566 Midterm Study Guide

WEEK 1

-Things to know about each of the major antibiotic drug classes

- Contraindications and high-risk patients
- Know examples of each of the major antibiotic drug classes
- Monitoring needs
- Which ones require renal dosing adjustments and how much (i.e., 25%, 50%, etc.)
- Patient education
- Lifespan considerations including pregnancy
- Indications for use

Penicillins

- **caution with patients allergic reactions to penicillins, cephalosporins, or carbapenems**
- **Treats infection cause by sensitive bacteria**
  check culture to identify infecting organism
- **Can order skin test to assess allergy status**
- **adjusted doses for patients with impaired renal fnx**

NARROW SPECTRUM PENICILLINS: PENICILLIN SENSITIVE(PEN G &PEN V)

-**Mechanism of Action: "Bactericidal"- Weakens the cell wall, causing bacteria to take up excessive amounts of water and rupture.**

Occurs by two actions simultaneously: inhibiting transpeptidases and activating autolysins which disrupts synthesis of the cell wall and promotes the active destruction resulting in cell lysis and death.

-Examples: Penicillin G (Prototype Drug), Penicillin V, Nafcillin, Oxacillin, Dicloxacillin, Ampicillin, Amoxicillin, Piperacillin

Penicillin G-

-First Penicillin Available and often referred to plainly as Penicillin
-Bactericidal for gram negative and gram positive bacteria
-Should be taken with medications whereas Penicillin V is stable in stomach acids.

-Side Effects: Allergic reactions, pain at IM injection sites, prolonged (but reversible) sensory and motor dysfunction if injected into peripheral nerves, and neurotoxicity (seizures, confusion, hallucinations- if levels too high)

.

-Life Span Considerations:

***Infants- Used safely in infants with bacterial infections including syphilis, meningitis, & group A streptococcus**
***Children/Adolescents- Common drug used to treat bacterial infections in children.**
***Pregnant- No well controlled studies but evidence suggests no 2nd or 3rd trimester fetal risk.**
***Breastfeeding- Amoxicillin is safe. Data is lacking about transmission of other PCNs from mother to infant through breast milk.**
***Older Adults- Doses should be adjusted in older adults with renal dysfunction.**

Penicillin Allergy:

-Most common drug allergy to date with severity ranging from minor rash to anaphylaxis
-Can possibly display cross sensitivity to cephalosporins and should not be used if possible
-observed 30 minutes minimum post drug injection for adverse reactions
-For history of PCN allergy, a skin allergy test can be done to assess current risk by injecting a tiny amount of allergen ID (only to be done where epinephrine and respiratory support is available if needed)

Penicillin V-

- **Stable in stomach acid (Pen G is not)**
- **Used for oral therapy, can be taken with meals**

NARROW SPECTRUM PENICILLIN: PENICILLIN RESISTANT: (Nafcillin, Oxacillin, Dicloxacillin)

-Treats S. aureus and S. epidermidis

Broad-Spectrum Penicillins (Ampicillin & Amoxicillin):

-Most common side effects are rash and diarrhea (rash usually 3-10 days post TX start).
-Therapy can be PO or IV and requires dosage adjustment for renal impairment
-Treats Haemophilus influenzae, E. Coli, proteus mirabilis, enterococci, and Neisseria gonorrhoeae

EXTENDED SPECTRUM PENICILLIN: (Piperacillin)

-Treats same diseases as broad spectrum PLUS: *pseudomonas aeruginosa*, enterobacter spp, proteus, bacteroides fragilis, klebsiella spp
-Can cause bleeding secondary to disrupting platelet function
-Usually administered IV
-Reduce dose in renal pt's

Cephalosporins (Cephalexin)

-Bactericidal drug (similar to PCNs)
-Increases activity against gram-negative agents
-Increases ability to reach cerebral spinal fluid (CSF)-3rd,4th,5th generations
-no routine lab monitoring
-Administered IM or IV
-Take cultures to determine sensitivity and infecting organism
-Contraindicated in pt's with severe allergic reaction to cephalosporins or penicillins
- CAN CAUSE C. DIFF INFECTION (tell pt. To monitor for frequent stools)
-Used to treat infants & neonates. Especially in otitis media and gonococcal and pneumococcal infections
-Adverse Effects: Maculopapular rash, bronchospasm, anaphylaxis
-Education: Patients should not consume alcohol

First generation: tx's staphylococci or streptococci
Cefadroxil, Cefazolin, Cephalexin
Second generation: TX's H. Influenza, Klebsiella, pneumococci, staphylococci
Cefaclor, Cefotetan, Cefoxitin, Cefurozime
Third generation: tx's pseudomonas aeruginosa, Neisseria gonorrhoeae, Klebsiella, Serratia
Cefdinir, Cefotaxime, Cefpodoxime, Ceftazidime, Ceftriaxone
Fourth generation: Pseudomonas aeruginosa
Cefepine, Ceftolozane/tazobactam
Fifth generation: Methicillin resistant Staphylococcus aureus
Ceftaroline

Carbapenems (Imipenem)

-Patients on valproate for seizures not to give
-Avoid in renal impairment pts
-Adverse effects: N/V/D, seizures (rare), rashes, pruritus

Vancomycin

-Used for C. Diff infection
-Treats S. Aureus and S. epidermidis, and MRSA
-Monitor Vanco drug levels
-Use caution in pt's with renal impairment

Telavancin

-Black Box Warning: when used to tx hospital acquire or ventilator-associated bacterial pneumonia with creatinine clearance of less thn 50 ml/min, increased chance of mortality. Not safe in pregnancy

Aztreonam

-Adverse effects: pain & thrombophlebitis at injection site
USES: -treats gram negative bacteria: E. Coli, salmonella, Shigella, Serratia, Klebsiellam Proteus, H. influenza, P. aeruginosa

Fosfomycin

-Single dose therapy in women with uncomplicated UTI
-Adverse effects: diarrhea, headache, vaginitis, nausea, abdominal pain, rhinitis, drowsiness, dizziness, rash

Tetracyclines (Tetracycline)

-Broad spectrum bacteriostatic
-Contraindication/Precautions:
- After the 4th month of pregnancy can stain deciduous teeth and stain permanent teeth of children ages of 4 month and 8 years
- If given to treat an STD, abstain from intercourse until med is finished.

- **Uses**
  - Disorders for which they ARE first-line drugs include:
    - Acne Vulgaris (topically and orally)
    - Rickettsial Disease (Rocky Mountain spotted fever, typhus fever, Q fever)
    - Infections caused by Chlamydia Trachomatis (trachoma, lymphogranuloma venereum, urethritis, cervicitis)
    - Brucellosis
    - Cholera
    - Pneumonia caused by *Mycoplasma pneumonia*.
    - Lyme Disease
    - Anthrax
    - Gastric Infection with *H.Pylori* -Peptic Ulcer Disease
  - Periodontal Disease

- Food decreases absorption

- **Complications**
  - GI discomfort (cramping, nausea, diarrhea, and esophageal ulceration)
    - § Taking Doxycycline and Minocycline with meals will with GI discomfort BUT food will reduce absorption.
    - § Avoid taking at bedtime to reduce the risk of esophageal ulceration.

- Yellow/Brown tooth discoloration, Hypoplasia of tooth enamel, Effects on bones
    - Avoid in children younger than 8 and women who are pregnant.
    - Can suppress the growth of long bones in premature infants.
- Hepatoxicity (lethargy, jaundice)
    - Avoid high daily doses IV.
    - Fatty infiltration of the liver
- Photosensitivity (exaggerated sunburn)
    - Use sunscreen with an SPF 30 or higher.
- Superinfection of the Bowel
    - C-diff associated diarrhea AKA antibiotic-associated pseudomembranous colitis. D/C med immediately
    - Yeast infections of the mouth, pharynx, vagina
- Dizziness. Lightheadedness (Minocycline)
- Renal Toxicity

- **Contraindication/Precautions**
    - After the 4th month of pregnancy can stain deciduous teeth and stain permanent teeth of children ages of 4 month and 8 years
    - If given to treat an STD, abstain from intercourse until med is finished.
- **Interactions**
    - Interaction with milk products, calcium, iron supplements, laxatives containing magnesium and antacids causes formation of nonabsorbable chelates, thus reducing the absorption of tetracyclines.
        - Administer 1 hour BEFORE or 2 hours ingestion of chelating agents.
    - Increase the risk of digoxin toxicity and increase INR by altering Vitamin K -producing flora in the gut.
    - Decrease efficacy of oral contraceptives – use alternative form of birth control.

Life Stage	Patient Care Concerns
Children/adolescents	Tetracyclines should not be used in children younger than 8 years because they may cause permanent discoloration of the teeth.
Pregnant women	Animal studies reveal that tetracyclines can cause fetal harm in pregnancy. Thus, this class of drugs should be avoided in pregnant women.
Breastfeeding women	Use of tetracyclines during tooth development can cause permanent staining. Tetracyclines should be avoided by breastfeeding women.
Older adults	Tetracyclines can interact with drugs, including digoxin. In the older adult who takes many medications, check for interactions.

Macrolides (Erythromycin)

- Uses
    - Treatment of choice for Corynebacterium diphtheria and may be used as an alternative to Penicillin G in patients with PCN allergy.
    - Treats chlamydial infections, pneumonia d/t *Mycoplasma pneumonia*, & streptococcal infections

- Fidaxomicin is a narrow spectrum macrolide that treats C.diff.

· Complications (S/E)
- GI Discomfort is the most common (nausea, vomiting, epigastric pain)
- Prolonged QT interval
  - § Torsade's de Pointes – dysrhythmia and sudden death.
- Ototoxicity with HIGH-dose therapy
  - § Report hearing loss, vertigo, and tinnitus.

· Contraindications/Precautions
- Liver Disease and QT Prolongation are contraindications.
  - § Avoid if patient has congenital QT prolongation and those taking class IA or III antidysrhythmic drugs.
  - § avoided by patients taking CYP3A4 inhibitors CCB, azole antifungals, HIV protease inhibitors and nefazodone.

· Interactions
- Erythromycin prevents binging of chloramphenicol and clindamycin – antagonizing their antibacterial effects.
- Erythromycin inhibits the metabolism of antihistamines, theophylline, carbamazepine, warfarin, and digoxin which can lead to TOXICITY.
  - § Monitor liver function if taken longer than 2 weeks.
  - § Monitor PT/INR

• **Minimizing Adverse Effects: Avoid use in patients with QT prolongation. GI disturbances can be reduced by administering with meals.**

Clindamycin

- Drug of choice for severe Group A Streptococcal infection and for gas gangrene
- Widely used and as an alternative to penicillin

· Complications
- *CDAD, formerly known as *antibiotic-associated pseudomembranous colitis* is the MOST SEVERE toxicity
  - § Symptoms may develop 4-6 weeks AFTER withdrawal.
  - § Drugs that decrease bowel motility (opioids, anticholinergics) may WORSEN symptoms and should NOT be used.
- Erosive Esophagitis

· Black BOX Warning
- *Clindamycin can cause fatal Clostridium difficile diarrhea. Patients should promptly report nay diarrhea.*

· Interactions
- May decrease oral contraceptive activity.

Linezolid

· **Uses**
- 5 Approved indications
  - § Infections caused by VRE
  - § Hospital Acquired pneumonia caused by *S. Aureus* (Methicillin—susceptible & methicillin-resistant strain or *S. pneumoniae* (penicillin-susceptible strain only)
  - § Community-associated pneumonia (CAP) caused by *S. pneumonia* (penicillin-susceptible strains only)

§ Complicated skin and skin structure infections caused by *S. aureus* (Methicillin—susceptible & methicillin-resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactia*.
§ Uncomplicated skin and skin structure infections caused by *S. aureus* (Methicillin—susceptible & methicillin-resistant strains) or *S. pyogenes*.

To delay the emergence of resistance Linezolid should generally BE RESERVED for infections caused by VRE or MRSA

- Aerobic and facilitative gram-positive bacteria
- It is NOT active against gram-bacteria.

· **Complications**

- *Most common are diarrhea, nausea, and headache.
- Oral suspension contains phenylalanine and must NOT be used by patients with phenylketonuria.
- May cause reversible myelosuppression – manifesting as anemia, Leukopenia thrombocytopenia or even pancytopenia – (Draw CBC weekly)
- *Rare, prolonged therapy has been associated with neuropathy.

· **Interactions**

- Weak inhibitor of Monoamine Oxidase (MAO) > risk for hypertensive crisis.
  § MAO inhibitors can cause severe hypertension if combined with indirect-acting sympathomimetics (epinephrine, pseudoephedrine, methylphenidate, cocaine) or with foods that contain large amounts of tyramine.
- Combining linezolid with a selective serotonin reuptake inhibitor (SSRI) (Paroxetine, duloxetine) can increase the risk for serotonin syndrome.

Tedizolid

• Uses

- Skin and soft tissue infections caused by MRSA, *Streptococcus* and *Enterococcus*
  - **Complications**
    - *Most Common side effects are diarrhea, nausea, vomiting, dizziness, and headache.
  - **Interactions**
    - Weak inhibitor of MAO and pose a risk for hypertensive crisis.
    - Same principle applies to the SSRIs.

Aminoglycosides (Gentamicin, Tobramycin, Amikacin)

· **Uses**

- Gentamicin: Bacterial infections caused by aerobic gram-negative bacilli: Pseudomonas aeruginosa Enterobacteriaceae
- Kanamycin: Bacterial infections caused by gram-negative bacilli—not to be used for Serratia and Pseudomonas, as these bacteria are now resistant
- Neomycin: Topical infection Prevention in minor cuts Ocular bacterial infections
- Amikacin: Bacterial infections caused by gram-negative bacilli
- Tobramycin: Bacterial infections caused by aerobic gram-negative bacilli: Pseudomonas aeruginosa Enterobacteriaceae
- Streptomycin: Used in combination with other drugs to treat tuberculosis; also used to treat tularemia and plague

-Oral or IV

· **Complications**

- **Ototoxicity**

§ Cochlear damage (hearing loss), vestibular damage (loss of balance) is largely **IRREVERSIBLE**.
§ *First sign of impending COCHLEAR damage is high-pitched tinnitus.
· *(Amikacin & Kanamycin) = auditory*
§ *First sign of VESTIBULAR damage is headache. Followed by nausea, unsteadiness, dizziness, and vertigo.
· *(Gentamycin & Tobramycin) = vestibular*
§ AUDIOMETRIC testing is needed.

- **Nephrotoxicity**
  - § Correlates with:
    - · The *total cumulative dose* of aminoglycosides
    - · *High Trough* levels
  - § Usually manifest as acute tubular necrosis. Prominent symptoms are proteinuria, casts in the urine, production of dilute urine and elevations in serum creatinine and blood urea nitrogen (BUN)
  - § Cells of the proximal tubule REGENERATE, injury to the kidneys usually **REVERSES**.

· **Contraindications/Precautions**

- cautious in patients with kidney impairment, hearing loss and myasthenia gravis.
- if taking ethacrynic acid (increases the risk for ototoxicity), amphotericin B, cephalosporins, vancomycin (increases the risk for nephrotoxicity) and neuromuscular blocking agents (tubocurarine).

· **Black BOX Waring**

- **Aminoglycoside> Neurotoxicity/Ototoxicity**
  - § ***Use of aminoglycosides is associated with irreversible ototoxicity. Neurotoxic symptoms: numbness, tingling, muscle twitching and seizures. This risk increases in patients on high doses or with prolonged use and in patients with preexisting renal impairment.***
- **Aminoglycoside >Nephrotoxicity**
  - § ***. This risk increases in patients using high does, with prolonged use and in patients with preexisting renal impairment.***
- **Aminoglycoside-Induced Neuromuscular Blockade**
  - § ***inhibit neuromuscular transmission, causing flaccid paralysis and potentially fatal respiratory depression. Most episodes of neuromuscular blockade have occurred after intraperitoneal or intrapleural instillation of aminoglycosides.***

· **Beneficial Drug Interactions**

- *Penicillin* disrupts the cell wall and thereby facilitate access of aminoglycosides to their site of action.
- *Cephalosporins & Vancomycin* weaken the bacterial cell wall to enhance bacterial kill when used with aminoglycosides.

· **Adverse Drug Interactions**

- Risk for injury to the inner ears is increased by concurrent use of loop diuretics.
- Penicillin inactivates aminoglycosides when in the same IV solution.

· **Monitoring Serum Drug Levels**

- Once -A-Day-Dosing: It is only necessary to obtain blood sample for measuring *trough levels* .
- Divided Doses

§ *Peak*: 30 min AFTER administration of aminoglycoside IM or 30 min AFTER COMPLETION of an IV infusion
§ *Trough*: Right BEFORE the next dose

Patient-Centered Care Across the Life Span
Aminoglycosides

Life Stage	Patient Care Concerns
Infants	treat bacterial infections in infants younger than 8 days. Dosing is based on weight and length of gestation.
Children/adolescents	safe for use against bacterial infections
Pregnant women	can harm the fetus.
Breastfeeding women	Gentamicin is probably safe to use during lactation. There is limited information regarding its use in this way
Older adults	Caution must be used regarding decreased renal function in the older adult

Summary of Key Prescribing Considerations
Aminoglycosides

- **Therapeutic Goal:** Treatment of serious infections caused by gram-negative aerobic bacilli.
- **Baseline Data:** Blood and/or urine cultures.
- **Monitoring:** Aminoglycoside levels (peaks and troughs) and renal function must be monitored.
- **Identifying High-Risk Patients:** caution in patients with renal impairment, preexisting hearing impairment, and those receiving ototoxic and nephrotoxic drugs.
- **Evaluating Therapeutic Effects:** Patients must be monitored for indications of antimicrobial effects, including reduction in fever, pain, or inflammation.
- **Minimizing Adverse Effects:** Caution must be exercised when aminoglycosides are used in combination with other nephrotoxic or ototoxic drugs. Patients must be instructed to report symptoms of ototoxicity.

Sulfonamides

- Uses
  - Broad spectrum of microbes comprising gram-positive cocci (including methicillin-resistant *Staphylococcus aureus*),
  - Gram-negative bacilli, *Listeria monocytogenes*, actinomycetes (e.g., *Nocardia*), chlamydiae (e.g., *Chlamydia trachomatis*)
  - Some protozoa (e.g., *Toxoplasma* species, plasmodia, *Isospora belli*)
  - 2 fungi: *Pneumocystis jirovecii* (formerly thought to be *Pneumocystis carinii*) and *Paracoccidioides brasiliensis*.
  - Sulfasalazine is used to treat Ulcerative Colitis.

*Their applications are now limited due to the introduction of bactericidal antibiotics that are less toxic than the sulfonamides, and the development of sulfonamide resistance. Today, UTI is the principal indication for these drugs.

- **Complications**
  - Hypersensitivity Reactions
    - § Stevens-Johnson Syndrome if the most severe- widespread lesions of the skin and mucous membranes
  - Blood Dyscrasias
    - § Hemolytic Anemia, agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia
      - Obtain blood samples for baseline and periodic CBC counts to detect disorders.
      - Observe for bleeding, sore throat and pallor.
  - Kernicterus
    - § A disorder in newborns cause by deposition of bilirubin in the brain.
    - § Because of the risk for kernicterus, sulfonamides should not be administered to infants younger than 2 months. In addition, sulfonamides should not be given to pregnant patients after 32 weeks of gestation or to those who are breastfeeding.
  - Renal Damage
    - § Older sulfonamides tended to come out of solution in the urine, forming crystalline aggregates in the kidneys, ureters, and bladders. These aggregates cause irritation and obstruction, sometimes resulting in anuria and even death.
    - § Sulfamethoxazole is the only intermediate-acting sulfonamide available. The risk for renal damage from crystalluria can be reduced by maintaining adequate hydration.
- **Interactions**
  - Sulfonamides can intensify the effects of warfarin, phenytoin, and sulfonylurea-type oral hypoglycemics (glipizide, glyburide). These drugs may require a reduction in dosages to prevent toxicity.

Patient Education
Sulfonamides

- Instruct patients to complete the prescribed course of treatment even though symptoms may abate before the full course is over.
- Patients taking oral sulfonamides should drink at least 8 to 10 glasses of water or other noncaffeinated fluids per day to decrease the risk for crystalluria. (Caffeine may be taken in addition to the other fluids.)
- To prevent photosensitivity reactions, advise patients to avoid prolonged exposure to sunlight, to wear protective clothing, and to apply sunscreen to exposed skin. Tanning beds are to be avoided.
- Patients should be instructed to observe for alterations that may indicate hypersensitivity (e.g., rash) and to report these promptly if they occur.

Patient-Centered Care Across the Life Span
Sulfonamides

Life Stage	*Patient Care Concerns*
Infants	*younger than 2 months can cause kernicterus, a potentially fatal condition.*
Pregnant women	*Systemic sulfonamides may cause birth defects, especially if taken during the first semester. If taken near term, the infant may develop kernicterus.*
Breastfeeding women	*Sulfonamides are secreted in breast milk. Breastfeeding women on sulfonamides should be warned that breastfeeding an infant younger than 2 months can cause kernicterus.*
Older adults	*Older patients are more likely to experience adverse effects, and when experienced, the effects are more likely to be severe. Life-threatening effects—including neutropenia, Stevens-Johnson syndrome, and toxic epidermal necrolysis—occur more frequently in older adults.*

Trimethoprim

- **Uses**
  - Approved only for the initial therapy of acute, uncomplicated UTIs due to susceptible organisms (e.g., *E. coli*, *P. mirabilis*, *K. pneumoniae*, *Enterobacter* species, and coagulase-negative *Staphylococcus* species, including *S. saprophyticus*).
  - Combined with sulfamethoxazole, trimethoprim has considerably more applications.
- **Complications**
  - Hematologic Effects
    - § Rare effects—*megaloblastic anemia*, *thrombocytopenia*, and *neutropenia*—occur only in individuals with preexisting folic acid deficiency.
    - § Caution is needed when trimethoprim is being administered to patients in whom folate deficiency might be likely (e.g., patients with excessive alcohol intake, pregnant women, debilitated patients).
    - § If early signs of bone marrow suppression occur (e.g., sore throat, fever, pallor), complete blood counts should be performed.
  - Hyperkalemia
    - § Suppresses renal excretion of potassium and can thereby promote hyperkalemia.
    - § Greatest risk is those taking high doses, those with renal impairment, and those taking other drugs that can elevate potassium, including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), potassium-sparing diuretics, aldosterone antagonists, and potassium supplements.
    - § Patients older than 65 years who are taking an ACEI or ARB are at especially high risk. Risk can be reduced by checking serum potassium, preferably 4 days after starting treatment (hyperkalemia typically develops within 5 days of starting treatment).
  - Effects in Pregnancy and Lactation

§ Large doses of trimethoprim have caused fetal malformations in animals.
§ Readily crosses the placenta - avoiding its routine use during pregnancy.
§ Excreted in breast milk and may interfere with folic acid utilization by the nursing infant.

Patient Education
Trimethoprim

• Inform patients about early signs of blood dyscrasias (e.g., sore throat, fever, pallor) and instruct them to report these promptly if they occur.

Trimethoprim/Sulfamethoxazole

- **Uses**
  - Preferred or alternative medication for a variety of infectious diseases. The combination is especially valuable for UTIs, otitis media, bronchitis, shigellosis, and pneumonia caused by *P. jirovecii*.
- **Complications**
  - The most common are nausea, vomiting, and rash.
  - Like sulfonamides, the combination can cause the following:
    - § • Hypersensitivity reactions (including Stevens-Johnson syndrome)
    - § • Blood dyscrasias (hemolytic anemia, agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia)
    - § • Kernicterus in neonates
    - § • Renal damage
  - Like trimethoprim, the combination can cause the following:
    - § • Megaloblastic anemia (but only in patients who are folate deficient)
    - § • Hyperkalemia (especially in patients on high doses, in those with renal impairment, and in those taking other drugs that can raise potassium levels)
    - § • Birth defects (especially during the first trimester)
  - TMP/SMZ may also cause adverse CNS effects (headache, depression, hallucinations).
  - Patients suffering from AIDS are unusually susceptible to TMP/SMZ toxicity.
- **Drug Interactions**

  > like sulfonamides used alone, SMZ in the combination can intensify the effects of warfarin, phenytoin, and sulfonylurea-type oral hypoglycemics (e.g., glipizide). when combined with TMP/SMZ, a reduction in their dosage may be needed.
  - TMP/SMZ may also intensify bone marrow suppression in patients receiving methotrexate.
  - As noted, drugs that raise potassium levels can increase the risk for hyperkalemia from TMP.

Summary of Key Prescribing Considerations
Trimethoprim/Sulfamethoxazole

- **Therapeutic Goal:** Absence of infection
- **Baseline Data:** Establish infection: Urinalysis (if UTI is suspected) with culture and sensitivity as indicated. (Collect urine sample before starting therapy but don't wait for results before prescribing treatment; treat empirically until results are available.) Obtain complete blood count (CBC) with white cell differential if indicated or if treatment will be prolonged. Renal function should be checked if there is concern that it may be compromised.

· **Monitoring:** CBC should be monitored if the patient develops signs or symptoms of blood disorders, as should CD4+ count for patients with HIV infection. Signs and symptoms of hypersensitivity reactions and of resolution of infection should also be assessed. If hyperkalemia is suspected due to use of trimethoprim, potassium must be checked 4 days after starting treatment.

· **Identifying High-Risk Patients:** Sulfonamides are contraindicated for nursing mothers, pregnant women in the first trimester and also those near term, and infants younger than 2 months. An alternative antibiotic must be chosen for patients with G6PD deficiency.

It is important to *exercise caution* in prescribing sulfonamides for patients with renal impairment.

In patients with renal impairment (creatinine clearance of 15–30 mL/min), dosage should be decreased by 50%. If creatinine clearance falls below 15 mL/min, drug use must be discontinued.

Trimethoprim is *contraindicated* in patients with folate deficiency (manifested as megaloblastic anemia). When possible, trimethoprim should be avoided during pregnancy and lactation.

Patients with renal dysfunction require a reduced dosage.

Trimethoprim should be avoided when folate deficiency is likely (e.g., in patients with alcoholism or debilitation and in women who are pregnant).

· **Evaluating Therapeutic Effects:** Absence of evidence of infection (negative urinalysis, white cell differential returns to normal, signs and symptoms resolve).

Fluoroquinolones

· **Uses**
  - o Ciprofloxacin - Infections of the respiratory tract, urinary tract, GI tract, bones, joints, skin and soft tissues, Inhalational anthrax
  - o Ofloxacin - Infections of the respiratory tract, urinary tract, GI tract, skin and soft tissues
  - o Levofloxacin - infections of the respiratory tract, urinary tract, GI tract, skin and soft tissues, Inhalational anthrax
  - o Moxifloxacin - Infections of the respiratory tract, intra-abdominal infections, skin and skin structures
  - o Gemifloxacin - Respiratory tract infections (1) CAP & (2) Acute bacterial exacerbation of chronic bronchitis

· **Complications**
  - o GI Discomfort (nausea, vomiting, diarrhea)
    - § May take oral dose with food except for dairy products.
  - o Achilles Tendon Rupture
    - § Damage tendons by disrupting the extracellular matrix of cartilage in immature animals. A similar mechanism may underlie tendon rupture in humans.
    - § Tendon injury is reversible if diagnosed early, -discontinue at the first sign of tendon pain, swelling, or inflammation. Refrain from exercise until tendinitis has been ruled out.
  - o CNS Effects
    - § (dizziness, headache, restlessness, confusion).
  - o Superinfection
    - § *Candida* infections of the pharynx and vagina may develop during treatment.

§ Increase the risk for developing C. Difficile.

- Phototoxicity (Severe Sunburn)
  - Characterized by burning, erythema, exudation, vesicles, blistering, and edema. Can occur after exposure to direct sunlight, indirect sunlight, and sunlamps—even if a sunscreen has been applied.

- **Black BOX Warning**
  - ***Fluroquinolones and Tenson Rupture***
    - ***Cipro and other fluoroquinolones have caused tendon rupture, usually of the Achilles tendon. People highest risk are those 60 years of age and older, those taking glucocorticoids, and those who have undergone heart, lung or kidney transplantation.***
  - ***Ciprofloxacin and Myasthenia Gravis***
    - ***Ciprofloxacin and other fluoroquinolones can exacerbate muscle weakness in patients with myasthenia gravis. Accordingly, patients with a history of myasthenia gravis should not receive these drugs.***
- **Contraindications/Precautions**
  - Do not administer to children younger than 18 years of age d/t risk of Achilles tendon rupture.
  - Increases the risk for C-diff because it destroys normal intestinal flora.
- **Interactions**
  - Cationic compounds (aluminum- or magnesium- containing antacids, iron salts, sucralfate, dairy products) decrease the absorption.
    - Administer cationic compounds 6 hours before cipro or 2 hours after cipro.
  - Increase plasma levels of several drugs, including theophylline (used for asthma), warfarin (an anticoagulant), and tinidazole (an antifungal drug). Toxicity could result.
    - Warfarin - prothrombin time should be monitored, and the dosage of warfarin reduced.

Patient-Centered Care Across the Life Span
Antibacterial Drugs

Life Stage	Patient Care Concerns
Children/adolescents	Ciprofloxacin and levofloxacin are the only fluoroquinolones approved for use in children. Because of concerns regarding tendon injury, fluoroquinolones are generally avoided in this population.
Pregnant women	Although data reveal little potential for fluoroquinolone toxicity in the fetus, these data are limited. Risks and benefits must be considered for administration during pregnancy.

Breastfeeding women	Effects of fluoroquinolones on the nursing infant are largely unknown. Other medications should be considered if possible.
Older adults	Fluoroquinolones are generally well tolerated in older adults. For safe dosing, creatinine clearance should be calculated.

Summary of Key Prescribing Considerations
Fluoroquinolones

- **Therapeutic Goal:** Treatment of fluoroquinolone-sensitive infections
- **Baseline Data:** None indicated
- **Monitoring:** None recommended
- **Identifying High-Risk Patients:** Fluoroquinolones are contraindicated in patients with a history of myasthenia gravis. They should be used with caution in patients with renal impairment, patients over 60 years of age, and patients taking glucocorticoids.
- **Evaluating Therapeutic Effects:** Patients should be monitored for indications of antimicrobial effects such as reduction in fever, pain, or inflammation.
- **Minimizing Adverse Effects:** Patients must be instructed to report early signs of tendon injury and to avoid prolonged sun exposure.

· **Complications**
  - o GI Discomfort (nausea, vomiting, diarrhea)
    - § May take oral dose with food except for dairy products.
  - o Achilles Tendon Rupture
    - § Damage tendons by disrupting the extracellular matrix of cartilage in immature animals. A similar mechanism may underlie tendon rupture in humans.
    - § Tendon injury is reversible if diagnosed early, -discontinue at the first sign of tendon pain, swelling, or inflammation. Refrain from exercise until tendinitis has been ruled out.
  - o CNS Effects
    - § (dizziness, headache, restlessness, confusion).
  - o Superinfection
    - § *Candida* infections of the pharynx and vagina may develop during treatment.
    - § Increase the risk for developing C. Difficile.
  - o Phototoxicity (Severe Sunburn)
    - o Characterized by burning, erythema, exudation, vesicles, blistering, and edema. Can occur after exposure to direct sunlight, indirect sunlight, and sunlamps—even if a sunscreen has been applied.

· **Black BOX Warning**
  - o ***Fluroquinolones and Tenson Rupture***

§ ***Cipro and other fluoroquinolones have caused tendon rupture, usually of the Achilles tendon. People highest risk are those 60 years of age and older, those taking glucocorticoids, and those who have undergone heart, lung or kidney transplantation.***

- ***Ciprofloxacin and Myasthenia Gravis***
  - § ***Ciprofloxacin and other fluoroquinolones can exacerbate muscle weakness in patients with myasthenia gravis. Accordingly, patients with a history of myasthenia gravis should not receive these drugs.***

- **Contraindications/Precautions**
  - Do not administer to children younger than 18 years of age d/t risk of Achilles tendon rupture.
  - Increases the risk for C-diff because it destroys normal intestinal flora.
- **Interactions**
  - Cationic compounds (aluminum- or magnesium- containing antacids, iron salts, sucralfate, dairy products) decrease the absorption.
    - § Administer cationic compounds 6 hours before cipro or 2 hours after cipro.
  - Increase plasma levels of several drugs, including theophylline (used for asthma), warfarin (an anticoagulant), and tinidazole (an antifungal drug). Toxicity could result.
    - Warfarin - prothrombin time should be monitored, and the dosage of warfarin reduced.

Patient-Centered Care Across the Life Span
Antibacterial Drugs

Life Stage	Patient Care Concerns
Children/adolescents	Ciprofloxacin and levofloxacin are the only fluoroquinolones approved for use in children. Because of concerns regarding tendon injury, fluoroquinolones are generally avoided in this population.
Pregnant women	Although data reveal little potential for fluoroquinolone toxicity in the fetus, these data are limited. Risks and benefits must be considered for administration during pregnancy.
Breastfeeding women	Effects of fluoroquinolones on the nursing infant are largely unknown. Other medications should be considered if possible.

Older adults	Fluoroquinolones are generally well tolerated in older adults. For safe dosing, creatinine clearance should be calculated.

Summary of Key Prescribing Considerations
Fluoroquinolones

- **Therapeutic Goal:** Treatment of fluoroquinolone-sensitive infections
- **Baseline Data:** None indicated
- **Monitoring:** None recommended
- **Identifying High-Risk Patients:** Fluoroquinolones are contraindicated in patients with a history of myasthenia gravis. They should be used with caution in patients with renal impairment, patients over 60 years of age, and patients taking glucocorticoids.
- **Evaluating Therapeutic Effects:** Patients should be monitored for indications of antimicrobial effects such as reduction in fever, pain, or inflammation.
- **Minimizing Adverse Effects:** Patients must be instructed to report early signs of tendon injury and to avoid prolonged sun exposure.

-Community Acquired Pneumonia (CAP)

- Causative agents
    1. Most common - **Streptococcus pneumoniae**
    2. General Population -
        1. **Streptococcus pneumoniae (gram positive)**
        2. **Atypical bacteria (mycoplasma pneumoniae)**
        3. **Viruses (H. influenzae and RSV)**
        4. **Staphylococcus aureus**
- Treatment options
    - Empiric treatment when culture results are not available
        1. **1st line treatments for CAP in patients with no comorbidities/risk factors**
            1. **Amoxicillin, Macrolides (Erythromycin or clarithromycin), and Doxycycline**
        2. **If treated with antimicrobial agent in last 90 days (risk of drug resistance):**
            1. **Give Fluoroquinolones**
    - Understand the use of macrolides in pregnancy and children under the age of 8 with CAP or M. Pneumoniae (**not sure if they meant to state tetracyclines instead of macrolides??)**
        1. **Macrolides and tetracyclines are drugs of choice for Mycobacterium pneumoniae.**
            1. **Erythromycin (macrolides) may be prescribed safely throughout pregnancy.**
            2. **Tetracycline**
                1. **Should be avoided during pregnancy because of potential tooth damage and staining.**

2. **Should avoid in children under 8 because of potential for permanent discoloration of the teeth.**

- When to prescribe fluoroquinolone for CAP
    1. **If treated with antimicrobial agent in last 90 days (risk of drug resistance):**
        1. **Give Fluoroquinolones**

· Progression of infectious process
- Treatment expectations

· Know the most likely pathogen causing CAP according to patient population
1. **Smokers & COPD**
    1. **Haemophilus influenzae (gram negative)**
2. **Cystic Fibrosis**
    1. **Pseudomonas aeruginosa (gram negative)**

-Treatment of chlamydial pneumonia **(info from CDC)**
1. **Macrolides (Azithromycin - 1st line therapy)**
2. **Tetracyclines (tetracycline and doxycycline)**
3. **Fluoroquinolones**

-Understand empiric treatment and when to use
1. **Severe infection and need to initiate treatment before culture or gram stain results are back.**
2. **Drug selection must be based on clinical evaluation and knowledge of which microbes are most likely to cause infection in a particular site.**
3. **Use a broad spectrum if needed to start off, then switch to a narrow spectrum (a more selective drug) when the organism is identified.**
4. **Get samples of exudates and body fluids BEFORE INITIATION OF TREATMENT.**

-Understand broad spectrum vs narrow spectrum agents
· What are they
1. **Broad Spectrum**
    1. **Active against a wide variety of microbes**
    2. **Gram negative and gram positive**
2. **Narrow**
    1. **Are active against only a few species of microorganisms.**
    2. **Narrow-spectrum drugs are generally preferred to broad-spectrum drugs.**

· Drugs under each category
1. **Narrow**
    1. **Gram-positive cocci and gram-positive bacilli**

1. **Penicillin G and V**
2. **Penicillinase-resistant penicillins: oxacillin and nafcillin**
3. **Vancomycin**
4. **Erythromycin**

5. **Clindamycin**

2. **Gram-negative aerobes**
    1. **Aminoglycosides: gentamicin and others**
    2. **Cephalosporins (first and second generations)**
3. **Mycobacterium tuberculosis**
    1. **Isoniazid**
    2. **Rifampin**
    3. **Ethambutol**
    4. **Pyrazinamide**

2. **Broad Spectrum**
    1. **Gram-positive cocci and gram-negative bacilli**
        1. **Broad-spectrum penicillins: ampicillin and others**
        2. **Extended-spectrum penicillins: piperacillin and others**
        3. **Cephalosporins (third generation)**
        4. **Tetracyclines: tetracycline and others**
        5. **Carbapenems: imipenem and others**
        6. **Trimethoprim**
        7. **Sulfonamides: sulfisoxazole and others**
        8. **Fluoroquinolones: ciprofloxacin and others**

· How they work (local vs. systemic)
1. **Broad**
    1. **Systemic - covering a large basis**
2. **Narrow**
    1. **Local - more targeted to certain areas of the body where the infection may be taking place.**

· When to use each
1. **Broad**
    1. **Use when an organism is unknown and treatment needs to start immediately.**
2. **Narrow**
    1. **Use when an organism is known and the practitioner is able to target the antimicrobial therapy from the test results.**

-If someone is allergic to one antibiotic group, which do you prescribe in its place?

· Allergic to penicillin- what would you prescribe?
1. **Cephalosporins - if penicillin allergy is mild**

· Allergic to sulfa drugs- what would you prescribe?

-Clostridium difficile

· How to treat- **Vancomycin and Flagyl**
1. **Stop antibiotic that caused the C. diff infection**
2. **For initial (1st timer C. diff) infections**
    1. **Treat with oral vancomycin or fidaxomicin (narrow spectrum macrolide)**
    2. **Metronidazole can be used if vancomycin or fidaxomicin is not available.**

3. **If fulminant infection (one by shock, megacolon, or hypotension)**
    1. **Oral vancomycin**

- Which antibiotics are more likely to cause?
    1. **All categories of Cephalosporins (mainly 2nd and 3rd generation) can promote C diff, instruct patients to report frequent stools**
    2. **Clindamycin**
    3. **Fluoroquinolones**
        1. **Cipro and levofloxacin - responsible for spread of NAP1/BI/027 strain**

Which antibiotics require renal dose adjustments? Penicillins, vancomycin and aminoglycoside?

1. **Sulfonamides**
    1. **CrCl is 15-30mL decrease dose by 50%**
    2. **CrCl is <15mL - stop drug completely**

- What types of infections are usually viral and do not warrant antibacterial agents?

Otitis Media

Community acquired pneumonia

WEEK 2

-Know how to treat

- **Different types of Tinea**
    1. **Scalp - Tinea Capitis (ringworm)**
        1. Griseofulvin PO x 6-8 weeks (book info) or 8-10 weeks (module info)
        2. 2-4 weeks of PO terbinafine (may be more effective)
    2. **Skin - Tinea Corporis (ringworm)**
        1. Terbinafine - Topical (module info)
        2. Also responds to topical azole or allylamine (book info)
        3. Severe infection may require systemic agent - griseofulvin
    3. **Foot - Tinea Pedis (athlete's foot) - MOST COMMON**
        1. Terbinafine - Topical
        2. Advise patients to wear cotton socks, change their shoes often, and dry their feet after bathing.
    4. **Tinea Cruris (Jock Itch)**
        1. Topical Therapy - continue meds at least 1 week after symptoms have cleared.
        2. **If severely inflamed:**
            1. **Systemic antifungal drug - Clotrimazole**
            2. **May need topical or systemic glucocorticoids**
- **Oral candidiasis**
    1. **Mouth - Candida (thrush)**
        1. Nystatin - Topical
        2. Fluconazole - PO
- **Aspergillosis**

1. Drug of Choice
    1. **Voriconazole**
        1. 6mg/kg day 1, followed by 4mg/kg IV BID x 7 days, then 100mg PO q12h
2. Alternatives
    1. Amphotericin B, isavuconazonium, itraconazole, posaconazole, caspofungin, micafungin

-Voriconazole and Phenobarbital should not be combined due to CYP450

· **Phenobarbital is a CYP450 inducer which can reduce the levels of drugs like voriconazole.**

-Adverse reactions/Patient Teaching

· **Itraconazole**

1. Adverse Reaction
    1. **Cardiac Suppression**
        1. **Negative inotrope**
            1. Transient decrease in ventricular ejection fraction.
            2. Cardiac functions returns to normal after 12 hours of dosing.
            3. Can still be used to treat only SERIOUS FUNGAL INFECTIONS in HF patients - closing monitoring required.
                1. If HF starts to worsen, STOP TREATMENT.
            4. BLACKBOX WARNING
                1. Do not use for superficial fungal infections (dermatomycoses or onychomycosis) in patients with HF or hx of HF, or other indications with ventricular dysfunction
    2. Liver Injury
    3. Can inhibit drug-metabolizing enzymes and raise levels of other drugs
2. **Patient Teaching**
    1. Take this medication 1 hour before or 2 hours after taking antacids, H2 antagonists, or PPIs.
    2. Instruct patients to report signs of liver dysfunction.
    3. Avoid use with drugs that are metabolized by CYP3A4 (warfarin, cyclosporin, digoxin, and quinidine).

· **HIV: Nucleotide Reverse Transcriptase Inhibitors (NRTIs)**

- Instruct patients to adhere closely to the prescribed dosing schedule.
- Emphasize the need to avoid taking any over-the-counter drugs or supplements without first checking with the provider to verify safety.
- Teach patients how to access and use drug interaction checkers.
- All NRTIs, except didanosine, may be taken without regard to meals
- MITOCHONDRIAL TOXICITY - IMPAIRED MITOCHONDRIAL FUNCTION
    - **Mitochondrial impairment causes:**

- Patients taking NRTIs are at risk of lactic acidosis and hepatic steatosis.
    - Lactic Acidosis
        - S/S: nausea, malaise, fatigue, anorexia, and hyperventilation
    - Hepatic Steatosis and Hepatomegaly
        - Abdominal Pain
- Pancreatitis and Myopathies
- Inform patients that, even when HIV RNA is undetectable, they are still infectious and should avoid behaviors that can transmit HIV.

· **Example drugs of NRTIs**

- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

-How to measure therapeutic effect of HIV therapy

Success is indicated by reduction in plasma HIV RNA (Viral Load). Plasma HIV RNA should decline to 10% of baseline within 2 to 8 weeks of treatment. After 16-20 weeks of treatment, plasma HIV RNA should reach its minimum.

CD4 Tcell counts- As viral load decreases, CD4 T cell counts may rise indicating some restoration of immune function.

-Diagnostics & Monitoring for anthelmintics

- Diagnostics: Pregnancy test
- **Monitoring:**
    - **Albendazole (liver function and CBC with differential)**
    - **Mebendazole (liver function, CBC with differential, and renal function)**
    - **Praziquantel (liver function)**
    - **Ivermectin and moxidectin (ophthalmologic exam if abnormal at baseline)**

-Identifying High-Risk Patients with the following drugs

· Albendazole

- Because bone marrow suppression, impaired liver function, and possibly renal function may occur, patients with liver or kidney disease, anemia, bleeding disorders, and infections are at increased risk

· Mebendazole

- Because bone marrow suppression and liver impairment may occur, patients with liver disease, anemia, bleeding disorders, and infections are at increased risk.

· Pyrantel pamoate

- Patients with liver impairment are at a higher risk for adverse effects. Neonates should not be prescribed formulations containing benzyl alcohol or its derivatives

· **Ivermectin**
- Patients with hypotension or taking antihypertensive drugs may be at risk for increased hypotension and falls

· **Moxidectin**
- (Same as ivermectin) - Patients with hypotension or taking antihypertensive drugs may be at risk for increased hypotension and falls

· **Didanosine**
- Pancreatitis is increased by a history of alcoholism or pancreatitis and by use of IV pentamidine.

· **Zidovudine**
- Hematologic toxicity is increased by a low granulocyte count; low levels of hemoglobin, vitamin B12, or folic acid; and concurrent use of drugs that are myelosuppressive, nephrotoxic, or toxic to circulating blood cells.

· **Lopinavir**
- **Contraindicated for full-term infants (until 14 days after birth) and preterm infants (until 14 days after their predicted due date).**
- **Caution in patients with structural heart disease, cardiac conduction disturbances, and ischemic heart disease, and in those taking other drugs that prolong the PR interval.**

-Adverse Effects

· **Albendazole**
- Mild to moderate liver impairment
  - Liver function should be assessed before each cycle of treatment and 14 days later
- Suppresses bone marrow function
  - Causes granulocytopenia, agranulocytosis, and even pancytopenia.
- Some patients developed renal failure
- Teratogenic in animals
  - Should not be used during pregnancy
  - If pregnancy occurs, the drug should be discontinued immediately.

· **Pyrantel pamoate**
- Neonates given formulations with benzyl alcohol or its derivatives had developed a potentially fatal “gasping syndrome” with complications that include respiratory distress, cardiovascular collapse, seizures, and metabolic acidosis.
- Most common effects are GI reactions (nausea, vomiting, diarrhea, stomach pain, and cramps).
- Possible central nervous system effects include dizziness, drowsiness, headache, and insomnia.

· **Mebendazole**
- Most concerning are bone marrow suppression (neutropenia) and liver impairment

        - Typically only a problem with high doses or prolonged treatment
    - Patients with massive parasitic infestations, transient abdominal pain and diarrhea may occur.
    - Relatively low doses are embryotoxic and teratogenic in some animal reproduction studies.

· Ivermectin

- Patients treated for onchocerciasis commonly develop pruritus, rash, fever, lymph node tenderness, and bone and joint pain
    - Reaction known as a Mazotti reaction, an allergic and inflammatory response to the death of *O. volvulus* rather than a reaction to the drug.
- Abdominal pain and headache are seen in less than 5% of patients
- Hypotension develops rarely
- Teratogenic in mice, rats, and rabbits.
- Cleft palate is the most common effect.
    - There are no adequate data on teratogenesis in humans
    - Until more is known, ivermectin should be avoided during pregnancy.

· **Moxidectin**

- Patients typically experience the flu-like symptoms of the Mazotti-response
- Adverse effects mirror those of ivermectin

· Lopinavir/ritonavir

- Dangerous drug interactions, hepatotoxicity, pancreatitis, PR interval prolongation, QT interval prolongation, hyperglycemia or diabetes (new onset or exacerbation), immune reconstitution syndrome, redistribution of adipose tissue, hyperlipidemia, renewed bleeding in patients with hemophilia, headache, nausea, vomiting, abdominal discomfort, indigestion, weakness

· Saquinavir

- Dangerous drug interactions (including danger with ritonavir), PR interval prolongation, QT interval prolongation, diabetes (new onset or exacerbation), immune reconstitution syndrome, redistribution of adipose tissue. renewed bleeding in patients with hemophilia, exacerbation of comorbid hepatic disease, hyperlipidemia, nausea, vomiting, abdominal pain, diarrhea, fatigue

· Enfuvirtide

- Injection site reactions (98%), hypersensitivity, postinjection bleeding, immune reconstitution syndrome, pneumonia, nausea, diarrhea, fatigue.
- Inform patients of injection site reaction pain, tenderness, erythema, induration, nodules, cysts, pruritus, and ecchymosis—and forewarn them that these occur in nearly everyone.
    - Reduce occurrence by rotating sites, avoiding sites with active reactions, and avoid unnecessary deep site injections.
- Risk for bacterial pneumonia is increased
    - Cough, fever, and breathing difficulties.

-Lifespan Considerations

· Which medications are safe during pregnancy or childhood

**Additional Notes:

- Drugs that decrease gastric acid should be administered at least 2 hours apart from other drugs due to decreased drug absorption.

- Prompt recognition of liver injury is essential with oral antifungal drugs. AST, ALT, alkaline phosphatase, and bilirubin should be monitored prior to initiation of therapy, monthly for 3 to 4 months, and frequently thereafter during treatment.

WEEK 3

-Treatment of glaucoma

· Pros and Cons of beta blocker use

Beta Blockers approved for topical use in treating open-angle glaucoma are ***betaxolol*, carteolol, levobunolol, metipranolol, and *timolol*.** These drugs treat glaucoma by reducing IOP which can slow or even stop the disease progression. Beta blockers lower IOP by decreasing production of aqueous humor. They are suitable for initial therapy, maintenance therapy and emergency management of acute angle closure glaucoma.

Adverse Effects

Local- stinging, conjunctivitis, blurred vision, photophobia and dry eyes

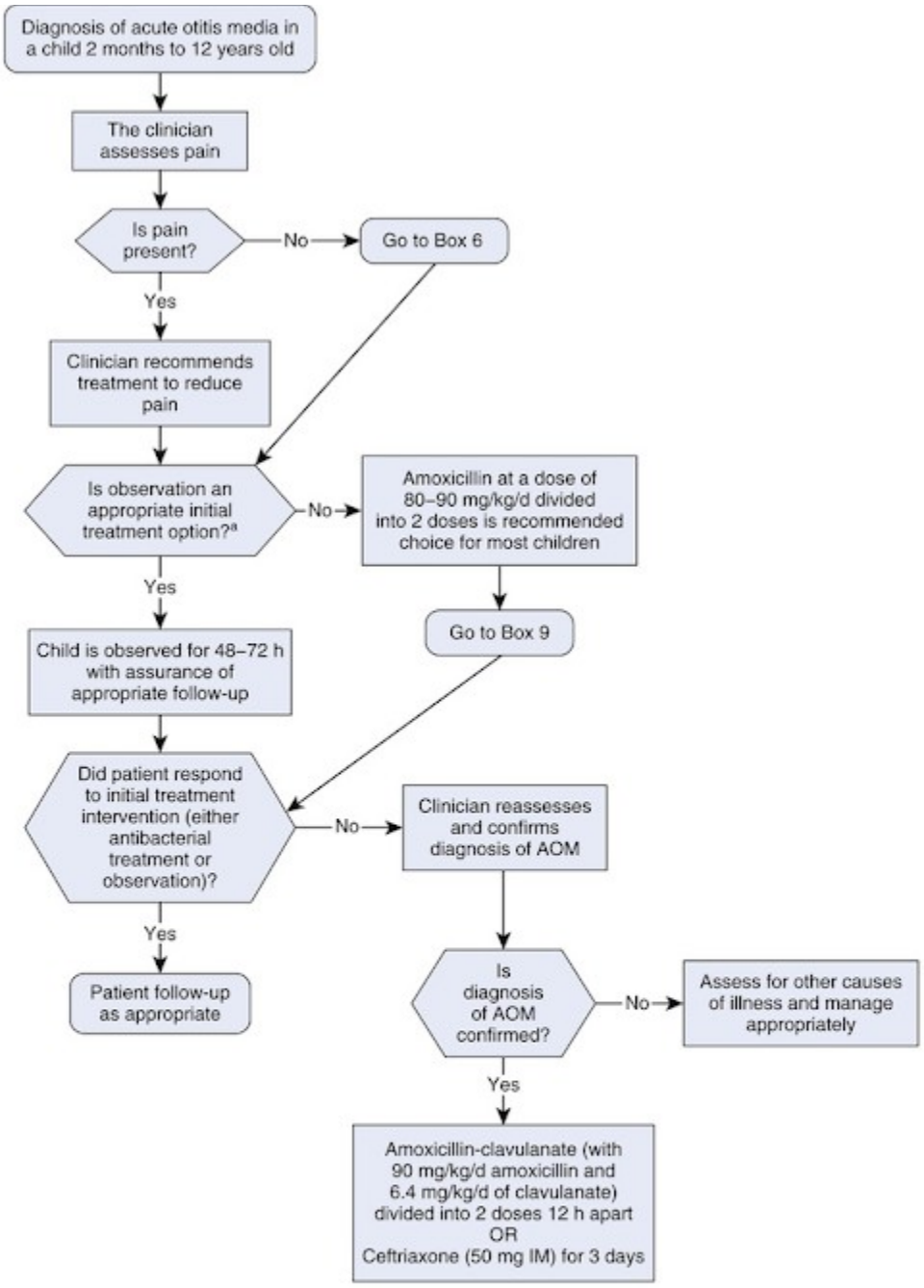
Systemic- 1 dop of .5% timolol in each eye can produce the same blood level as taking 10 mg of timolol by mouth. Bradycardia and AV heart block can also occur. Pulse should be monitored. **USE WITH CAUTION IN PATIENTS WITH HEART FAILURE. Can also cause Bronchospasm**

· **How to treat someone with glaucoma and either asthma or COPD**

Use only betaxolol as treatment of choice because it's beta 1 selective.

-Treatment of Otitis Media and associated symptoms

- **ASSOCIATED S/S:**
  - Ear pain (children will pull ear), fever, vomiting, anorexia, irritability, sleeplessness, and diarrhea
  - Bulging tympanic membrane, inflammation and swelling of the eustachian tube



[a] Criteria for antibacterial treatment or observation in children with uncomplicated AOM[b]

1) <6 months: antibacterial treatment
2) 6 months - 2 years: antibacterial treatment if AOM diagnosis is certain unless AOM is unilateral without otorrhea
3) 2 yr and older: antibacterial treatment if severe pain >48 h, fever ≥39°C (102.2°F) during the preceding 48 h, or if there is a possibility that the caregiver may not reliably arrange for follow-up, if needed. For mild earache of <48 h or if temperature is <39°C, observation is appropriate

[b]Caregiver is informed and agrees to the option of observation.
Caregiver is able to monitor child and return should condition worsen.
Systems are in place for ready communication with the clinician, evaluation, and obtaining medication if necessary.

[a]Appropriate medication alternatives should be used for the child with penicillin allergy.

Patient Group	RECOMMENDED DRUGS

and Illness Severity	For Most Patients	For Patients With Penicillin Allergy[a]
Patients Receiving Immediate Antibiotic Therapy		
Nonsevere illness	Amoxicillin, 40–45 mg/kg bid	*Non–type I allergy:* Cefdinir, 14 mg/kg per day in one dose or two divided doses, *or* Cefuroxime, 15 mg/kg bid, *or* Cefpodoxime, 5 mg/kg bid *Type I allergy:* Azithromycin, 10 mg/kg on day 1, then 5 mg/kg on days 2, 3, 4, and 5. *or* Clarithromycin, 7.5 mg/kg bid
Severe illness	Amoxicillin, 45 mg/kg bid *plus* clavulanate, 3.2 mg/kg bid[b]	Ceftriaxone, 50 mg/kg IM for 1 or 3 days
Patients With Persistent Symptoms After 48–72 h of Observation (With No Antibiotic Therapy)		
	Same as for patients receiving immediate antibiotic therapy	
Patients With Persistent Symptoms After 48–72 h of Antibiotic Therapy (Indicating Drug Resistance)		
Nonsevere illness	Amoxicillin, 45 mg/kg bid *plus* clavulanate, 3.2 mg/kg bid[b]	*Non–type I allergy:* Ceftriaxone, 50 mg/kg IM or IV for 3 days *Type I allergy:* Clindamycin, 30–40 mg/kg/d in 3 divided doses
Severe illness	Ceftriaxone, 50 mg/kg IM for 3 days	Clindamycin (plus a third-generation cephalosporin if non–type I penicillin allergy) and tympanocentesis

-Treatment of Otitis Externa and associated symptoms

- Bacterial vs. Fungal
  - **Bacterial:**
    - Common cause: Pseudomonas aeruginosa and Staphylococcus aureus
    - s/s: Hearing impairment, purulent discharge (may occur), pruritus, ear fullness, tenderness or manipulation of the external ear, edema , or erythema

Treatment for bacterial: analgesics for pain control and ear drops of acetic acid and alcohol, if this treatment fails give ciprofloxacin drops

- Oral medication is indicated if infection extends beyond the external auditory canal and involves the pinna. Give oral ciprofloxacin in patients over 18 years and Cephalexin (Keflex) in children

Fungal (otomycosis): Common pathogen: Aspergillus and candida

S/S: intense pruritus and erythema, with or without pain or hearing loss.

Treatment: cleansing and application of 2% acetic acid solution 3-4 times a day for 7 days. If treatment fails, prescribe 1% clotrimazole (Lotrimin) drops twice daily for 7 days, if treatment fails prescribe oral antifungal such as itraconazole (sporanox) or Fluconazole (Diflucan).

-Treatment of acne (fig 88.1)

· **Mild:** Benzoyl peroxide or topical retinoid (Vitamin A) or topical combo therapy of benzoyl peroxide plus antibiotic or retinoid plus benzoyl peroxide

· **Moderate:** Topical combo therapy. Benzoyl + antibiotic or retinoid + benzoyl + antibiotic OR oral antibiotic + topical retinoid + benzoyl + topical antibiotic

· **Severe (two agents):** Oral antibiotic (Doxycycline or minocycline) and topical combo therapy of benzoyl peroxide plus antibiotic or retinoid plus benzoyl peroxide or oral or retinoid + benzoyl + antibiotic OR isotretinoin (Accutane)

Side effects associated with Benzoyl peroxide and retinoids: local irritation including burning, blistering, scaling, swelling and hypersensitivity reactions

Side effects of Isotretinoin:nose bleeds, inflammation of lips and eyes, dryness of skin, nose and mouth. high risk of severe structural and cognitive defects in fetus, contraindicated in pregnancy, use protection from sunlight, avoid alcohol. STOP TETRACYCLINE BEFORE STARTING THIS THERAPY! ALCOHOL CAN POTENTIATE HYPERTRYGLYCERIDEMIA.

-Treatment of eczema and complications that may arise

First line therapy: moisturizers and topical glucocorticoids (complications include skin atrophy, hypopigmentation, permanent focal red lesions, and in high doses adrenal suppression).
If topical glucocorticoids are ineffective, a topical immunosuppressant (tacrolimus and pimecrolimus) can be used. They may pose risk for skin cancer and lymphoma- use as second line therapy only if first line fails. Avoid the use of tanning beds or direct sunlight and use sunscreen if treated with these therapies. Prolonged treatment should be avoided.

-Key ingredient needed in organic sunscreen

- **Organic**
  - Aminobenzoic Acid Derivatives
  - Cinnamates
  - Salicylates
  - Benzophenones
  - Others:
    - **Avobenzone, Ecamsule, Ensulizole, Meradimate, and Octocrylene**
- **Inorganic**
  - Titanium Dioxide
  - Zinc Oxide
- **Avobenzone to protect against UVA1 rays.**
- **Need coverage for protection against UVA and UVB rays and SPF of at least 15**

-Mechanism of Action

· **Expectorants** (know examples)

MOA: Renders cough more productive by stimulating the flow of respiratory tract secretions

Example: Guaifenesin (Mucinex, Humibid)

Max dose of Guaifenesin: 200 to 400 mg PO every 4 hours as needed. **Max**: 6 **doses**/day (2400 mg/day)

-Adverse Effects & Patient Teaching

· **Montelukast:**

Adverse Reactions: Neuropsychiatric effects including agitation, aggression, hallucinations, depression, insomnia.

Patient teaching: monitor for neuropsychiatric effects.

· **Intranasal Glucocorticoids**

Adverse reactions: Most common is drying of the nasal mucosa and a burning or itching sensation. Throat pain, epistaxis, and headache. Systemic effects including adrenal suppression and slowing of linear growth in children is rare but possible.

Patient teaching: give daily, may take a week for effects to develop

· **Sympathomimetics**

- **Phenylephrine**

  Rebound congestion if topical use

  Restlessness, irritability, anxiety, and insomnia in oral use

  Systemic vasoconstriction

- **Pseudoephedrine**

  Potential for abuse

· **Brimonidine-** Topical a adrenergic agonist for glaucoma

Adverse: dry mouth, ocular hyperemia, local burning and stinging, headache, blurred vision, foreign body sensation, and itching. Also can cause drowsiness, fatigue, and hypotension

Patient teaching: can be absorbed through soft contact lens, at least 15 minutes should elapse between drug admin and lens installation

· **Prostaglandin analog**s- first line therapy for glaucoma

Adverse: harmless heighed brown pigmentation of the iris and eyelid. Blurred vision, burning, stinging, conjunctival hyperemia/edema, and punctate keratopathy.

Teaching: Apply 1 drop in the evening daily. Take meds as prescribed, notify provider of vision loss, severe eye pain, headache, or N/V. Do not touch dropper to the eyes or fingers- can cause contamination, Close the eyes for 3 minutes after administering to help with absorption

· **Salicylic Acid for Acne**

Adverse: systemic salicylate toxicity (salicylism)- tinnitus, hyperpnea, and psychological disturbance

Teaching:Avoid prolonged use of high concentrations on large areas

· **Benzoyl peroxide**

Adverse: local irritation including burning, blistering, scaling, swelling and hypersensitivity reactions

Teaching: Avoid sun exposure, avoid irritant soaps, wash and dry skin before use, keep away from eyes, mouth, and mucus membranes, report severe irritation, blistering, and burning/swelling

· **Isotretinoin (Acutane)**

Adverse: :nose bleeds, inflammation of lips and eyes, dryness of skin, nose and mouth, depression

Teaching: high risk of severe structural and cognitive defects in fetus, contraindicated in pregnancy, use protection from sunlight, avoid alcohol. Avoid driving at night, women who can become pregnant need to be on 2 kinds of reliable birth control, avoid supplements that contain vitamin A, avoid waxing, laser therapy, or microdermabrasion

-Be familiar with which medications control which set of symptoms:

- Intranasal glucocorticoids, such as fluticasone propionate, are the most effective drugs for prevention and treatment of seasonal and perennial, because they prevent or suppress all the major symptoms of allergic rhinitis (congestion, rhinorrhea, sneezing, nasal itching, and erythema).
- Pseudoephedrine is an oral sympathomimetic used to reduce nasal congestion associated with allergic rhinitis. It has no effect on other symptoms.
- Loratadine, an oral antihistamine, reduces sneezing, rhinorrhea, and nasal itching only and is less effective than intranasal glucocorticoids.
- Intranasal cromolyn sodium is moderately effective in the treatment of allergic rhinitis, but the benefits are much less than those of intranasal glucocorticoids.

-How to manage rebound congestion

Larger and more frequent dose of medication- can lead to a cycle of escalating congestion and increased drug use. Use intranasal glucocorticoid in both nostrils for 2 to 6 weeks, starting 1 week before discontinuing the decongestant. Limit topical decongestant application to 3-5 days to reduce the development of rebound congestion.

-Understand role of biologics in treating allergies

Omalizumab is a biologic that works against IgE, an immunoglobulin (antibody) that plays a central role in the allergic release of inflammatory mediators from mast cells and basophils. Omalizumab is approved only for allergy-mediated asthma; however, several studies have demonstrated significant improvement of allergic symptoms. Because patients with ragweed-induced seasonal allergic rhinitis have achieved symptom relief with omalizumab when other drugs have been ineffective, this drug is sometimes prescribed off-label for management while clinical trials continue.

<u>WEEK 4</u>

-Treatment of obesity

- Evaluation of phentermine/topiramate

Schedule IV drug indicated for chronic weight loss. Phentermine suppresses appetite while topiramate increases satiety. Most common side effects are dry mouth, constipation, blurred vision, & numbness and tingling
Serious side effects are memory impairment, difficulty concentrating, HTN, tachycardia increased risk of hypoglycemia for diabetics
Contraindicated for patients with glaucoma or hyperthyroid
Should not be given with MAO inhibitors. Stop MAO inhibitors 2 weeks before starting medication and visa versa. Administration with carbonic anhydrase increases risk for metabolic acidosis and administration with diuretics that are not potassium sparing increases sick of hyperkalemia.

-Adverse Effects and/or Patient Teaching

- Orlistat
    - **Oily rectal leakage, flatulence with discharge, fecal urgency, and fatty or oily stools.**
    - **Increased defecation and fecal incontinence.**
    - **Rare cases of severe liver damage**
        - **Itching, vomiting, jaundice, anorexia, fatigue, dark urine, and light-colored stools.**
    - **Acute pancreatitis and kidney stones.**
    - **CONTRAINDICATIONS**
        - **Malabsorption syndrome or cholestasis**
- Lorcaserin
    - **Headaches, back pain, decrease in lymphocytes, and URIs.**
    - **Diabetics will experience an increase in hypoglycemic episodes.**
    - **Less common:**
        - **Blood dyscrasias, cognitive impairment, psychiatric disorders, priapism, pulmonary hypertension, and valvular heart disease.**
    - **Contraindications:**
        - **Associated with different aspects of lifespan.**
        - **Children:**
            - **Liraglutide, lorcaserin, and the combination drugs phentermine/topiramate and naltrexone/bupropion are not approved for children. Orlistat is not approved for children younger than 12 years. Diethylpropion and phentermine are not recommended for children younger than 16 years.**
        - **Pregnant Women**
            - **Weight loss is not advisable for pregnant women. All drugs mentioned in this chapter are contraindicated during pregnancy with the exception of diethylpropion. Diethylpropion is not a teratogen; however, neonates born to women who take this drug may experience withdrawal symptoms.**
        - **Breastfeeding**
            - **For all drugs listed, breastfeeding is not recommended.**
        - **Older adults**
            - **For patients with moderate renal impairment, naltrexone/bupropion should be limited to one tablet daily. If the creatinine clearance is less than 50, phentermine/topiramate should be limited to one 7.5/46 capsule daily. If the creatinine clearance is less than 30, lorcaserin should not be given.**
            - **For patients with hepatic impairment, both naltrexone/bupropion and phentermine/topiramate should be limited to one tablet daily.**

Phentermine/topiramate should not be prescribed for patients with severe hepatic impairment. The manufacturer of liraglutide recommends caution when prescribing for patients with renal or hepatic impairment.

- **Dosage adjustments are not indicated for orlistat, diethylpropion, and phentermine.**

· Naltrexone

- **Decrease the ability of opioid analgesics to relieve pain.**
- **Do not take within 2 weeks of a MAO inhibitor.**

· Naltrexone/Bupropion

- **10% of patients - N/V, constipation, headache, dizziness, and insomnia**
- **5% of patients - increase in blood pressure, dry mouth, diarrhea, abdominal discomfort, anxiety, and fatigue.**
- **Suicide risk also present.**
- **BLACK BOX WARNING**
  - **Increased risk of suicidal ideation and suicide attempts in children, adolescents, and young adults.**
- **Contraindications**
  - **Patients taking other forms of bupropion.**
  - **Do not use in select conditions:**
    - **Uncontrolled HTN**
    - **Seizure disorder**
    - **Eating disorders such as anorexia or bulimia**
  - **Patients undergoing alcohol, barbiturate, or benzodiazepine withdrawal.**

-Drug Interactions

· Orlistat

- **May cause hypothyroidism in patients taking levothyroxine by decreasing the absorption of thyroid hormone.**
- **If both drugs are needed:**
  - **Administer them at least 4 hours a part.**
- **Orlistat can reduce absorption of cyclosporine.**
  - **Give the 2 drugs 3 hours a part.**

-Baseline data and ongoing assessment needs for prescribing

· Liraglutide

- **Baseline Data:**
  - **Baseline HbA_{1c}, lipids, renal function**
  - **Baseline assessment of ability of patient or family to administer injections**
- **Ongoing Assessments**
  - **HbA1c, every 6 months if stable; more often as needed**
  - **Periodic monitoring of triglycerides, if indicated**

        - **Assess for s/s of cholecystitis, pancreatitis, depression, and suicidal thoughts**
- Orlistat
    - **Baseline Data:**
        - **None noted in book or module**
    - **Ongoing Assessments**
        - **Assess for s/s of deficiency in fat soluble vitamins (Vitamins A, D, E, and K)**
- Lorcaserin
    - **Baseline Data:**
        - **Baseline assessment to rule out valvular disorders and pulmonary hypertension**
    - **Ongoing Assessments**
        - **Ongoing monitoring for cognitive changes**
        - **CBC with differential for s/s of blood dyscrasias**
- Phentermine
    - **Baseline Data:**
        - **Baseline cardiac assessment**
    - **Ongoing Assessments**
        - **Ongoing assessment of cardiac status**
- Naltrexone/bupropion
    - **Baseline Data**
        - **Baseline blood glucose, liver function, renal function, and mental status**
    - **Ongoing Assessments**
        - **Periodic assessment for blood glucose, liver and renal function, s/s depression, anxiety or panic attacks, suicidal ideation, and mania**

-Drug interactions

- Lorcaserin
    - **Lorcaserin is an inhibitor of the CYP2D6 isoenzyme of cytochrome P450. When given with CYP2D6 substrates (i.e., drugs metabolized by CYP2D6 isoenzymes), the serum levels of the substrates can be increased. To decrease the risk for toxicity when both drugs are prescribed, the substrate may have to be prescribed at a lower dose.**
    - **Risk for serotonin syndrome is associated with serotonergic drugs. When serotonergic drugs such as lorcaserin are given with other serotonergic drugs, this risk increases.**

-Role of topiramate in the treatment for obesity

- **Topiramate induces a sense of satiety.**
- **Possible mechanisms for topiramate include antagonism of glutamate (an excitatory neurotransmitter), modulation of receptors for γ-aminobutyric acid, and inhibition of carbonic anhydrase**

-Obesity stages

· BMI at each stage & Treatment recommendations for each stage

- **Stage 0: A BMI of 25 or more with no complications**
  - **Lifestyle therapy**
  - **Drug therapy to be considered if lifestyle therapy alone is ineffective**
- **Stage 1: A BMI of 25 or more in the presence of one or more mild to moderate complications amenable to moderate weight loss**
  - **Lifestyle therapy**
  - **Drug therapy to be considered if lifestyle therapy alone is ineffective or if BMI is 27 or more**
- **Stage 2: A BMI of 25 or more at least one complication requiring significant weight loss**
  - **Lifestyle therapy**
  - **Drug therapy to be considered for BMI of 25 to 26**
  - **Drug therapy to be initiated for BMI of 27 or more**
  - **Bariatric surgery to be considered for BMI of 35 or more**

-DEA Schedules of drugs used to treat obesity

- **Lorcaserin (Belviq, Belviq XR) - Schedule IV**
- **Diethylpropion (generic) - Schedule IV**
- **Phentermine (Adipex-P, Lomaira) - Schedule IV**
- **Phentermine/Topiramate (Qsymia) - Schedule IV**
- **Liraglutide (Saxenda) - Not A Controlled Drug**
- **Orlistat (Alli and Xenical) - Not A Controlled Drug**
- **Bupropion/Naltrexone (Contrave) - Not A Controlled Drug**

PRESCRIPTION WRITING

-Medications you will need to know for the prescription writing questions include:

· **Amoxicillin**

For Adults 750-1750mg po q8 hours
For children 20-90 mg/kg q8 hours

· **Tetracycline**

Adult 1000-2000mg po q6 hours
Pediatric 25-50 mg/kg po q6 hours

· **Benzoyl Peroxide Cr.**

Benzoyl peroxide is available in a variety of formulations (lotion, cream, gel, foam) and concentrations range from 2.5% to 10%. For initial therapy one daily application is recommended. Over time, the frequency can be increased to three times a day. Patients should be advised to keep the drug away from eyes, mouth and mucous membrane as well as inflamed skin

· **Acyclovir**

Topical ointment 5% ointment applied 6 times a day at 3 hour intervals for 7 days
Topical Cream 5% cream applied 5 times a day for 4 days

educate patients to wear finger cot or rubber glove to avoid viral transfer to other body sites or other people

Oral acyclovir is available in 200 mg, 400mg and 800mg.

For initial espides of herpes the dose is 400 mg 3 times a day for 7-10 days

Episodic recurrence the dose is 400 mg 3 times a day for 5 days

Long term suppression therapy 400 mg twice a day for up to 12 months

Acute therapy of herpes zoster 800 mg 5 times a day for 7-10 days

Chickenpox is 20mg/kg 4 times a day for 5 days. Treatment should begin at the earliest sign of the rash

- **Timolol ophthalmic**

  .25% solution, .5% solution, - 1 drop once or twice a day

  .25% gel., .5% gel - 1 drop once a day

- Betaxolol

  .25% suspension 1 drop twice a day

Betaxolol