Learning Objectives

- **Learning Objectives:**
  - Describe appropriate treatment of patients with pneumonia, urinary tract infections, central nervous system infections, skin and soft tissue infections, osteomyelitis, intra-abdominal infections, and endocarditis.
  - Identify appropriate preventive therapy for pneumonia, central nervous system infections, endocarditis, and surgical wound infections.

Agenda

- Pneumonia
- Urinary Tract Infections
- Central Nervous System Infections
- Skin and Soft Tissue Infections
- Osteomyelitis
- Intra-abdominal Infections
- Endocarditis
- Clostridium difficile Infection
- Surgical Prophylaxis

Pneumonia

- RL is a 68 year old male
- Chief complaint: cough and shortness of breath
- HPI: Symptoms began 4 days ago and have worsened over the last 24 hours. He is coughing up yellowish-green sputum and complains of chills with a fever to 102.4°F
- PMH: CAD with an MI 5 years ago, CHF, hypertension and osteoarthritis.

Conflict of Interest Disclosures

Curtis Smith, Pharm.D.
- I have no conflicts of interest related to this presentation.

Pneumonia

- SH: rarely drinks alcohol; quit smoking
- Meds on admission: lisinopril 10mg daily, hydrochlorothiazide 25mg daily and acetaminophen 650mg QID.
- PE: alert and oriented - VS: Temp 101.8°F, HR 100, RR 24, BP 142/94.
- Labs: nl except BUN=32 mg/dl (Scr=1.23 mg/dl).
- Blood gases: pH 7.44, pCO2 35, pO2 82, O2 sat 90%.
- Sputum specimen is not available.
Pneumonia

- Community-acquired
  - Symptoms in RL: cough with sputum, SOB, chills, fever
  - Potential for complicated course:
    - > 65
    - comorbid illnesses
    - high fever
    - CURB-65 score = 2
  - Most common organisms
    - S. pneumoniae
    - M. pneumoniae
    - H. influenzae

Pneumonia

Which is the best empiric therapy for RL?

A. Ampicillin/sulbactam 1.5g IV q6h
B. Piperacillin/tazobactam 4.5g IV q6h plus gentamicin 180mg IV q12h
C. Ceftriaxone 1g IV q24h plus azithromycin 500mg IV daily
D. Doxycycline 100mg IV q12h

Pneumonia

- Community-acquired - Outpatient Therapy
  - Previously healthy / No antibiotics in 3 months
    - Macrolide (clarithromycin or azithromycin)
    - Doxycycline
  - Comorbidities / Antibiotics in 3 months
    - Fluoroquinolone (levo- 750mg, moxi-, gemi-)
    - Macrolide (or doxycycline) with high-dose amoxicillin (1g TID) or amoxicillin/clavulanate (2g BID) or cephalosporin (ceftriaxone, cefotaxime, cefpodoxime)

Pneumonia

- Community-acquired (Moderately severe) – Inpatient Therapy
  - Fluoroquinolone (levo- 750mg, moxi-, gemi-)
  - Macrolide (or doxycycline) plus 3rd generation cephalosporin
  - Macrolide (or doxycycline) plus ampicillin
  - Macrolide (or doxycycline) plus ertapenem

Pneumonia

- Community-acquired (Severe) – Requiring ICU Therapy
  - ampicillin/sulbactam plus a respiratory fluoroquinolone or azithromycin
  - 3rd generation cephalosporin plus a respiratory fluoroquinolone or azithromycin
  - may also need broader antibacterial activity
  - MRSA empirical therapy:
    - ICU admission
    - Necrotizing or cavitary infiltrates
    - Empyema

Pneumonia

Which is the best empiric therapy for RL?

A. Ampicillin/sulbactam 1.5g IV q6h
B. Piperacillin/tazobactam 4.5g IV q6h plus gentamicin 180mg IV q12h
C. Ceftriaxone 1g IV q24h plus azithromycin 500mg IV daily
D. Doxycycline 100mg IV q12h
BP is a 66 year old female
HPI: CABG x2 8 days ago, now on ventilator in ICU. She is spiking temps and a tracheal aspirate shows many WBCs and Gram-negative rods.
PMH: CAD with an MI 2 years ago, COPD, and hypertension.

Which is the best empiric therapy for BP?

A. Ceftriaxone 1 g IV daily plus gentamicin 480 mg IV every 24 hours plus linezolid 600 mg IV q12h
B. Piperacillin/tazobactam 4.5 g IV every 6 hours
C. Levofloxacin 750 mg IV daily plus linezolid 600 mg IV q12h
D. Cefepime 2 g IV every 12 hours plus tobramycin 480 mg IV every 24 hours plus vancomycin 15 mg/kg IV q12h

Nosocomial pneumonia

- Hospital-acquired pneumonia
- Ventilator-associated pneumonia
- Health-care associated pneumonia

Risk factors in BP
- Mechanical ventilation
- Recent CABG
- ICU stay/Prolonged hospitalization
- Elderly
- Underlying chronic lung disease
- Gram-negative organisms and S. aureus predominate

Nosocomial pneumonia – Early onset (< 5 days) and no risk factors for MDR organisms
- Third-generation cephalosporin (cefotaxime or ceftriaxone)
- Fluoroquinolone (levofloxacin, moxifloxacin, ciprofloxacin)
- Ampicillin-sulbactam
- Ertapenem

Nosocomial pneumonia – Late onset (≥ 5 days) or risk factors for MDR organisms
- Cefazidime or cefepime plus aminoglycoside or fluoroquinolone (ciprofloxacin, levofloxacin)
- Imipenem or meropenem or doripenem plus aminoglycoside or fluoroquinolone (ciprofloxacin, levofloxacin)
- Piperacillin-tazobactam plus aminoglycoside or fluoroquinolone (ciprofloxacin, levofloxacin)
- Vancomycin or linezolid should be used only if methicillin-resistant S. aureus (MRSA) is strongly suspected
  - History of MRSA infection/colonization, recent hospitalization or antibiotics, or presence of invasive health-care devices, or there is a high incidence locally (>5-10%).

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Pneumonia

- Nosocomial pneumonia
  - Risk factors for MDR organisms
    - Antibiotic therapy within the last 90 days
    - Hospitalization ≥ 5 days
    - High resistance in community or hospital unit
    - Risk factors for health-care associated pneumonia (recent hospitalization, nursing home, home care, home infusion, chronic dialysis)
    - Immunosuppressive disease and/or therapy

Which is the best empiric therapy for BP?

A. Ceftriaxone 1 g IV daily plus gentamicin 480 mg IV every 24 hours plus linezolid 600 mg IV q12h
B. Piperacillin/tazobactam 4.5 g IV every 6 hours
C. Levofloxacin 750 mg IV daily plus linezolid 600 mg IV q12h
D. Cefepime 2 g IV every 12 hours plus tobramycin 480 mg IV every 24 hours plus vancomycin 15 mg/kg IV q12h

What vaccinations would you recommend?

A. BP does not need any vaccinations
B. BP should receive pneumococcal now and influenza vaccine in the fall
C. BP should receive influenza in the fall but due to her current infection pneumococcal vaccine is not needed
D. BP should receive pneumococcal now but influenza vaccine is not needed

Vaccinations

- Pneumococcal vaccine
  - Persons aged ≥ 65 years
  - Persons 2-64 with chronic diseases
  - Persons 2-64 who are asplenic
  - Persons 2-64 living in special environments
  - Immunocompromised patients
  - Persons 18-64 who smoke or have asthma
- Influenza vaccine
  - Everyone older than 6 months should receive the vaccine annually

Vaccinations

- Influenza Vaccine
  - Intranasal live attenuated vaccine (FluMist)
    - indicated for persons 2-49 years of age without underlying illnesses
    - inactivated vaccine preferred for vaccinating household members, health-care workers, and others who have close contact with immunosuppressed
  - High dose trivalent influenza vaccine (High Dose Fluzone)
    - indicated for people over 64 years of age
    - at this time the CDC does not have a preference for using this vaccine over the regular influenza vaccine.
**Pneumonia**

What vaccinations would you recommend?

- A. BP does not need any vaccinations
- B. BP should receive pneumococcal now and influenza vaccine in the fall
- C. BP should receive influenza in the fall but due to her current infection pneumococcal vaccine is not needed
- D. BP should receive pneumococcal now but influenza vaccine is not needed

**Urinary Tract Infections**

- GN is a 62 year old female
- Chief complaint: 3 day history of urinary frequency and dysuria.
- HPI: Over the last 24 hours she has had nausea, vomiting and flank pain.
- PMH: Type 2 DM, HTN, multiple DVTs
- Meds on admission: glyburide 5mg po daily, enalapril 10mg po BID, warfarin 3mg po daily and metoclopramide 10mg po QID.

**Urinary Tract Infections**

- PE: alert and oriented - VS: Temp 102.8°F, HR 120, RR 16, BP lying down: 140/75, standing 110/60.
- Labs: Normal except INR=2.7, BUN=26 mg/dl, Scr=1.88 mg/dl and WBC = 12,000/mm³.
- UA: turbid, 2+ glucose, pH 7.0, protein 100 mg/dl, 50-100 WBC, + nitrites, 3-5 RBC, bacteria and casts.

**Urinary Tract Infections**

How should GN be treated?

- A. TMP/SMZ DS po BID for 7 days
- B. Ciprofloxacin 400mg IV BID then 500mg po BID for 10 days
- C. Gentamicin 140mg IV q24h for 3 days
- D. Tigecycline 100 mg once, then 50 mg every 12 hours and then doxycycline 100 mg 2 times/day—duration of antibiotics: 10 days.

**Urinary Tract Infections**

- Community-acquired UTI organisms

**Urinary Tract Infections**

- Nosocomial UTI organisms

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Urinary Tract Infections

- Predisposing factors in GN:
  - age
  - female
  - diabetes mellitus

- Cystitis vs. Pyelonephritis
  - Symptoms: dysuria, frequency and urgency only vs. these symptoms plus nausea, vomiting, flank pain, fever, increased WBC, casts

- Male sex
- Hospital-acquired
- Pregnancy
- Anatomical abnormality of the urinary tract
- Childhood urinary tract infection
- Recent antimicrobial use
- Diabetes
- Indwelling urinary catheter
- Recent urinary tract instrumentation
- Immunosuppression

Urinary Tract Infections

- Acute uncomplicated cystitis
  - TMP/SMZ
  - Nitrofurantoin
  - Fosfomycin
  - Alternatives:
    - Fluoroquinolones
    - Beta lactams

- Acute uncomplicated pyelonephritis
  - Fluoroquinolone
    - If uropathogen resistance > 10% use initial dose of long acting beta lactam or once daily aminoglycoside
  - TMP/SMZ
    - If sensitivities unknown use initial dose as listed above
  - Beta lactam
    - Less effective – use initial dose as listed above

- Complicated UTIs
  - Fluoroquinolone
  - Aminoglycoside
  - Extended spectrum beta lactam (penicillin, cephalosporin, carbapenem)
  - Pregnancy
    - Amoxicillin
    - Nitrofurantoin
    - Cephalexin
    - TMP/SMZ

How should GN be treated?

A. TMP/SMZ DS po BID for 7 days
B. Ciprofloxacin 400mg IV BID then 500mg po BID for 10 days
C. Gentamicin 140mg IV q24h for 3 days
D. Tigecycline 100 mg once, then 50 mg every 12 hours and then doxycycline 100 mg 2 times/day—duration of antibiotics: 10 days.
Urinary Tract Infections
- Catheter-related UTIs
  - short-term indwelling catheters
  - long-term indwelling catheters
- Prostatitis
  - acute
  - chronic
- Epididymitis

Skin and Soft Tissue Infections
- Acute cellulitis
  - S. pyogenes, S. aureus (MRSA empirical therapy if purulent cellulitis or hospitalized patients with complicated SSTI)
- Erysipelas
  - S. pyogenes
- Necrotizing fasciitis
  - Streptococcal
  - Mixed - includes anaerobes
- Shingles vaccine (Zostavax®)

Diabetic Foot Infections
- GN now has right foot ulcer
- Ulcer: red, swollen, deep - ? osteomyelitis
  Which organism(s) is (are) responsible?
  A. S. pyogenes
  B. P. aeruginosa
  C. S. aureus
  D. Polymicrobial with Gm+, Gm- and anaerobes

Diabetic Foot Infections
- Due to neuropathy, vasculopathy, and immunologic defects
- Generally polymicrobial
- Preventative therapy:
  - examine feet
  - wear proper shoes
  - no barefoot walking
  - keep feet clean and dry
  - have toenails cut properly

Diabetic Foot Infections
- GN now has right foot ulcer
- Ulcer: red, swollen, deep - ? osteomyelitis
  Which organism(s) is (are) responsible?
  A. S. pyogenes
  B. P. aeruginosa
  C. S. aureus
  D. Polymicrobial with Gm+, Gm- and anaerobes

Diabetic Foot Infections
- Which is the best empiric therapy for GN?
  A. Nafcillin 2g IV q6h for 6-12 weeks
  B. Tobramycin 120mg IV q12h plus levofloxacin 750mg IV daily for 1-2 weeks
  C. Piperacillin/tazobactam 3.375g IV q6h for 1-2 weeks
  D. BKA followed by ceftriaxone 1g IV q24h for 1 week
**Diabetic Foot Infections**

- Shallow infection - treat like cellulitis
- Deep, limb-threatening - broad-spectrum agents
- Additional therapy
  - becaplermin (Regranex®) - topically
  - surgical amputation

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**Diabetic Foot Infections**

Which is the best empiric therapy for GN?

A. Nafcillin 2g IV q6h for 6-12 weeks
B. Tobramycin 120mg IV q12h plus levofloxacin 750mg IV daily for 1-2 weeks
C. Piperacillin/tazobactam 3.375g IV q6h for 1-2 weeks
D. BKA followed by ceftriaxone 1g IV q24h for 1 week

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**Osteomyelitis**

WA is a 55 year old male

- Chief complaint: weight loss, malaise and severe back pain and spasms that have progressed over the last 2 months; LE loss of sensation
- PMH: 4 months PTA – surgery for fx tibia and subsequent infection; also has hypertension and diverticulitis
- PE: alert and oriented - VS: Temp 99.4°F, HR 88, RR 14, BP 130/85

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**Osteomyelitis**

Labs: WNL. WBC = 14,300, ESR = 89 mm/hr and C-reactive protein = 12 mg/dL.

- MRI: bony destruction of the lumbar vertebrae 1 and 2. Confirmed by a bone scan.
- CT guided bone biopsy growing Gram-positive cocci in clusters.

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**Osteomyelitis**

How should WA be treated?

A. Vancomycin 15 mg/kg IV every 12 hours; total antibiotic duration 6 weeks
B. Nafcillin 2 g IV every 6 hours; total antibiotic duration 2 weeks
C. Levofloxacin 750mg oral daily; total antibiotic duration 6 weeks
D. Ampicillin/sulbactam 3g IV every 6 hours; total antibiotic duration 2 weeks

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**Osteomyelitis**

- Hematogenous spread
  - Primarily children
  - Risk factors: bacteremia, sickle cell disease
  - Organisms: usually monomicrobial
    - Children: *S. aureus*
    - Adult: *S. aureus*
    - Sickle cell: Salmonella, *S. aureus*
  - IV drug users: *Pseudomonas*
**Osteomyelitis**

- **Contiguous spread**
  - Primarily adults
  - Risk factors: ORIF, GSW, dental and soft tissue infections
  - Organisms: usually mixed
    - *S. aureus*
    - Other Gram positive (*S. epidermidis*, Strep)
    - Gram negative rods
    - Anaerobes

- **Vascular insufficiency**
  - Adults
  - Risk factors: DM, PVD
  - Organisms: usually polymicrobial
    - *S. aureus*, *S. epidermidis*, *Streptococcus*, Gram negative rods, anaerobes

**WA presentation / clinical findings:**

- Risk factors: recent surgery and infection
- S/S: Lower back pain, loss of sensation
- Labs: elevated WBC, ESR and CRP
- Bone changes on MRI and positive bone scan

**Neonates < 1 month**

- Nafcillin plus cefotaxime OR
- Nafcillin plus an aminoglycoside

**Infant (1-36 months)**

- Cefuroxime
- Ceftriaxone
- Nafcillin plus cefotaxime

**Pediatric (> 3 years)**

- Nafcillin or cefazolin or clindamycin

**Length of therapy**

- Acute osteomyelitis
  - 4-6 weeks
- Chronic osteomyelitis
  - 6-8 weeks of parenteral therapy and 3-12 months of oral therapy
Osteomyelitis

How should WA be treated?

A. Vancomycin 15 mg/kg IV every 12 hours; total antibiotic duration 6 weeks
B. Nafcillin 2 g IV every 6 hours; total antibiotic duration 2 weeks
C. Levofloxacin 750mg oral daily; total antibiotic duration 6 weeks
D. Ampicillin/sulbactam 3g IV every 6 hours; total antibiotic duration 2 weeks

CNS Infections

- DM is a 21 year old male
- Chief complaint: worst headache of his life; pain with neck movement
- PMH: none
- PE: extreme pain 10/10 - VS: Temp 102.4°F, HR 110, RR 18, BP 130/75

CNS Infections

- Labs: WNL. WBC = 22,500/mm³ (82 polys, 11 bands, 5 lymphs, 2 monos).
- LP: Glucose = 44 mg/dl (peripheral = 110), protein = 220 mg/dl, and WBC = 800/mm³ (85% neutrophils, 15% lymphocytes).
- Gram stain shows abundant Gram negative cocci.

CNS Infections - Etiology

<table>
<thead>
<tr>
<th>Age</th>
<th>Most likely organisms</th>
<th>Less common organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborns (&lt; 2 months)</td>
<td>Group B Streptococcus, Listeria monocytogenes, S. pneumoniae, H. meningitidis</td>
<td>E. coli, Klebsiella sp., Herpes simplex type 2</td>
</tr>
<tr>
<td>2 mo.- 2 years</td>
<td>S. pneumoniae, N. meningitidis, H. influenzae, Group B Streptococcus</td>
<td>Viruses, E. coli</td>
</tr>
<tr>
<td>2-50 years</td>
<td>N. meningitidis, S. pneumoniae</td>
<td>H. influenzae, Viruses</td>
</tr>
<tr>
<td>&gt; 50 years</td>
<td>S. pneumoniae, N. meningitidis, H. influenzae</td>
<td>L. monocytogenes, Group B Streptococcus, aerobic gram-negative bacilli, viruses</td>
</tr>
</tbody>
</table>

Meningitis

- Clinical Presentation
  - Symptoms in DM
    - Fever
    - Headache, nuchal rigidity
  - Lumbar puncture

<table>
<thead>
<tr>
<th>Component</th>
<th>Normal CSF</th>
<th>Bacterial Meningitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>30-70 mg/dl (¾ peripheral)</td>
<td>&lt; 50 mg/dl (≤0.4 CSF:blood)</td>
</tr>
<tr>
<td>Protein</td>
<td>&lt; 50 mg/dl</td>
<td>&gt; 150 mg/dl</td>
</tr>
<tr>
<td>WBC</td>
<td>&lt; 5/mm³</td>
<td>&gt; 1200/mm³</td>
</tr>
</tbody>
</table>

Meningitis - Etiology

- Lumbar Puncture
  - CSF stains
    - Gram stain (microorganisms)
    - Latex agglutination – high sensitivity, 50-100%, for common organisms; not routinely recommended
  - Laboratory findings
    - Increased WBC with a left shift
    - Positive CSF Gram stain
    - Positive CSF cultures (positive 75-80% of cases of bacterial meningitis)
Meningitis

How should DM be treated?

A. Penicillin G 4 million units IV every 4 hours plus dexamethasone 4mg IV every 6 hours
B. Ceftriaxone 2g IV every 12 hours
C. Ceftriaxone 2g IV every 12 hours plus dexamethasone 4mg IV every 6 hours
D. Ceftriaxone 2g IV every 12 hours plus vancomycin 1000mg IV every 12 hours

Meningitis

- Neonates < 1 month
  - Ampicillin plus aminoglycoside OR
  - Ampicillin plus cefotaxime
- Infant (1-23 months)
  - 3rd generation cephalosporin (cefotaxime or ceftriaxone) plus vancomycin

Meningitis

- Pediatric and Adult (2-50 years)
  - 3rd generation cephalosporin (cefotaxime or ceftriaxone) plus vancomycin
- Elderly (> 50 years)
  - 3rd generation cephalosporin (cefotaxime or ceftriaxone) plus ampicillin plus vancomycin
- Penetrating head trauma, post neurosurgery or CSF shunt
  - Vancomycin plus cefepime or ceftazidime or meropenem

Meningitis

- Therapy of specific pathogens

  - Length of therapy
    - *N. meningitidis* – 7 days
    - *H. influenzae* – 7 days
    - *S. pneumoniae* – 10-14 days

Meningitis

- Adjunctive Corticosteroid Therapy

  - Risks versus benefits
    - less hearing loss in children with *H. influenzae*
    - improved outcomes in adults with *S. pneumoniae*
    - may decrease antibiotic penetration
  - Dose and administration
    - give 10-20 mins before or same time as antibiotics
    - dexamethasone 0.15 mg/kg q6h for 2-4 days
    - use in children with *H. influenzae* meningitis or adults with pneumococcal meningitis, but may need to initiate before knowing specific causative bacteria.
Meningitis

Following diagnosis there is concern regarding prophylaxis. What is the best recommendation?

A. HCPs with close contact should receive rifampin 600mg every 12 hours for 4 doses.
B. Those in dorm and classes should receive rifampin 600mg daily for 4 days.
C. Those in ED should receive the meningococcal conjugate vaccine.
D. Those in ED should receive rifampin 600mg every 12 hours for 4 doses.

Neisseria menigitidis

Chemoprophylaxis – for close contacts (household or daycare) and exposure to oral secretions of index case

- Adults - rifampin 600mg q12h x 4 doses
- Children - rifampin 10 mg/kg q12h x 4 doses
- Infants (< 1 month) - rifampin 5 mg/kg q12h x 4 doses

Meningococcal conjugate [and polysaccharide] vaccine (lack serogroup B)

- All young adolescents (11-12 years)
- College freshman (especially living in dormitories)
- Military recruits
- Travel to “meningitis belt”
- Asplenia (anatomic or functional)
- Terminal complement component disorder
- Outbreaks
- Booster – 5 years later in adolescents and asplenic patients

Endocarditis

TS is a 48 year old male

Chief complaint: fever, chills, nausea/vomiting, anorexia, lymphangitis in his right hand and lower back pain.

PMH: kidney stones 4 years ago.

SH: TS is homeless and an IV drug abuser (heroin) for the past year but quit 2 weeks ago.

PE: alert and oriented - VS: Temp 100.8°F, HR 114, RR 12, BP 127/78; Cardiac: faint systolic ejection murmur; Ext: right hand is erythematous and swollen.

Labs: WNL. HIV negative.

Cultures: Blood culture - MSSA. Two more cultures were drawn that are both now growing Gram-positive cocci in clusters.

TEE: vegetation on the mitral valve.
Endocarditis

How should TS be managed?

A. Nafcillin IV therapy for 2 weeks
B. Nafcillin IV + rifampin therapy for 6 weeks
C. Nafcillin IV + gentamicin IV therapy for 2 weeks
D. Nafcillin IV for 6 weeks with gentamicin for the first 3-5 days

Endocarditis

TS presentation / clinical findings:
- Risk factors: IV drug use
- Fever, chills, low back pain
- PE: low-grade fever, cardiac murmur
- Positive blood culture

Endocarditis

Causative organisms

- Coag-neg Staph
- C. albicans
- Enterococci
- S. aureus
- Streptococci

Endocarditis

Viridans Streptococci
- penicillin G (± gentamicin)
- ceftriaxone (± gentamicin)
- vancomycin
  - treatment is for 2-4 weeks (gentamicin allows for shorter course of therapy)
  - treatment is for 6 weeks with prosthetic valve

Endocarditis

Methicillin sensitive S. aureus
- oxacillin or nafcillin (± gentamicin)
- cefazolin (± gentamicin)
- vancomycin

Endocarditis

Methicillin resistant S. aureus
- vancomycin
- daptomycin – native valve only
  - treatment is for 6 weeks (gentamicin for 3-5 days decreases bacterial load)
  - treatment is for ≥ 6 weeks plus gentamicin for 2 weeks in prosthetic valves – also add rifampin

Endocarditis

Enterococci
- penicillin G or ampicillin plus streptomycin or gentamicin
- vancomycin plus streptomycin or gentamicin
  - treatment is for 4-6 weeks
  - treatment is for 6 weeks in prosthetic valves
  - streptomycin or gentamicin must be given due to inherent resistance
**Endocarditis**

How should TS be managed?

A. Nafcillin IV therapy for 2 weeks

B. Nafcillin IV + rifampin therapy for 6 weeks

C. Nafcillin IV + gentamicin IV therapy for 2 weeks

D. Nafcillin IV for 6 weeks with gentamicin for the first 3-5 days

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**Endocarditis**

TS tooth extraction 6 months later. What do you recommend for prophylaxis?

A. Tooth extractions do not require prophylaxis.

B. Amoxicillin 2g, 1 hour before the extraction

C. Amoxicillin 3g, 1 hour before and 1.5g, 6 hours for 4 doses after the extraction.

D. TS does not need prophylaxis.

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**Endocarditis Prophylaxis**

- See tables for:
  - Endocarditis prophylaxis:
    - Conditions in which prophylaxis is necessary
    - Dental procedures that require prophylaxis
    - Other procedures that require prophylaxis
  - Dental or respiratory tract procedures:
    - Antibiotic dosed prior to procedure only
    - ampicillin, amoxicillin
    - clindamycin, cephalexin, cefazolin, ceftriaxone, macrolide

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**Peritonitis**

- Primary peritonitis
- Secondary peritonitis

**Therapy**

- Mild/moderate community acquired
  - Cefoxitin, cefazolin, cefuroxime, ceftriaxone or cefotaxime plus metronidazole, ticarcillin/clavulanate, ertapenem, moxifloxacin, ciprofloxacin or levofloxacin plus metronidazole, tigecycline

- High risk/Severe community or health-care acquired
  - Piperacillin/tazobactam, ceftazidime or cefepime plus metronidazole, imipenem, meropenem or doripenem, ciprofloxacin or levofloxacin plus metronidazole

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**Clostridium difficile Infection**

- Risk factors and Symptoms
- Therapy

  - Initial episode and first recurrence:
    - Metronidazole 500mg PO/IV TID-QID for 10-14 days
    - Vancomycin 125mg PO four times daily for 10-14 days
    - Fidaxomicin 200mg PO two times daily for 10 days

  - Second and third recurrences
    - Consider fidaxomicin is not already given
    - Consider higher doses of vancomycin
    - Taper therapy
    - Pulse therapy
    - Consider rifaximin 400mg twice daily for 14 days
Surgical Prophylaxis

Which of the following is the best practice for optimizing surgical prophylaxis:

A. Redose antibiotics for procedures longer than 4 hours or involving major blood loss.
B. Give antibiotics for 24 hours after the procedure – this will optimize prophylaxis.
C. Pre-operative antibiotics can be given up to 4 hours before the incision.
D. Vancomycin should be the antibiotic of choice due to its long t1/2 and activity against MRSA.

Surgical Prophylaxis

- Timing

Surgical Prophylaxis

- Duration
  - most only require antibiotics when the patient is in the OR
  - cardiac procedures may require 24-48 hours of antibiotics after surgery

Surgical Prophylaxis

- Antibiotic Spectrum
  - only need activity against skin flora
  - vancomycin should NOT routinely be used
  - clean-contaminated procedures may require additional antibiotics
  - colorectal surgery requires broad spectrum antibiotics
Surgical Prophylaxis

Which of the following is the best practice for optimizing surgical prophylaxis:

A. Redose antibiotics for procedures longer than 4 hours or involving major blood loss.
B. Give antibiotics for 24 hours after the procedure – this will optimize prophylaxis.
C. Pre-operative antibiotics can be given up to 4 hours before the incision.
D. Vancomycin should be the antibiotic of choice due to its long t1/2 and activity against MRSA.

Questions / Comments

Suggested References - Page 455
Self-assessment Questions – Pages 420, 421
Answers to Self-assessment Questions – Page 458-59

Self Assessment Questions

1. Which of the following would be the best empiric therapy for P.E.?
   a. Doxycycline 100 mg PO 2 times/day (BID)
   b. Cefuroxime axetil 250 mg PO 2 times/day (BID)
   c. Levofloxacin 750 mg PO daily
   d. Trimethoprim/sulfamethoxazole DS PO 2 times/day (BID)

2. HW should be given:
   a. Azithromycin 500mg, followed by 250mg orally for 4 more days.
   b. Amoxicillin/clavulanic acid 875 orally twice daily.
   c. Oseltamivir 75mg orally twice daily for 5 days.
   d. Symptomatic treatment only.

3. Which study design would be the most appropriate?
   a. Case series
   b. Case-control study
   c. Prospective cohort study
   d. Randomized clinical trial
Self Assessment Questions

4. Which of the following would be the best empiric therapy for NR?
   a. Oral nitrofurantoin ER 100 mg twice daily for 3 days.
   b. Ciprofloxacin 500mg oral twice daily for 7 days.
   c. Trimethoprim/sulfamethoxazole i DS oral twice daily for 3 days.
   d. Cephalexin 500mg oral four times daily for 3 days.

Self Assessment Questions

5. Which of the following is the best for BY?
   a. No therapy since she is chronically catheterized and has no symptoms.
   b. No antibiotic therapy but the catheter should be changed.
   c. Ciprofloxacin 500mg orally twice daily for 7 days and a new catheter.
   d. Ciprofloxacin 500mg orally twice daily for 14-21 days without a change in catheter.

Self Assessment Questions

6. MRSA endocarditis. An initial 1g dose of vancomycin is given. Wt = 72kg, vancomycin half-life = 35 hours, Vd is 0.7 L/kg. Which is the best assessment of when the patient will reach a concentration of 10 mcg/L?
   a. In approximately 18 hours from the first dose.
   b. In approximately 35 hours from the first dose.
   c. In approximately 70 hours from the first dose.
   d. The initial dose is not adequate to achieve a concentration of 10 mcg/ml.

Self Assessment Questions

7. Which of the following would be the best empiric therapy for VE?
   a. Nafcillin 2g IV q6h – infection may worsen and necrotizing fasciitis needs to be ruled out.
   b. Penicillin G 2 million units IV q4h – this is probably erysipelas.
   c. Piperacillin/tazobactam 3.375 g IV q6h – surgical debridement is vitally important.
   d. Enoxaparin 80mg SQ BID and warfarin 5mg po daily.

Self Assessment Questions

8. Which of the following would be the best empiric therapy for RK?
   a. This is aseptic meningitis and no antibiotics are necessary.
   b. Ceftriaxone 2g IV every 12 hours until the CSF cultures are proven negative for bacteria.
   c. Ceftriaxone 2g IV every 12 hours plus vancomycin 1000mg IV every 12 hours.
   d. Acyclovir 500 mg IV every 8 hours until the CSF culture results are complete.

Self Assessment Questions

9. What is the most appropriate therapy for LG?
   a. penicillin G plus gentamicin for 2 weeks
   b. vancomycin plus gentamicin for 2 weeks
   c. ampicillin plus gentamicin for 6 weeks
   d. cefazolin plus gentamicin for 6 weeks
Self Assessment Questions

10. Which of the following would be the best follow up antibiotics for NL?
   a. Vancomycin 1000mg IV every 12 hours plus metronidazole 500mg IV every 8 hours
   b. Ceftriaxone 1g IV daily plus ciprofloxacin 400mg IV every 12 hours.
   c. Ertapenem 1g IV daily.
   d. No antibiotics are needed following surgical repair of a perforated appendix.

Conflict of Interest Disclosures

Curtis Smith, Pharm.D.
– I have no conflicts of interest related to this presentation.

Learning Objectives

- Formulate an appropriate regimen to prevent or treat human immunodeficiency virus infections, including initiation and monitoring therapy.
- Discuss appropriate treatment of the various acquired immunodeficiency syndrome opportunistic infections, including primary and secondary prophylaxis.
- Describe appropriate treatment and preventive therapy for tuberculosis, including infections with drug-resistant organisms.
- Classify the various antifungal agents and explain their role in common fungal infections.

Agenda

- HIV
- HIV-related Opportunistic Infections
- Tuberculosis
- Antifungal Therapy

HIV

- Transmission
  - Sexual
  - Parenteral Exposure to Blood
    - Universal Precautions
  - Perinatal

2012 Updates in Therapeutics:
The Pharmacotherapy Preparatory Review & Recertification Course
HIV/Infectious Diseases
Curtis L. Smith, Pharm.D., BCPS
Ferris State University
HIV

- Diagnosis
  - ELISA – initial test
  - Western Blot – confirmation
  - Rapid HIV tests
  - HIV RNA (copies/ml)
    - signal amplification nucleic acid probe
    - reverse transcriptase PCR
    - nucleic acid sequence based amplification
    - < 200 copies/ml considered undetectable

HIV RNA test indications:
  - acute infection
  - newly diagnosed
  - every 3-6 months (on or off therapy) – also check CD4 count
  - 2-4 (no > 8) weeks after starting or changing therapy
  - following a clinical event or decreasing CD4

HIV RNA test indications:
  - acute infection
  - newly diagnosed
  - every 3-6 months (on or off therapy) – also check CD4 count
  - 2-4 (no > 8) weeks after starting or changing therapy
  - following a clinical event or decreasing CD4
HIV

Treatment
- Nucleoside Reverse Transcriptase Inhibitors
- Nucleotide Reverse Transcriptase Inhibitors
- Non-Nucleoside Reverse Transcriptase Inhibitors
- Protease Inhibitors
- Entry Inhibitors (enfuvirtide, maraviroc)
- Integrase Inhibitor (raltegravir)
* See tables on pages 469-471

Maternal-Fetal Transmission
- HIV-infected pregnant women with no antiretroviral therapy
  - potent combination antiretroviral therapy (wait until after 1st trimester if don’t meet criteria for starting therapy)
  - use zidovudine as a component if possible
  - avoid efavirenz in the first trimester
  - continue combination regimen through intrapartum period
- HIV-infected women receiving potent therapy
  - continue current regimen (preferably with ZDV)

Maternal-Fetal Transmission
- HIV-infected women in labor (+/- therapy)
  - zidovudine IV dosing guidelines (stop oral ZDV)
  - continue other antiretrovirals

Infants born to mothers who are HIV positive
- ZDV 4 mg/kg/dose every 12 hours for 6 weeks
- consider additional antiretrovirals if mother did not receive therapy during pregnancy

Exposure type
Severity
HIV Positive
Class*
Recommended Prophylaxis†
Percutaneous exposure
Less severe
Class 1
Basic 2-drug regimen

More severe
Class 1 or 2
Expanded 3-drug regimen
Mucous membrane and nonintact skin exposure
Small volume
Class 1 or 2
Basic 2-drug regimen

Large volume
Class 1
Basic 2-drug regimen

Class 2
Expanded 3-drug regimen

* Class 1 – asymptomatic HIV infection or low viral load (< 1500 copies/ml); Class 2 – symptomatic HIV infection or high viral load
† Basic 2-drug regimen: ZDV/3TC or FTC; or d4T/3TC or FTC; or TDF/3TC or FTC
† Expanded 3-drug regimen: add LPV/RTV, ATV, f-APV, IDV/RTV, SQV/RTV, NFV, or EFV

FG is a 27 year old asymptomatic HIV-positive patient.
- One year ago
  - CD4 count = 815/mm³, viral load = 1500/ml.
- Today
  - CD4 count = 240/mm³, viral load = 60,000/ml.

How should FG be treated?
A. No antiretroviral therapy because FGs CD4 count is still above 200/mm³.
B. Start FG on zidovudine since his CD4 count is still above 200/mm³.
C. Start FG on combination therapy of tenofovir, emtricitabine, and nevirapine.
D. Start FG on tenofovir, emtricitabine and atazanavir/ritonavir.
Initiating Therapy
- any symptomatic patient
- CD4 < 350/mm³
- Start regardless of CD4 count:
  - pregnant women
  - patients with HIV-associated nephropathy
  - patients coinfected with hepatitis B
- Recommended in patients with CD4 > 350-500/mm³ (lower strength of recommendation)

Preferred Therapy
- atazanavir/ritonavir or darunavir/ritonavir PLUS tenofovir with emtricitabine or lamivudine
- efavirenz PLUS tenofovir with emtricitabine or lamivudine
- raltegravir PLUS tenofovir with emtricitabine or lamivudine

Alternative Therapy
- atazanavir/ritonavir or darunavir/ritonavir PLUS abacavir with lamivudine
- fosamprenavir/ritonavir or lopinavir/ritonavir PLUS abacavir / lamivudine or tenofovir / emtricitabine
- efavirenz or rilpivirine PLUS abacavir / lamivudine or tenofovir / emtricitabine
- raltegravir PLUS abacavir / lamivudine

Acceptable Therapy
- efavirenz or rilpivirine PLUS zidovudine/ lamivudine
- nevirapine PLUS zidovudine or abacavir/ lamivudine or tenofovir/ emtricitabine
- atazanavir PLUS zidovudine or abacavir/ lamivudine
- atazanavir/ritonavir or darunavir/ritonavir or fosamprenavir/ritonavir or lopinavir/ritonavir PLUS zidovudine/ lamivudine

Regimens to be used with caution
- saquinavir/ritonavir PLUS two NRTIs (abacavir or zidovudine/ lamivudine or tenofovir/ emtricitabine)

Not Recommended Regimens
- all monotherapies
- dual NRTI regimens alone
- triple NRTI regimens other than abacavir / lamivudine / zidovudine
- any regimen with didanosine/ tenofovir
How should FG be treated?

A. No antiretroviral therapy because FGs CD4 count is still above 200/mm³.
B. Start FG on zidovudine since his CD4 count is still above 200/mm³.
C. Start FG on combination therapy of tenofovir, emtricitabine, and nevirapine.
D. Start FG on tenofovir, emtricitabine and atazanavir/ritonavir.

---

CD4 increases and viral load is undetectable. Two years later CD4 = 310/mm³ and viral load = 15,000 copies/ml. What would you do?

A. No changes - wait until viral load is above 50,000/ml.
B. Change the tenofovir to abacavir.
C. Change the tenofovir and emtricitabine to abacavir and lamivudine.
D. Change the entire regimen to abacavir, lamivudine and fosamprenavir/ritonavir.

---

Change therapy for:

- Virologic failure
  - not achieving HIV RNA < 200 copies/ml
  - two consecutive HIV RNA > 200 copies/ml after 24 weeks of therapy
  - HIV RNA > 200 copies/ml after initial suppression to undetectable
- Immuneologic failure
  - failure to increase CD4 50-100 cells/mm³ above baseline
  - failure to increase CD4 to above 350 cells/mm³

---

Options for Treatment Failures:

- Perform resistance testing
- Prior therapy with no resistance
  - Check adherence and address underlying causes (consider continuing same regimen)
  - Start a new regimen
  - Intensify or PK boost therapy

---

Options for Treatment Failures:

- Prior therapy with resistance
  - New regimen with 2, preferably 3 active agents
- Extensive therapy with resistance
  - Resuppress as possible to prevent clinical progression
- New regimen with 2 active agents not possible
  - Continue current regimen

---

CD4 increases and viral load is undetectable. Two years later CD4 = 310/mm³ and viral load = 15,000 copies/ml. What would you do?

A. No changes - wait until viral load is above 50,000/ml.
B. Change the tenofovir to abacavir.
C. Change the tenofovir and emtricitabine to abacavir and lamivudine.
D. Change the entire regimen to abacavir, lamivudine and fosamprenavir/ritonavir.
HIV

Which of the following should be monitored if FG is to receive fosamprenavir/ritonavir?

A. Peripheral neuropathy.
B. Drug interactions with CYP1A2.
C. Endocrine disturbances - hyperglycemia, fat redistribution, and lipid abnormalities.
D. Nephrolithiasis.

See drug tables on pages 469-471

HIV

Which of the following should be monitored if FG is to receive fosamprenavir/ritonavir?

A. Peripheral neuropathy.
B. Drug interactions with CYP1A2.
C. Endocrine disturbances - hyperglycemia, fat redistribution, and lipid abnormalities.
D. Nephrolithiasis.

See drug tables on pages 469-471

AIDS Opportunistic Infections

HIV/AIDS

Three years later FGs CD4 count has decreased to 135/mm³. What should he receive primary prophylaxis for?

A. Pneumocystis pneumonia.
B. Cryptococcal meningitis.
C. Cytomegalovirus.
D. Mycobacterium avium complex.

HIV/AIDS

Pneumocystis pneumonia (page 479)
- primary prophylaxis in patients with CD4 < 200/mm³

Cryptococcal meningitis (page 480)
- primary prophylaxis – not indicated

Cytomegalovirus retinitis (page 484)
- primary prophylaxis with CD4 < 50/mm³
  - Regular fundoscopic examinations

Mycobacterium avium complex (page 482)
- primary prophylaxis with CD4 < 50/mm³
  - clarithromycin 500mg po BID
  - azithromycin 1200mg po once weekly (generally recommended as drug of choice)
  - rifabutin 300mg QD (or 150mg po BID with food)

Toxoplasmosis (page 486)
- primary prophylaxis for Toxoplasma seropositive patients with CD4 ≤ 100/mm³
  - TMP/SMX or dapsone/pyrimethamine at PCP doses
HIV/AIDS

Three years later FGs CD4 count has decreased to 135/mm³. What should he receive primary prophylaxis for?

A. Pneumocystis pneumonia.
B. Cryptococcal meningitis.
C. Cytomegalovirus.
D. Mycobacterium avium complex.

AIDS OIs - PCP

BL is a 44 year old HIV positive male

Chief complaint: severe shortness of breath.

CXR: pulmonary infiltrates in both lung fields.

Labs: WNL except: BUN=38, LDH=386, pH=7.45, pO₂=63, pCO₂=32, O₂ saturation=85%.

Sputum gram stain and silver stain - negative.

AIDS OIs - PCP

How should BL be treated?

A. Pentamidine IV with adjuvant prednisone therapy for 21 days.
B. Trimethoprim/sulfamethoxazole for 21 days
C. Trimethoprim/sulfamethoxazole IV with adjuvant prednisone therapy for 21 days.
D. Atovaquone 750mg po TID for 21 days.

AIDS OIs - PCP

Pneumocystis jiroveci pneumonia (PCP) – Therapy

- Trimethoprim/sulfamethoxazole
- Pentamidine
- Trimethoprim/dapsone (mild to moderate PCP)
- Atovaquone (mild to moderate PCP)
- Clindamycin/primaquine

AIDS OIs - PCP

Adjuvant Therapy
- Corticosteroids
  - for severe PCP (As gradient ≥ 35 or PaO₂ ≤ 70)
  - 40mg BID prednisone for 5 days, then 40mg daily for 5 days, then 20mg daily for remainder of PCP therapy

Prophylaxis
- 2° prophylaxis in patients following PCP
- 1° prophylaxis in patients with CD₄ < 200/mm³
  - Stop if CD₄ > 200/mm³ for ≥ 3 months after ART

AIDS OIs - PCP

How should BL be treated?

A. Pentamidine IV with adjuvant prednisone therapy for 21 days.
B. Trimethoprim/sulfamethoxazole for 21 days.
C. Trimethoprim/sulfamethoxazole IV with adjuvant prednisone therapy for 21 days.
D. Atovaquone 750mg po TID for 21 days.
AIDS OIs - Cryptococcosis

- GH is a 33 year old HIV-positive male
- Chief complaint: severe headache
- HPI: headache has worsened over the past 3 weeks - memory problems and tiredness.
- Labs: CD4 count = 75/mm³.
- He is diagnosed with Cryptococcal meningitis and successfully treated.

AIDS OIs - Cryptococcosis

Which of the following is the most appropriate follow up treatment for GH?

A. No maintenance treatment needed.
B. Fluconazole 200mg po daily.
C. Amphotericin B deoxycholate 1mg/kg IV once weekly.
D. GH is protected as long as he is also receiving PCP prophylaxis

AIDS OIs - Cryptococcosis

- Therapy
  - Preferred: Amphotericin B deoxycholate: 0.7–1 mg/kg/day (or liposomal amphotericin 4-6 mg/kg/day) PLUS flucytosine 25 mg/kg every 6 hours for at least 2 weeks, followed by fluconazole 400 mg/day for at least 8 weeks—commonly used in patients with AIDS
  - Alternative: Amphotericin B deoxycholate: 0.7–1 mg/kg/day (or liposomal amphotericin 4-6 mg/kg/day) for 4-10 weeks (or 1 month after negative cultures); alternative in patients with AIDS

AIDS OIs - Cryptococcosis

- Prophylaxis
  - relapses usually occur in 1st year after therapy (less often with HAART therapy)
  - 2° prophylaxis – fluconazole 200mg daily
  - 1° prophylaxis – not indicated

AIDS OIs - Cryptococcosis

Which of the following is the most appropriate follow up treatment for GH?

A. No maintenance treatment needed.
B. Fluconazole 200mg po daily.
C. Amphotericin B deoxycholate 1mg/kg IV once weekly.
D. GH is protected as long as he is also receiving PCP prophylaxis
GH started on potent combination antiretroviral therapy
- Two months CD4 count = 212/mm³.
- Six months CD4 count = 344/mm³.
- Eight months CD4 count = 484/mm³.

Which of the following is the most appropriate follow up treatment for GH?
A. Continue the fluconazole maintenance
B. Continue maintenance therapy for at least 1 year and then stop since CD4 counts have increased
C. Continue maintenance therapy until the CD4 counts are greater than 500/mm³
D. Maintenance therapy with fluconazole can be discontinued

Prophylaxis
- relapses usually occur in 1st year after therapy
- 2° prophylaxis – fluconazole 200mg daily
- May stop if CD4 > 100/mm³ for ≥ 3 months after ART (restart if drop < 100/mm³)
- 1° prophylaxis – not indicated

How should JC be treated or prophylaxed?
A. Clarithromycin plus ethambutol for 2 weeks followed by clarithromycin maintenance.
B. Azithromycin plus ethambutol for at least 12 months.
C. Clarithromycin plus INH for 2 weeks followed by maintenance with clarithromycin alone.
D. Ethambutol plus rifabutin for at least 12 months.

JC is a 36 year old HIV positive female
- Chief complaint: severe anemia.
- HPI: She has been tested for iron deficiency and has been taken off zidovudine and TMP/SMZ. She has also started to lose weight and have severe diarrhea.
- Blood culture is positive for MAC.
**AIDS OIs - MAC**

- **Therapy**
  - clarithromycin 500mg (7.5-15mg/kg) BID or azithromycin 500-600mg (10-20mg/kg) daily
  - **PLUS** ethambutol 15mg/kg/day
  - other agents:
    - rifabutin 150-600 mg/day
    - ciprofloxacin 750 mg (10-15 mg/kg) 2 times/day
    - amikacin 10-15 mg/kg/day intravenously

**AIDS OIs - MAC**

- **Prophylaxis**
  - stop chronic maintenance therapy / 2° prophylaxis after 12 months if CD4 > 100/mm³ for 6 months and patient is asymptomatic
  - primary prophylaxis with CD4 < 50/mm³
    - clarithromycin 500mg po BID
    - azithromycin 1200mg po once weekly
    - rifabutin 300mg daily (or 150mg po BID)
    - Stop if CD₄ > 100/mm³ for ≥ 3 months after ART

**AIDS OIs - CMV**

- PL is a 44 year old HIV positive male
- Diagnosed with CMV retinitis
- Currently on zidovudine/lamivudine/efavirenz, dapsone and fluconazole

**AIDS OIs - CMV**

- **Therapy**
  - Valganciclovir 900mg po BID for 14-21 days (or ganciclovir 5mg/kg IV q12h for 14 days) or implant plus valganciclovir
  - Foscarnet 60mg/kg IV q8h or 90mg/kg IV q12h
  - Cidofovir 5mg/kg IV every week for 2 weeks

---

How should JC be treated or prophylaxed?

A. Clarithromycin plus ethambutol for 2 weeks followed by clarithromycin maintenance.
B. Azithromycin plus ethambutol for at least 12 months.
C. Clarithromycin plus INH for 2 weeks followed by maintenance with clarithromycin alone.
D. Ethambutol plus rifabutin for at least 12 months.

Which is the best empiric therapy?

A. Valganciclovir orally and change zidovudine/lamivudine to tenofovir/emtricitabine.
B. Ganciclovir intravenously and change dapsone to atovoquone.
C. Foscarnet intravenously and change efavirenz to atazanavir/ritonavir.
D. Acyclovir intravenously with no other changes.
AIDS OIs - CMV

- **Secondary Prophylaxis**
  - Valganciclovir 900mg po daily (or ganciclovir 5mg/kg IV daily) or implant plus valganciclovir
  - Foscarnet 90-120mg/kg IV daily
  - Cidofovir 5mg/kg IV every other week
  - Stop if CD₄ > 100/mm³ for ≥ 3-6 months

- **Primary Prophylaxis**
  - CD₄ < 50/mm³ – regular fundoscopic exams

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AIDS OIs - CMV

Which is the best empiric therapy?

- A. Valganciclovir orally and change zidovudine/lamivudine to tenofovir/emtricitabine.
- B. Ganciclovir intravenously and change dapsone to atovoquone.
- C. Foscarnet intravenously and change efavirenz to atazanavir/ritonavir.
- D. Acyclovir intravenously with no other changes.

---

AIDS OIs - Toxoplasmosis

- **Therapy:**
  - pyrimethamine 50-75mg daily (LD=200mg in 2 doses) plus sulfadiazine 1-1.5g every 6 hours

- **Alternative Therapy:**
  - pyrimethamine 50-75mg per day plus clindamycin 600-1200mg every 6-8 hours OR atovaquone 1500mg po BID OR azithromycin 900-1200mg po daily

---

AIDS OIs - Toxoplasmosis

- **Primary Prophylaxis:**
  - Toxoplasma seropositive patients with CD₄ ≤ 100/mm³
  - TMP/SMZ or dapsone/pyrimethamine/leukovorin or atovaquone/pyrimethamine at PCP doses
  - Stop if CD₄ > 200/mm³ for ≥ 3 months

---

AIDS OIs - Toxoplasmosis

- **Secondary Prophylaxis:**
  - pyrimethamine 25-50mg per day with sulfadiazine 2-4g per day (plus leucovorin)
  - clindamycin 600mg every 8 hours can be substituted if sulfa intolerance occurs
  - atovaquone 750mg q6-12h ± pyrimethamine
  - Stop if CD₄ > 200/mm³ for ≥ 6 months after ART

---

Tuberculosis

- **Epidemiology**

![Reported TB Cases United States, 1992–2010*](image)
Tuberculosis

- Epidemiology
- Pathophysiology
- Diagnosis
  - Signs and symptoms
  - Radiology
  - Microbiology
  - PPD
  - Interferon-gamma release assays

- Latent Tuberculosis Infection
  - PPD positive if ≥ 10mm induration **AND**
    - Immigrants (< 5 years) from high prevalence
    - IVDA
    - Residents and employees of homeless shelters, nursing homes, prisons and hospitals
    - Patients with diseases increasing the TB risk (DM, silicosis, Hodgkin’s disease, ESRD)
    - Children < 4 yrs or any child exposed to adults at high-risk

- Late Latent Tuberculosis Infection
  - Always PPD positive if ≥ 15mm induration
  - Patients at low risk should NOT be tested
    - Exception: at entry into a work site where risk of exposure to TB is anticipated
  - QuantiFERON-TB Gold and T-SPOT.TB
    - Blood tests
    - Less sensitivity but greater specificity

**TB Case Rates, United States, 2010**

*Cases per 100,000.

**Number of TB Cases in U.S.-born vs. Foreign-born Persons United States, 1993–2010**

**Epidemiology**

**Pathophysiology**

**Diagnosis**

**Latent Tuberculosis Infection**

**QuantiFERON-TB Gold and T-SPOT.TB**

**Blood tests**

**Less sensitivity but greater specificity**
Tuberculosis

JM is a 42 year old male - works at LTCF
18mm induration 48 hours after PPD placement
First PPD reaction; CXR is negative

Which is the best therapy for JM?
A. No treatment is necessary - another PPD in 1 year.
B. Another PPD should be performed in one week to see if this is a booster effect.
C. JM should be monitored closely but no treatment is necessary because he is over 35 years of age.
D. Start isoniazid 300mg po daily for 6 months.

Therapy of Latent Tuberculosis Infection
- Treat if PPD positive AND
  - Close contact
  - Health care worker at facilities with TB patients
  - Foreign born person
  - Homeless person
  - Workers or residents of LTC facility
  - HIV infected
  - Recent converter (within 2 years)
  - Abnormal chest x-ray
  - Patients with certain medical conditions

HIV-negative:
- INH 300mg daily or 900mg twice weekly for 6-9 months (9 preferred, 6 accepted)
- RIF 600mg daily for 4 months
- Rifapentine 900mg plus INH 900mg weekly for 12 weeks
- RIF 600mg plus INH 300mg daily for 3 months

HIV-positive
- INH 300mg daily for 9 months
- INH 900mg twice weekly for 9 months

RJ is a 32 year old male
CC: increased weight loss and night sweats, as well as a cough productive of sputum.
PMH: HIV-positive
Current meds: fosamprenavir/ritonavir, zidovudine, lamivudine, fluconazole, and TMP/SMZ.
Sputum: positive for AFB. RJ lives in an area that has a low incidence of MDR TB.
Tuberculosis

What is the best therapy for RJ?

A. Start INH, rifampin, PZA, with no change in his HIV medications.
B. Start INH, rifampin, and PZA and increase the dose of fosamprenavir/ritonavir and rifampin.
C. Start INH, rifabutin, PZA, and EMB and decrease the dose of rifabutin.
D. Start INH, rifabutin, PZA, and EMB and decrease the dose of fosamprenavir/ritonavir.

Tuberculosis - Therapy

- HIV-negative patients:
  - INH + RIF + PZA + EMB for 2 months (daily, BIW, TIW) then INH + RIF for 4 more months (daily, BIW, TIW)
  - INH + RIF + EMB for 2 months (daily or 5x/week) then INH + RIF for 7 more months (daily or 5x/week)

- HIV-positive patients:
  - INH + RIF + PZA + EMB for 2 months (daily, TIW) then INH + RIF for 4 more months (daily, TIW)
  - INH + RIF + EMB for 2 months (daily or 5x/week) then INH + RIF for 7 more months (daily or 5x/week)

Tuberculosis - Therapy

- NO rifampin with PIs or NNRTIs (except efavirenz / nevirapine)
- Washout period once rifampin stopped
- Substitute rifabutin but:
  - monitor HIV RNA levels closely
  - decrease rifabutin dose with PIs

Tuberculosis

How should RJ be followed-up?

A. Treatment with the initial drugs for 6 months.
B. Change to INH and a rifamycin after 2 months for a total treatment of 18-24 months.
C. Change to INH and a rifamycin after 2 months for a total treatment of 6 months – monitor HIV RNA levels closely during therapy.
D. Change to INH, a rifamycin, and either PZA or EMB after 2 months for a total treatment of 6 months – monitor HIV RNA levels closely.

Tuberculosis

How should RJ be followed-up?

A. Treatment with the initial drugs for 6 months.
B. Change to INH and a rifamycin after 2 months for a total treatment of 18-24 months.
C. Change to INH and a rifamycin after 2 months for a total treatment of 6 months – monitor HIV RNA levels closely during therapy.
D. Change to INH, a rifamycin, and either PZA or EMB after 2 months for a total treatment of 6 months – monitor HIV RNA levels closely.
Antifungal Therapy

- Amphotericin B
- Azole Antifungals
- Echinocandins

Questions / Comments

Suggested References - Page 497
Self-assessment Questions - Pages 462-464
Answers to Self-assessment Questions – Page 500-501

Self Assessment Questions

1. What is the best treatment for KE to prevent HIV transmission to her child?
   a. No drug therapy is needed – the risks to the baby outweigh any benefits.
   b. Zidovudine throughout the pregnancy, during labor and, to the baby for 6 weeks.
   c. No drug therapy now but a single dose of nevirapine at the onset of labor.
   d. A highly-active antiretroviral regimen that includes zidovudine throughout the pregnancy.

Self Assessment Questions

2. What is the best counseling?
   a. Watch for jaundice as atazanavir can cause hyperbilirubinemia.
   b. If you’re having a drug related adverse effect cut the dose in half of all of your drugs.
   c. Talk to your pharmacist about drug interactions because atazanavir and tenofovir inhibit CYP3A4.
   d. Tenofovir and emtricitabine cause additive peripheral neuropathy so let your pharmacist know if you experience tingling.

Self Assessment Questions

3. One year later RE asks you if he should make some changes. What do you tell him?
   a. His therapy should be changed only if he is deteriorating clinically.
   b. His therapy should be changed if his viral load is detectable after initial suppression.
   c. His fosamprenavir/ritonavir should be changed to nelfinavir.
   d. Resistance most commonly occurs with emtricitabine so this should be changed to lamivudine.

Self Assessment Questions

4. What is the best management for FVs drug-related symptoms?
   a. Add simvastatin for the lipid abnormalities and treat according to the NCEP guidelines.
   b. Add pioglitazone for glucose abnormalities.
   c. Change zidovudine to tenofovir.
   d. Change lopinavir/ritonavir to efavirenz.
Self Assessment Questions

5. What is the best therapy for PP?
   a. Fluconazole 200mg po daily.
   b. Amphotericin B deoxycholate 0.3 mg/kg/day alone.
   c. Amphotericin B deoxycholate 0.3 mg/kg/day plus flucytosine 37.5 mg/kg every 6 hours.
   d. Amphotericin B deoxycholate 0.7 mg/kg/day plus flucytosine 25 mg/kg every 6 hours for 2 weeks followed by fluconazole 400mg/day.

Self Assessment Questions

6. Which one of the following best represents the patients needed to treat with INH over RIF to prevent one progression to active disease?
   a. 5
   b. 50
   c. 200
   d. There is insufficient information to calculate this number.

Self Assessment Questions

7. What is the best treatment for GT?
   a. Atovaquone for 4-6 weeks.
   b. High dose trimethoprim/sulfamethoxazole plus clindamycin for 6 weeks.
   c. Pyrimethamine plus sulfadiazine for 6 weeks.
   d. Pyrimethamine plus clindamycin and leucovorin for 6 weeks.

Self Assessment Questions

8. HIV+ with Cryptococcal meningitis on amphotericin B and flucytosine. Flucytosine TR 50-100 mcg/ml. Which of the following is the best dose to achieve a peak concentration within the desired range?
   a. 12.5 mg/kg
   b. 37.5 mg/kg
   c. 75 mg/kg
   d. 150 mg/kg

Self Assessment Questions

9. Which would be the best therapy for PI?
   a. INH 300mg po daily for 6 months.
   b. INH, rifampin, pyrazinamide, and ethambutol for 2 months followed by INH and rifampin for 4 more months.
   c. INH and rifampin for 6 months.
   d. Leave her on the levofloxacin for both TB and other bacterial causes of pneumonia.

Self Assessment Questions

Prospective, DB comparison of antiretroviral therapy with protease inhibitor vs. efavirenz in 350 HIV-positive patients.

10. Which is the best statistical test for a mean change in viral load or CD4 counts?
    a. analysis of variance
    b. chi square test
    c. students t-test
    d. Wilcoxon Rank Sum test
2012 Updates in Therapeutics:
The Pharmacotherapy Preparatory Review & Recertification Course
Nephrology
Edward F. Foote, PharmD, FCCP, BCPS
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Agenda
I. Acute Kidney Injury
II. Drug Induced Kidney Disease (Radiocontrast)
III. Chronic Kidney Disease
IV. Drug Dosing

Patient Case – Questions 1
H.D. is a 48-year-old African American man admitted to the intensive care unit after an acute myocardial infarction. He has a medical history/social history of type 2 diabetes mellitus, hypertension, and tobacco use. Current medications include metformin 500 mg orally 2 times/day, lisinopril 20 mg daily, nicotine patch 14 mg/day applied each morning, and naproxen 500 mg/day orally. Before admission, his kidney function was normal (SCr 1.0 mg/dL); however, during the past 24 hours, his kidney function has declined (BUN 20 mg/dL, SCr 2.1 mg/dL). His urine shows muddy casts. He has been anuric for 6 hours. His current BP is 110/70 mm Hg. He has edema and pulmonary congestion. Which one of the following is the best assessment of H.D.’s kidney function?
A. 26.2 mL/minute (CrCl using Cockcroft and Gault)
B. 44 ml/min/1.73 m² (GFR using abbreviated MDRD)
C. 23.1 mL/min/70kg (CrCl using the Brater equation)
D. Assumed CrCl < 10 ml/min

Patient Case – Question 2
2. Which one of the following represents the most likely cause of kidney dysfunction in this patient?
A. Prerenal
B. Intrinsic
C. Postrenal
D. Functional

Acute Kidney Injury (AKI)
A. Definitions and Background
1. AKI is defined as an acute decrease in kidney function. Associated with accumulation of waste products and (usually volume).
   a. Acute Kidney Injury Network (AKIN)
      i. An abrupt (<48 hr) increase in SCr of more than 0.3 mg/L or a 50% increase in baseline OR
      ii. Urine output less than 0.5 ml/kg/hr for more than 6 hours
   b. RIFLE Criteria. Used to stage. (Risk, Injury, Failure, Loss or ESRD)
Patient Case – Questions 3 and 4

3. Which of the following medications is best to discontinue at this time?
   A. Lisinopril
   B. Naproxen
   C. Metformin and Lisinopril
   D. Metformin, Naproxen and Lisinopril

4. Which one of the following interventions is most appropriate at this time?
   A. Add intravenous 0.9% NaCl.
   B. Add hydrochlorothiazide.
   C. Add furosemide.
   D. Add fluid restriction

Acute Kidney Injury

D. Prevention of AKI

1. Avoid nephrotoxic drugs when possible.
2. Ensure adequate hydration (2L/day). If intravenous, 0.9% sodium chloride (NaCl) is preferred.
3. Patient education.
4. Drug therapies to decrease incidence of contrast-induced nephropathy – see drug nephrotoxicity section.
Patient Case – Question 5

E.P. is a 67-year-old man referred to cardiology for intermittent chest pain. The patient has a medical history significant for CKD, type 2 diabetes mellitus, and hypertension. Medications include enalapril, hydrochlorothiazide, and pioglitazone. Laboratory values include SCr 1.8 mg/dL, glucose 189 mg/dL, hemoglobin 12mg/dL, and hematocrit 36%. His physical examination is normal. The plan is to undergo elective cardiac catheterization. Which one of the following approaches is the best choice for hydration?

A. 0.45% NaCl.
B. 0.9% NaCl.
C. D5 (5% dextrose) / 0.45% NaCl.
D. Oral hydration with water.

Patient Case – Question 6

6. In addition to intravenous fluid, which one of the following therapies is best to use in E.P. to decrease his likelihood of developing contrast-induced nephropathy.

A. Fenoldopam
B. Acetylcysteine
C. Ascorbic acid
D. Hemofiltration

II. Drug-Induced Kidney Disease

See Pages 510-516 for overview of drug classes and types of DiKD. Will focus on Contrast-induced nephropathy

Drug-Induced Kidney Damage

3. Radiographic contrast media nephrotoxicity (intravenous contrast). Consists of isoosmolar (300 mOsm/kg), low osmolar (780-800 mOsm/kg), and high-osmolar (more than 1000 mOsm/kg) agents. Also categorized as ionic versus nonionic.
   a. Incidence
      i. Third leading cause of inpatient AKI
      ii. Less than 2% and up to 50% of patients (based on risk)
      iii. Associated with a high (34%) in-hospital mortality rate
   b. Pathogenesis
      i. Direct tubular toxicity due to reactive oxygen species
      ii. Also may cause renal ischemia because of intrarenal hemodynamic alterations. Most contrast agents are hyperosmolar (more than 900 mOsm/kg), which leads to an osmotic diuresis and dehydration. Some contrast agents also cause systemic hypotension on injection and renal vasoconstriction
   c. Presentation
      i. Initial transient osmotic diuresis, followed by tubular proteinuria
      ii. SCr rises and peaks after about 2 – 5 days
      iii. 50% develop oliguria, and some will require dialysis
   d. Risk factors for toxicity
      i. Pre-existing kidney disease (Scr > 1.5 mg/dL or CrCl less than 60 mL/minute)
      ii. Diabetes
      iii. Volume depletion
      iv. Age older than 75
      v. Anemia (hematocrit less than 39% men, less than 36% women)
      vi. Conditions with decreased blood flow to the kidney (e.g., CHF)
      vii. Hypotension
      viii. Other nephrotoxins
      ix. Large doses of contrast (more than 140 mL) and/or hyperosmolar contrast agents
Contrast-Induced Kidney Damage

e. Prevention

i. Hydration. Intravenous isotonic saline considered most effective. Begin 6-12 hours before procedure to maintain urine output greater than 150 mL/hour. The addition of sodium bicarbonate is widely used, but there are conflicting data on efficacy.

ii. Use an alternative imagining study if possible.

iii. Discontinue nephrotoxic agents. Avoid diuretics.

iv. Use low-osmolar or iso-osmolar contrast agents in patients at risk (more expensive).

v. Medications used to prevent contrast-induced nephropathy:

a) Acetylcysteine – antioxidant and vasodilatory mechanism. Accumulation of glutathione takes time and may not be as effective in emergency cases. Various dosing recommendations. Safe.

b) Ascorbic acid – antioxidant. One large study showed benefit when used immediately before. Not confirmed. Give ascorbic acid 3 g before procedure and 2 g 2 times/day x two doses after procedure. May have role in emergency cases.

c) Fenoldopam

d) Theophylline/Aminophylline – Avoid

Patient Case – Questions 7-8

7. P.P. is a 55-year-old male patient with a history of hypertension and newly diagnosed type 2 diabetes mellitus. He denies alcohol use but does smoke cigarettes (1 pack/day). His medications include atenolol 50 mg/day and a multivitamin. He was recently initiated on metformin. At your pharmacy, his BP is 149/92 mm Hg. A 24-hour urine collection reveals 0.4 g of albumin. A recent SCr is 1.9 mg/dL. His eGFR is 50 mL/minute. How would you stage this patient’s kidney disease?

A. Stage 2.
B. Stage 3.
C. Stage 4.
D. Stage 5.

8. Assuming that non-pharmacological approaches have been maximized, which one of the following actions is best for P.P. to limit the progression of his kidney disease?

A. Add nifedipine.
B. Add diltiazem
C. Add enalapril
D. Increase atenolol.

Chronic Kidney Disease

A. Background

Stages of CKD

1. Kidney damage with GFR > 90 mL/minute/1.73m²
2. Kidney damage with GFR 60-89 mL/minute/1.73m²
3. GFR 30-59 mL/minute/1.73m²
4. GFR 15-29 mL/minute/1.73m²
5. GFR < 15 mL/minute/1.73m² or on dialysis

E. Assessment of kidney function

1. Serum creatinine
   a. Avoid use as the sole assessment of kidney function
   b. Dependent on age, sex, weight, and muscle mass
   c. Most laboratories use standardized Cr. Affects equations differently.

2. Measurement of GFR. Inulin, iothalamate, and others are not routinely used.

3. Measurement of CrCl through urine collection
   a. Reserve for vegetarians, patients with low muscle mass, patients with amputations, and patients needing dietary assessment, as well as when documentation need to start dialysis
   b. Urine collection will give a better estimate in patients with very low muscle mass. In most cases, equations will overestimate kidney function because Cr concentrations will be low in patients with very low muscle mass.
Chronic Kidney Disease

E. Assessment of kidney function (continued)

4. Estimated CrCl using Cockcroft-Gault – overestimates GFR. Even less accurate with standardized Scr.

5. Estimated GFR with MDRD study data
   a. Estimated GFR (mL/minute/1.73 m²) in patients with known CKD (less than 90 mL/minute)
   b. Abbreviated MDRD formula correlates well with the original MDRD formula, simpler to use
   c. CKD-EPI. New. More accurate in patients with eGFR > 60 mL/minute/1.73 m²

6. Children - Schwartz and Counahan-Barratt

F. Diabetic Nephropathy

4. Management / slowing progression
   a. Intensive blood glucose control.
      Glycosylated hemoglobin less than 7%.
      Less aggressive with more advanced CKD
   b. Protein restriction – There are insufficient data in diabetes but 0.8 g/kg day might slightly reduce progression. Patients should avoid high-protein diets.

Patient Case – Question 9

9. Two weeks later, he presents back to his physician. His BP is 139/89 mm Hg. A repeat SCr is 2.3 mg/dL, and the serum K is 5.2 mEq/L. Which one of the following is the best recommendation for this patient?
   B. Add chlorthalidone 50 mg daily. Monitor BP, SCr, and K in 2 weeks.
   D. Increase atenolol.

Case – Questions 12 and 13

R.T. is a 60-year-old HD patient who has had ESRD for 10 years. His HD access is a left arteriovenous fistula. He has a history of hypertension, CAD, mild CHF, type 2 diabetes mellitus, and a seizure disorder. Medications: Epoetin 14,000 units 3 times/week at dialysis; multivitamin (Nephrocaps) once daily; atorvastatin 20 mg/day; insulin; calcium acetate 2 tablets 3 times/day with meals; phenytoin 300 mg/day; and intravenous iron 100 mg/month. Laboratory values: Hemoglobin 10.2 g/dL; immunoassay for PTH (iPTH) 800 pg/mL; Na 140 mEq/L; K 4.9 mEq/L; Cr 7.0 mg/dL; calcium 9 mg/dL; albumin 2.5 g/dL; and phosphorus 7.8 mg/dL. Serum ferritin is 200 mg/mL, and transferrin saturation is 32%. The RBC indices are normal. His WBC is normal. He is afebrile. Which one of the following is most likely contributing to relative epoetin resistance in this patient?
   A. Iron deficiency
   C. Phenytoin Therapy
   D. Infection
   E. Hyperparathyroidism

Case – Questions 12 and 13

13. In addition to diet modification and emphasizing adherence, which one of the following is the best approach to managing this patient’s hyperparathyroidism and renal osteodystrophy?
   a. Increase calcium acetate
   b. Change calcium acetate to sevelamer and add cinacalcet
   c. Hold calcium acetate and add intravenous vitamin D analog
   d. Add intravenous vitamin D analog
Complications of CKD - Anemia

Anemia

A. Anemia
1. Several factors are responsible for anemia in CKD: decreased erythropoietin production (most important), shorter life span of red blood cells, blood loss during dialysis, iron deficiency, anemia of chronic disease, and renal osteodystrophy.
2. Signs and symptoms. Symptoms of anemia of CKD are similar to anemia associated with other causes.
3. Treatment. Treatment of anemia in CKD can decrease morbidity/mortality, reduce LVH, increase exercise tolerance, and increase quality of life. Recent studies have suggested that treatment to high hemoglobin concentrations (greater than 13 g/dL) increases cardiovascular events. TREAT trial failed to show a benefit in outcomes but was associated with increased stroke in CKD.

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Anemia

a. Anemia work-up. Initiate evaluation when CrCl is less than 60 mL/minute or hemoglobin is less than 11 g/dL.
   i. Hemoglobin/hematocrit
   ii. Mean corpuscular volume
   iii. Reticulocyte count
   iv. Iron studies:
      Transferrin saturation (total iron / total iron-binding capacity) – assesses available iron and ferritin – measures stored iron. Other tests available.
   i. Stool guaiac

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Anemia

b. Erythropoietic stimulating agents (ESAs). Note, ESA’s now under FDA’s REMS program. Includes Epoetin and Darbepoetin

c. Goal Hemoglobin. 2007 Update to the guidelines suggest a goal of 11-12 g/dL and the avoidance of Hb concentration > 13 g/dL.

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Anemia

e. Iron therapy
   i. Most patients with CKD who are receiving ESA therapy require parenteral iron therapy to meet needs (increased requirements, decreased oral absorption).
   ii. For adult patients who undergo dialysis, an empiric 1000-mg dose is usually given and equations are rarely used.
   iii. Follow transferrin saturation and ferritin as noted during ESA therapy.
   iv. Four commercial iron preparations are approved in the United States (Table 2).
   v. Oral iron not recommended in CKD patients on HD.

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Complications of CKD – Bone Disease

B. Renal Osteodystrophy and Secondary Hyperparathyroidism

1. Pathophysiology: Complex. See notes.
   - Hyperphosphatemia
   - Decreased production/activation of vitamin D
   - Hypocalcemia.

   Hyperparathyroidism causes increased resorption of calcium from the bone and resultant osteodystrophy.

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CKD – Bone Dz

B. Renal Osteodystrophy and Secondary Hyperparathyroidism

4. Treatment
   a. Therapy goals - (Table 3)
   b. Nondrug therapy
      a. Dietary phosphorus restriction
      b. Dialysis
      c. Parathyroidectomy

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CKD – Bone Dz

c. Drug therapy.
   i. Phosphate binders: (Can combine different binders).
      Take prior to meals.
      a) Aluminum-containing phosphate binders Avoid (see notes).
      b) Calcium-containing phosphate binders
         1) Widely used binder. Considered initial binder of choice for stage 3 and 4 CKD. Carbonate is relatively inexpensive
         2) Calcium acetate. Better binder than carbonate, so less calcium given
         3) Use may be limited by development of hypercalcemia.
         4) Total elemental calcium per day = 2000 mg/day (1500-mg binder; 500-mg diet)

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Patient Case – Question 14

13. P.P. is a 40-year-old dialysis patient with a history of grand mal seizures. He takes phenytoin 300 mg/day. His albumin concentration is 3.0 g/L. His total phenytoin concentration is 5.0 mg/dL. Which one of the following is the best interpretation of the phenytoin concentrations?
   A. The concentration is subtherapeutic, and a dose increase is warranted.
   B. The concentration is therapeutic, and no dosage adjustment is needed.
   C. The concentration is toxic, and a dose reduction is needed.
   D. The level is not interpretable

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VI Dosage Adjustment in Kidney Disease

A. National Kidney Disease Education Program (NKDEP) of the NIH/NIDDK suggest that either eGFR or eCrCl can be used for drug dosing. (Controversial)

VI Dosage Adjustment in Kidney Disease

b. PK Alterations with Phenytoin. Free fraction of phenytoin in normals is 10%. With uremia and or hypoalbuminemia, free fraction is elevated (as high as 30%) resulting in lower total concentrations despite having normal free concentration. Do not need to adjust doses of phenytoin in CKD.
c. There are equations available to "adjust" observed concentrations. More often we now check free levels.

Patient Cases – 10 and 11

9. R.R. is a 70-year-old man being evaluated for hemodialysis access. He has a history of diabetes mellitus and hypertension but is otherwise healthy. Which of the following dialysis accesses has the lowest rate of complications and longest life span?
   A. Subclavian catheter
   B. Tenckhoff catheter
   C. Arteriovenous graft
   D. Arteriovenous fistula

10. W.Y. is a chronic hemodialysis patient who experiences intradialytic hypotension. After nonpharmacologic approaches have been maximized, which one of the following medications is best to manage his low blood pressure?
   A. Levocarnitine
   B. NaCl tablets
   C. Fludrocortisone
   D. Midodrine

Renal Replacement Therapy

A. Indications for Renal Replacement Therapy
   A — acidosis (not responsive to bicarbonate)
   E — electrolyte abnormality (hyperkalemia; hyperphosphatemia)
   I — intoxication (boric acid; ethylene glycol; lithium; methanol; phenobarbital; salicylate; theophylline)
   O — fluid overload (symptomatic pulmonary edema)
   U — uremia (pericarditis and weight loss)

B. Two Primary Modes of Dialysis
   i. Hemodialysis – most common modality
   Peritoneal dialysis

Renal Replacement Therapy

C. Hemodialysis (Intermittent for end-stage renal disease)
   i. Access
      a. Arteriovenous fistula-preferred access!
      i. Natural, formed by anastomosis of artery and vein
      ii. Lowest incidence of infection and thrombosis, lowest cost, longest survival
      iii. Takes weeks/months to "mature"
      b. Arteriovenous graft
      i. Synthetic (polytetrafluoroethylene)
      ii. Often used in patients with vascular disease
   c. Catheters
      i. Commonly used if permanent access not available
      ii. Problems include high infection and thrombosis rates. Low blood flows lead to inadequate dialysis.

Renal Replacement Therapy

C. Hemodialysis (continued)
   i. Intradialytic
      i. Hypotension – primarily related to fluid removal. Tx: limit fluid gains between sessions, give normal or hypertonic saline, nitroprusside. Less well-studied agents include fludrocortisone, selective serotonin reuptake inhibitors
      ii. Cramps – vitamin E or quinine (controversial because of side effect profile). Associated with rapid fluid removal.
      iii. Nausea/vomiting
      iv. Headache/chest pain/back pain
   b. Vascular access complications – most common with catheters.
      i. Infection – S. aureus. Need to treat aggressively. May need to pull catheter
      ii. Thrombosis - suspected with low blood flows. Oral anticoagulants for prevention not used because of lack of efficacy. Can treat with alteplase 1 mg per lumen.
The End