ALT is  $<$  2X ULN

## Adverse Drug Events Hepatotoxicity

- Should other TB therapy be started?
  - If it is likely there will be a delay of  $>$  2-3 wks, consideration can be given to starting a “liver friendly” regimen (EMB, fluoroquinolone, aminoglycoside) while waiting for LFT’s to normalize

## Adverse Drug Events Hepatotoxicity

- What treatment should be considered when ALT returns to  $< 2X$  normal?
  - RIF/EMB X 3-7 days
    - Monitor LFT's twice weekly
  - If LFT's stable after 3-7 days, add INH
    - Continue to monitor LFT's twice weekly
  - If LFT's stable, EMB can be discontinued and pt. returned to BIW dosing and tx. completed with INH/RIF

## Adverse Drug Events Immune Reactions

- Maculopapular rash and pruritis
  - Evaluating the rash
    - When did it start?
    - Where is it?
    - What does it look like now? Is that different?
    - Has it spread?
    - What makes it better or worse?
    - Does it itch?
    - Have you had an insect bite?

# Adverse Drug Events Immune Reactions

- Other possible causes
  - Scabies
  - Insect bites
  - Contact dermatitis
    - Question patient about new soaps, lotions, perfumes, laundry detergents, etc.
  - Sunburn
  - Dry skin
  - Other drugs, especially new agents
  - Viral or fungal infections
  - Etc.

# Adverse Drug Events Immune Reactions

- Drug rash
  - Usually begins on chest and later spreads to upper arms and thighs
  - Itches
  - Maculopapular
  - Urticaria/hives that are new
  - May be associated with more severe symptoms of airway compromise, angioedema, etc.
  - Occurs and worsens after medications



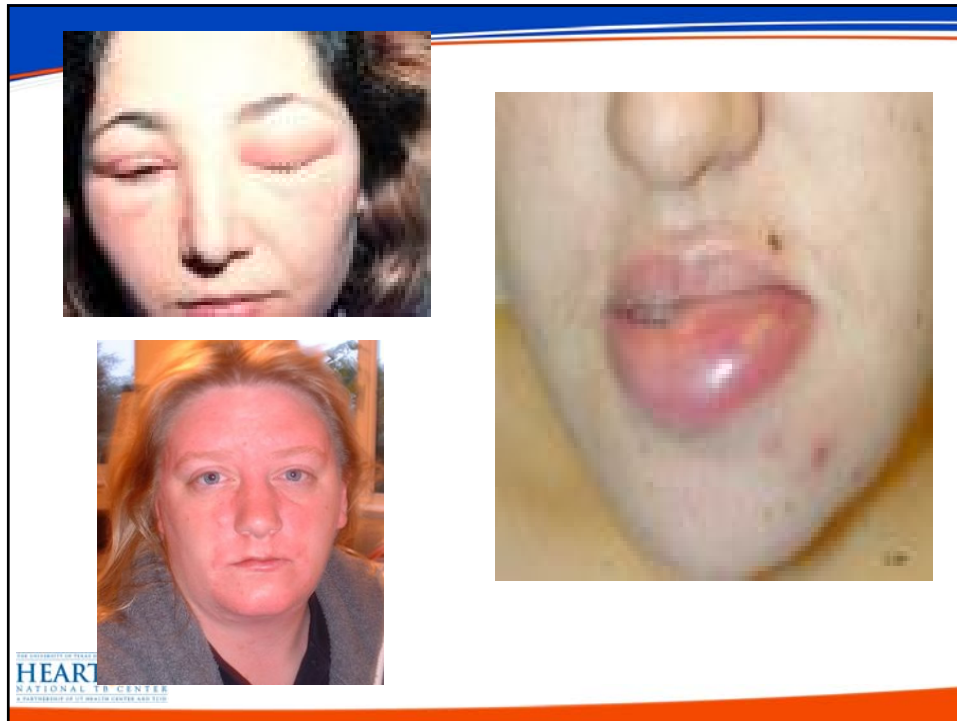
## Adverse Drug Events Immune Reactions

- Mild, limited maculopapular rashes and/or itching
  - Common
  - Often resolve after first several weeks of treatment
  - Usually do not require stopping medication
  - Treated symptomatically with Benadryl, other antihistamines, low-dose prednisone
- Petechial rash
  - May be a sign of a rifampin hypersensitivity reaction and thrombocytopenia
    - Hold medications and check platelet count
    - If low, stop rifampin and monitor platelet count until it returns to baseline
    - Do not restart rifampin



## Adverse Drug Events Immune Reactions

- Urticaria/Hives
  - Hold medications until reaction resolves
  - If no evidence of anaphylaxis, angioedema, airway compromise, may elect to attempt a drug rechallenge or desensitization under controlled conditions
- Severe Drug Reactions
  - Generalized rashes associated with fever, other systemic symptoms, mucous membrane involvement are characteristic of Stevens-Johnson Syndrome
    - Do not attempt to rechallenge or desensitize patient to the drugs



## Adverse Drug Events Immune Reactions

- Case study
  - 77 yo female contact to daughter, a PTB suspect
  - 1/31: initial CV
    - TST + (15 mm)
    - C/O several weeks of productive cough, now asymptomatic
    - CXR: blunting of CPA
    - Sputum AFB smear + (<1/HPF); culture pending
    - PMH: arthritis, 71 yr tobacco hx, hospitalized 1 mo prior for pneumonia/bronchitis
  - 2/4: started RIPE standard regimen
    - Baseline LFT's WNL

## Adverse Drug Events Immune Reactions

- 2/13: ER visit; c/o generalized rash, swelling of lower lip
  - RX: injection (?) plus prednisone 20 mg. BID
  - TB medications held
- Local TB physician consulted
  - Reinitiate one drug at a time to identify offending agent
  - Request consult from State TB expert physician consultant

## Adverse Drug Events Immune Reactions

- 2/17: received dose of INH 300 mg. in TB clinic
  - Prior to dose, c/o itching of scalp, no visible rash or swelling
  - Clinic RN requested consult from State TB physician consultant that day
- What concerns might you have in rechallenging this patient with TB medications?

## Adverse Drug Events Immune Reactions

- F/U
  - Provider given rechallenge protocol, but elected to hold TB medications pending further evaluation
  - All sputum cultures eventually reported negative for AFB
  - CXR: minimal abnormality, not suggestive of TB
  - Patient remained asymptomatic
  - + TST may be from recent exposure to daughter or may represent old infection in a 77 yo female living along the US/Mexico border
  - Consider risks vs. benefits of treatment

## Adverse Drug Events Ophthalmic Toxicity

- Drugs: EMB, rifabutin
- Baseline and monthly assessment
  - Question patient regarding visual disturbances
  - Observe children for eye rubbing, excessive blinking, sitting closer to TV, difficulty with accurate grasping
  - Baseline acuity testing with Snellen, Illiterate or Kindergarten charts and color discrimination testing with Ishihara plates
    - Monthly screening if EMB doses > 15-25 mg/kg, receiving EMB for > 2 mo., or renal insufficiency
  - Educate patient to report any changes in vision, erythema or eye pain

## Visual Acuity Screening

Initial Snellen Reading	Reading Indicating Significant Decrease	Significant Number of Lines	Decrease in Number of Points
20/13	20/25	3	12
20/15	20/25	2	10
20/20	20/30	2	10
20/25	20/40	2	15
20/30	20/50	2	20
20/40	20/70	2	30
20/50	20/70	1	20

## Adverse Drug Events Ophthalmic Toxicity

- Optic neuropathy
  - EMB is most common drug causing toxicity to optic nerve
    - Although a small number of patients have developed sudden, irreversible vision loss, most experts feel that doses of 15 mg. per kg. given for 2 months or less are rarely associated with toxicity to the optic nerve
  - Decreased visual acuity, color blindness, scotoma (“blind spots”)
  - Stop EMB
  - Refer to ophthalmologist
  - Do not restart EMB unless another cause is identified

# Adverse Drug Events Ophthalmic Toxicity

- Uveitis
  - Rifabutin given in higher doses or with drugs that decrease renal clearance, e.g., protease inhibitors can cause generalized inflammation of the eye
  - Painful, erythematous eyes and blurred vision
  - Hold rifabutin until symptoms resolve
    - Rifabutin can be reinstated at a lower dose
  - Consider referral to ophthalmologist to rule-out other causes
  - If infection ruled-out, steroid eye drops may be used
  - If recurring uveitis, stop rifabutin

# Adverse Drug Events Ophthalmic Toxicity

- Case study
  - 21 yo male dx'ed with PTB in October
    - February-May: incarcerated in county jail
    - May: onset of illness (fever, chills, productive cough, chest pain, night sweats, wt. loss)
    - 10/7: initial CV
      - CXR: LUL cavitary infiltrate
      - AFB smear + (1-10/HPF)
  - 10/12: started RIPE standard regimen
  - 11/9: isolate reported INH/SM resistant
    - Pt. improving: afebrile, 6 lb wt. gain, night sweats resolved, cough improving
    - INH discontinued; continued on RIF, PZA, EMB to complete 9 mo. tx.

## Adverse Drug Events Ophthalmic Toxicity

- March: pt. c/o difficulty driving, reading road signs
  - Advised by LHD nurse to see “eye doctor”
    - 3/21: seen by optometrist and given RX for corrective lenses (3/30)
  - EMB continued
- 5/3: pt c/o worsening vision
  - Visual acuity: 20/200 both eyes
    - Baseline visual acuity (October): 20/20 both eyes
  - 5/5: EMB discontinued; continued on RIF, PZA and LV added to regimen to complete 9 mo of tx.
  - Referred to retinal specialist

## Adverse Drug Events Ophthalmic Toxicity

- F/U
  - Seen by retinal specialist in May and June
    - DX: EMB optic neuropathy
    - Central scotoma on right and parascotoma on left
    - Vision uncorrected: 20/200
    - Vision best corrected: 20/60
  - LHD nurse admitted not performing visual acuity screening (Snellen chart), only color discrimination testing (Ishihara plates)

## Adverse Drug Events Neurotoxicity

- Peripheral neuropathy
  - Drugs: INH, EMB, (ethionamide, cycloserine)
    - INH binds with pyridoxine (Vitamin B6), limiting supply
  - Dose related: 0.2% - 1.2% at recommended doses
  - More common in patients with
    - Diabetes
    - Alcoholism
    - HIV infection
    - Hypothyroidism
    - Pregnancy/Breastfeeding
    - Older age
    - Renal failure
  - Inadequate dietary intake of pyridoxine



## Adverse Drug Events Neurotoxicity

- Initial symptoms: numbness, tingling, prickling, burning in balls of feet/tips of toes; may progress to hands and arms
  - Usually symmetrical
  - May progress to sensory loss (light touch, pain, position), muscle aches/weakness, loss of reflexes, unsteady gait
- Pyridoxine prophylaxis
  - 25-50 mg. daily usually adequate for standard treatment regimen
    - May be increased to 100-150 mgs. daily
    - At higher doses, toxicity may develop in patients with ESRD



# Adverse Drug Events Central Nervous System

- Drugs: INH, fluoroquinolones, amikacin, (ethionamide, cycloserine)
- Mild effects
  - Drowsiness, headaches, loss of concentration, irritability, agitation, mild mood changes, insomnia
  - Usually occur early in therapy and tend to lessen with time
  - Usually not necessary to discontinue medication
  - Intervention
    - Give medication at time of day to minimize effects
    - Analgesics/NSAID's may relieve headache
    - Limit caffeine intake
    - Exercise

# Adverse Drug Events Central Nervous System

- Depression
  - Situational vs. drug induced
  - Intervention
    - Assess/address underlying psychosocial issues
    - Assess for co-existing substance abuse and refer for counseling
    - Assess for suicidal ideation
    - If significant, refer for psychiatric evaluation/consideration for trial of antidepressant therapy
- Psychosis

## Adverse Drug Events Central Nervous System

- Case study
  - 48 yo female with drug susceptible PTB
  - PMH significant for treatment for depression 1992-1996
  - 1/15: started RIPE standard regimen
  - 1/24: reported to ER with c/o insomnia, loss of energy, fatigue, anorexia, difficulty concentrating, unable to work, uncontrollable crying spells, suicidal ideation
    - Prescribed Effexor-XR
    - Discharged to her home under husband's supervision with f/u appointment for psychiatric evaluation

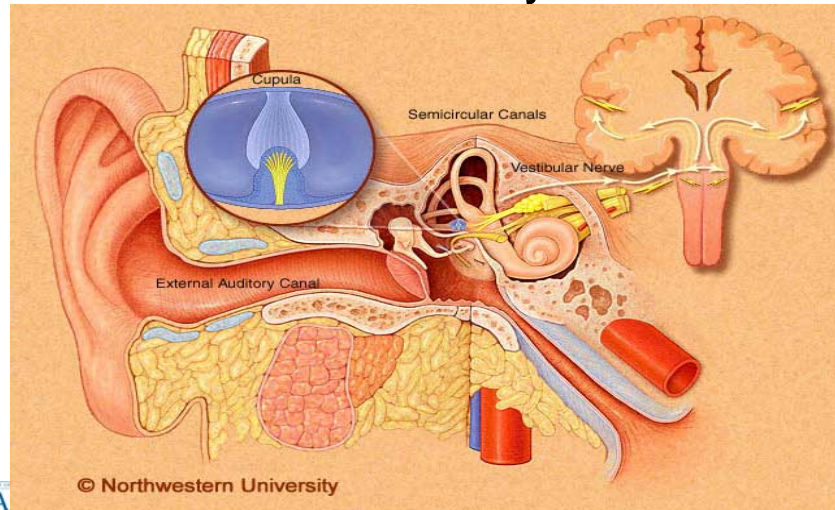
THE UNIVERSITY OF TEXAS HEALTH CENTER AT DALLAS  
**HEARTland**  
NATIONAL TB CENTER  
A PARTNERSHIP OF UT HEALTH DALLAS AND UTMSU

## Adverse Drug Events Central Nervous System

- 1/26: initial evaluation by psychiatrist
  - Dx'ed with substance induced mood disorder
  - INH held; continued on RIF, PZA, EMB
- 2/1: CV for DOT
  - Described as “like a different person”; reported feeling better, mood and affect brighter, make-up applied, neatly dressed, denied suicidal ideation
- 2/10: f/u by psychiatrist
  - No evidence of depressive signs/symptoms
  - Effexor-XR continued

THE UNIVERSITY OF TEXAS HEALTH CENTER AT DALLAS  
**HEARTland**  
NATIONAL TB CENTER  
A PARTNERSHIP OF UT HEALTH DALLAS AND UTMSU

## Adverse Drug Events Ototoxicity



HEA  
NATIONAL TD CENTER  
UNIVERSITY OF ILLINOIS HEALTH CENTER AND IUCR

## Adverse Drug Events Ototoxicity

- Drugs
  - Aminoglycosides: AK, KM, SM
    - SM most commonly associated with ototoxicity
  - Capreomycin
- 8<sup>th</sup> cranial nerve
- Auditory and/or vestibular toxicity

HEART Land  
NATIONAL TD CENTER  
UNIVERSITY OF ILLINOIS HEALTH CENTER AND IUCR

## Adverse Drug Events Ototoxicity

- Risk factors
  - Advanced age
  - Total dose: cumulative effect
    - Duration of therapy (>10 days)
  - Renal impairment
  - Dehydration
  - Co-administration of “loop” diuretics (Lasix, Bumex, Demadex)
  - Increased trough and/or peak serum drug levels
  - Prior aminoglycoside/capreomycin exposure

## Adverse Drug Events Auditory Toxicity

- Signs and symptoms
  - Early
    - Fullness, ringing, roaring, hissing, or “buzzing” in ears
    - High frequency hearing loss (not conversational frequencies)
      - “s”, “th”, and “fff” sounds may be missed or confused
      - Speech of women and children may be more difficult to understand
  - Generally reversible

## Adverse Drug Events Auditory Toxicity

### – Later

- Impairment at lower frequencies (conversational frequencies)
  - Problem hearing on the telephone?
  - Trouble hearing when noisy background or when two or more people are talking at once?
  - Times when people seem to mumble or not speak clearly?
  - Often asking people to repeat themselves?
  - People complain that you turn the TV volume up too high?
- Permanent or only partially reversible

## Adverse Drug Events Auditory Toxicity

- Perform audiometry at baseline and repeat monthly
  - Identify pre-existing hearing loss
  - Refer for evaluation if any decrease from baseline

## Adverse Drug Events Vestibular Toxicity

- Signs and symptoms
  - Parallel cochlear damage
  - Early
    - Fullness and intermittent ringing in ears
      - 2-3 times per week dosing may allow continued use of injectable agent for another month or more
        - » Close observation for progression of S/S: tinnitus and unsteadiness
        - » Careful monitoring of TDL's

## Adverse Drug Events Vestibular Toxicity

- Later
  - If tinnitus or unsteadiness develop, hold all drugs for several days to see if symptoms improve
    - If due to vestibular toxicity, symptoms generally do not improve
  - If injectable agent continued/substituted, permanent S/S of toxicity will develop
    - Vertigo
    - Dizziness
    - Nausea
    - Ataxia
    - Nystagmus

## Adverse Drug Events Vestibular Toxicity

- General prevention and monitoring
  - If >59 yrs., decrease dose to 10 mg./kg., 5-7 days/week
  - Baseline and periodic assessment of renal function
    - BUN, Cr/GFR
    - CrCl, if any concerns and monitor Cr/GFR weekly for 1<sup>st</sup> several weeks, then monthly
    - If baseline CrCl <70 ml./min., adjust dose to 12-15 mg./kg., 2-3 days/week

## Adverse Drug Events Vestibular Toxicity

- Initial and periodic monitoring of TDL's with appropriate dose adjustments
- Reduce dosing interval to 3 times/week after 4-6 months, if culture (-)
- Avoid "loop" diuretics
- Maintain adequate hydration
- Vestibular toxicity monitoring
  - Baseline and monthly vestibular screen
    - Assess
      - Hearing: fullness, stuffiness, unusual noises, hearing loss
      - Dizziness, unsteadiness, giddiness, lightheadedness, floating sensation

## Adverse Drug Events Vestibular Toxicity

- Weakness
- Nausea
- General gait and balance: weaving, swaying, staggering
- Heel-to-Toe walk: jerkiness, excess swaying, falling
- Romberg: excess swaying, falling
- Past-Pointing: consistent deviation to one side

## Adverse Drug Events Musculoskeletal

- Myalgias/Arthralgias
  - Drugs: PZA, levofloxacin, rifabutin (at higher doses)
  - Usually not necessary to discontinue medications
  - NSAID's usually helpful in relieving discomfort
  - If acute swelling, erythema, warmth present, evaluate for infection, autoimmune disease, gout
    - PZA causes asymptomatic increase in uric acid, but rarely causes gout except in patients with preexisting gout or decreased renal function
  - If receiving injectable therapy, consider possible electrolyte imbalance; draw serum electrolytes and correct deficiencies

## Adverse Drug Events Musculoskeletal

- Tendonitis/Tendon Rupture
  - Drugs: levofloxacin/other fluoroquinolones
  - Tendon rupture (usually Achilles) is rare
  - If tendon inflammation mild:
    - Rest the joint/NSAID's
    - Evaluate dose and reduce if possible
    - If symptoms progress, stop the fluoroquinolone
  - If tendon inflammation is significant
    - Stop the fluoroquinolone
    - Rest the joint/NSAID's
    - Evaluate risks and benefits of continuing drug in regimen



## Adverse Drug Events Nephrotoxicity

DRUG	CHANGE IN FREQUENCY	DOSE/FREQUENCY (CrCl < 30 ml/min or Hemodialysis)
INH	No Change	300 mg q day or 900 mg TIW
RIF	No Change	600 mg q day or 600 mg TIW
EMB	Yes	15-25 mg/kg TIW
PZA	Yes	25-35 mg/kg TIW
Levofloxacin	Yes	750-1000 mg TIW
Aminoglycosides	Yes	12-15 mg/kg TIW



## Adverse Drug Events Nephrotoxicity

- Drugs: amikacin/other aminoglycosides, (capreomycin)
- Baseline serum creatinine
  - 24-hour creatinine clearance if baseline serum creatinine abnormal
- Lower initial dose in patients over age 59 yrs. (10 mg. per kg.; max. dose 750 mg.)
- If baseline creatinine clearance less than 70ml./min., consider use of intermittent dosing initially
- Monitor peak and trough serum drug levels and adjust dose accordingly
- Encourage hydration



## Adverse Drug Events Nephrotoxicity

- Monthly serum creatinine; repeat 24-hour creatinine clearance if necessary
- Observe for decreased urine output and/or edema
- If renal function decreases during treatment
  - Hold injectable agent 1-2 weeks until renal function stabilizes
  - Ensure adequate hydration
  - Check serum electrolytes and correct, if needed
  - Evaluate/Adjust dosing of other drugs, as needed
  - Consider intermittent dosing with appropriate dosing adjustment
  - Monitor peak/trough serum drug levels
  - Monitor renal function carefully

