

Antibiotic Basics for the Pharmacy Technician

Arkansas Association of Health-System Pharmacists Fall Seminar
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October 3, 2014

Learning Objectives

- Describe the signs and symptoms of infection
- Define the following terms: broad vs. narrow spectrum; bacteriostatic vs. bactericidal; empiric vs. definitive therapy,
- Discuss the mechanism of action of different antibiotic classes
- Discuss various drug toxicities associated with antibiotics
- Describe appropriate compounding of parenteral and liquid antibiotics to ensure correct dosing for patients
- Discuss general counseling for antibiotics and the importance of auxiliary labels
- Describe the role of the antibiogram and infectious disease references

Abbreviations

- ABX – antibiotic
- MOA – mechanism of action
- RTI – respiratory tract infection
- VRE – vancomycin resistant enterococcus
- MRSA – methicillin resistant staph aureus
- VAP – ventilator associated pneumonia
- CAP – community acquired pneumonia
- UTI – urinary tract infection
- SSTI – skin and soft tissue infection

Rayanne Story reported that no relevant financial relationships exist.



Infection

- Refers to the invasion of tissue by a foreign substance such as a microorganism
 - bacteria
 - virus
 - fungi
 - protozoa
 - parasites
- Tissue damage can occur from the invading organisms or from the white blood cells (WBCs) sent to fight the organism

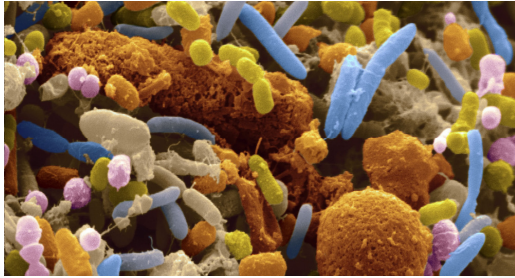
Infection

- The body can also raise its temperature to help kill the organisms
- Common signs of infection:
 - fever
 - pain
 - heat
 - redness
 - swelling



<http://imageshack.com/a/img812/286/p5c3.jpg>

- Some organisms are not harmful and some are helpful such as bacteria that live in the gut.

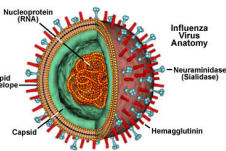
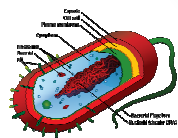
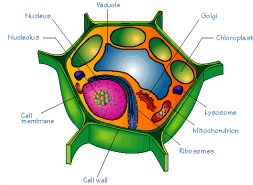


<http://i.imgur.com/3m0054l/thumb?o=GIF&ACT3RA&facebook&g>

Infection

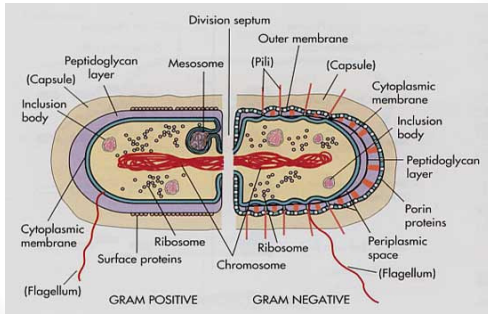
- May occur when there are too many organisms encountered or when the body's defenses cannot overcome the organism
- Antimicrobials are used when the body's defense needs help fighting an infection or there may be long term effects from the infection

- Antibiotics → bacteria
- Antivirals → virus
- Antifungals → fungus



<http://www.csa.com/discoveryguides/avian/images/virus.jpg>

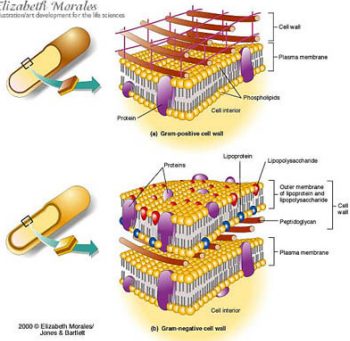
Basic Types of Bacteria



http://classconnection.s3.amazonaws.com/775/flashcards/729775/png/diagram_cells1327518364396.png

Elizabeth Morales

Microbiology Development for the life sciences



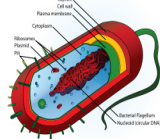
<http://faculty.ksu.edu/sa/shoeb/Pictures%20Library/Gram%20Positive%20and%20Negative%20Cell%20Wall.jpg>

Antibiotics

- Pharmacology

- Antibiotics interfere with:

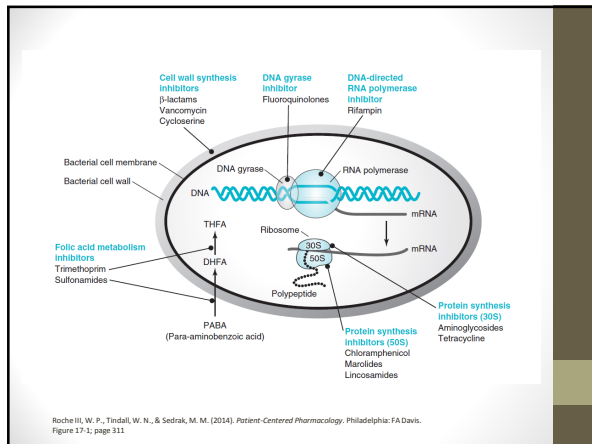
- Bacterial cell wall
 - DNA
 - RNA
 - protein synthesis



- Antibiotics can be:

- Bactericidal – kill bacteria
 - Bacteriostatic – inhibit the growth of the bacteria

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Antibiotic Terminology

- Spectrum of activity:
 - Narrow spectrum** – inhibits gram-positive or gram-negative
Examples: aztreonam, vancomycin
 - Broad-spectrum** – inhibits a variety of gram-positive and gram-negative organisms
Examples: imipenem/cilastatin, levofloxacin

Antibiotics

- Terminology
 - Classes of antibiotics:
 - Penicillins – ends in ‘**cillin**’
 - Cephalosporins – starts with ‘**Cef** or **Ceph**’
 - Carbapenems – ends in ‘**-penem**’
 - Monobactams – ends in ‘**-actam**’
 - Macrolides – ends in ‘**-romycin**’
 - Sulfonamides – Trimethoprim/Sulfamethoxazole
 - Tetracyclines – ends in ‘**-cycline**’
 - Fluoroquinolones – ends in ‘**-floxacin**’
 - Glycopeptides – **Vancomycin** or end in “**vancin**”
 - Nitroimidazole – ends in ‘**-idazole**’
 - Oxazolidinones – end in “**olid**”

Beta-lactam Ring Structure

Accessed at <http://student.ccbcmd.edu/courses/bio141/lecguide/unit3/control/images/betalactam.jpg> on Feb 20, 2014

Penicillins

- Inhibit bacterial cell wall synthesis
- Coverage and usage vary with each penicillin class:
 - Natural Penicillins
 - Anti-staphylococcal Penicillins
 - Aminopenicillins
 - Anti-pseudomonal Penicillins

Natural Penicillins

Coverage:
Streptococci
Meningococci
 Limited activity against *staphylococci*

Uses:
 Syphilis (drug of choice)
 Endocarditis (*Streptococcal*)

Examples:
 Penicillin G – only IV
 Penicillin V – usually oral

Penicillinase-Resistant Penicillins (antistaphylococcal)

Coverage:

Similar to natural penicillins, WITH increased activity against *staphylococci* (MSSA)

Uses:

Skin and soft tissue infections
Endocarditis (MSSA)

Examples:

Nafcillin (IV)
Oxacillin (IV)
Cloxacillin (oral)
Dicloxacillin (oral)

METHICILLIN

Aminopenicillins

Coverage:

Broader spectrum (gram-positive cocci, gram-negative rods):

Uses:

Upper respiratory tract infections (RTIs)
Otitis media

Examples:

Ampicillin (IV and oral)
Amoxicillin (oral only)

Broad-spectrum Penicillins (Antipseudomonal)

Coverage:

Same as aminopenicillins, AND including:
Pseudomonas
Enterobacter
Klebsiella

Uses:

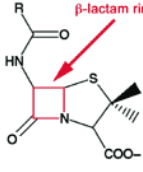
Sepsis, Intrabdominal surgery, Skin infections,
RTIs, SSTIs, UTIs

Examples:

Piperacillin (IV)
Ticarcillin (IV)

Antibiotic Resistance

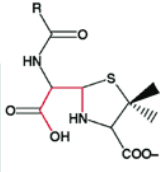
Penicillin Resistance



Penicillin

β-lactamase

β-lactamase breaks a bond in the β-lactam ring of penicillin to disable the molecule. Bacteria with this enzyme can resist the effects of penicillin and other β-lactam antibiotics.



Penicilloic acid

Accessed at http://www.wiley.com/college/pratt/0471993888/student/activities/bacterial_drug_resistance/beta_lactamase_rxn.pdf on February 7, 2010

Antibiotic Combinations with a β-lactamase inhibitor:

- β-lactamase inhibitor binds irreversibly and inactivates bacterial β-lactamase
- restores activity of antibiotic

Examples:

- Amoxicillin + Clavulanate (**Augmentin**®)(oral)
- Ampicillin + Sulbactam (**Unasyn**®)(IV)
- Piperacillin + Tazobactam (**Zosyn**®)(IV)

Allergy

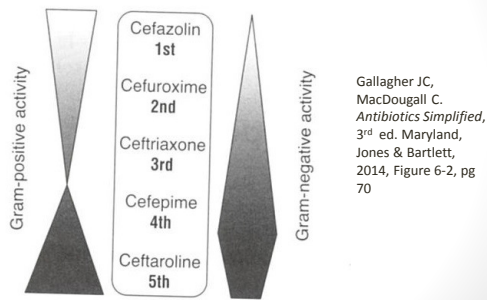
- **Cross reactivity** between beta lactam antibiotics
 - Patients with penicillin allergies can also have allergic reactions to other beta lactam antibiotics

Beta Lactam Antibiotics	PCN Allergy Cross Reactivity
Cephalosporin	Yes (less than 10%)
Carbapenem	Yes (up to 50%)
Monobactam	No, except ceftazidime

Cephalosporins

- Work the same way as penicillins
- Resistant to some β -lactamases
- Bacterial coverage and usage is varied by generation
- Longer half-life compared to penicillins, so less frequent dosing
- Small chance for cross-reactivity with PCN allergy (less than 10%)

Cephalosporin Activity



First-generation Cephalosporins

- **Uses:**
 - Respiratory tract
 - Skin
 - Urinary tract
 - Bone and joint
 - Surgical prophylaxis
- **Examples:**
 - Cefazolin (IV)
 - Cephalexin (PO)
 - Cefadroxil (PO)

Second-generation Cephalosporins

Uses:

- Urinary tract
- Gynecologic infections
- Septicemia
- Surgical prophylaxis
- Intra-abdominal infections

• **Examples:**

- Cefuroxime (Zinacef®, Cefitin) (IV, PO)
- Cefoxitin (Mefoxin®) (IV)
- Cefotetan (Cefotan®) (IV)
- Cefaclor (Ceclor®) (PO)

Third-generation Cephalosporins

Uses:

- Lower RTIs,
intra-abdominal
urinary tract
- uncomplicated gonorrhea
- bacterial septicemia
- meningitis

• **Examples:**

- Ceftriaxone (Rocephin®) (IV)
- Cefotaxime (Claforan®) (IV)
- Ceftazidime (Fortaz®) (IV)
- Cefixime (Suprax®) (PO)
- Cefpodoxime (Vantin®) (PO)
- Cefdinir (Omnicef®) (PO)

Cephalosporin Antibiotics

– **Cefdinir**

- Stool can appear red in color due to insoluble cefdinir-iron complex



Cephalosporin Activity

Gram-positive activity

Cefazolin
1st

Cefuroxime
2nd

Ceftriaxone
3rd

Cefepime
4th

Ceftaroline
5th

Gram-negative activity

Gallagher JC,
MacDougall C.
Antibiotics Simplified,
3rd ed. Maryland,
Jones & Bartlett,
2014, Figure 6-2, pg
70

Fourth-generation Cephalosporin

Coverage: broad spectrum

Uses:

- Nosocomial infections
- UTIs
- Febrile neutropenia
- Pneumonia
- Complicated intra-abdominal infections

• **Examples:**

- Cefepime (Maxipime®)(IV)

Fifth-generation Cephalosporin

• **Uses:**

- Community acquired pneumonia (CAP)
- Skin & soft tissue infections

• **Example:**

- Ceftaroline (Teflaro®)(IV)

Monobactam

Uses:

- urinary tract infections,
- lower respiratory tract infections,
- septicemia
- intra-abdominal infections
- gynecological infections

Example:

Aztreonam (Azactam®)(IV)

Carbapenems

Coverage: broad spectrum

Uses:

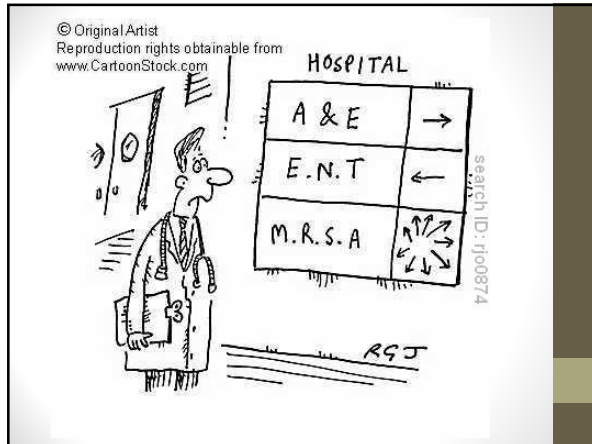
- Lower respiratory tract
- Urinary tract
- Intra-abdominal
- Gynecologic
- Bone and joint
- Skin and skin structure
- Polymicrobial infections as well as bacterial septicemia

Examples:

- Imipenem/cilastatin (Primaxin®)(IV)
- Meropenem (Merrem®)(IV)
- Doripenem (Doribax®)(IV)
- Ertapenem (Invanz®)(IV)

Beta-lactam Antibiotics

- Penicillins, Cephalosporins, Carbapenems, and Monobactams
- All beta-lactams can cause hypersensitivity reactions (rashes →anaphylaxis) and there is some cross-sensitivity
- Seizures can result from high doses so adjust for renal impairment in most agents (esp. imipenem, cefepime)



Glycopeptides

Coverage:
Gram-positive bacteria including MRSA

Uses:

- Pneumonia
- Skin and soft tissue infections
- Endocarditis
- Osteomyelitis
- Meningitis

• **Examples:**

- vancomycin (Vancocin®) (IV, PO)
- telavancin (Vibativ®) (IV)
- dalbavancin (Dalvance®) (IV) **NEW 2014**

Adverse reactions of glycopeptides:

- **vancomycin & telavancin**
 - Nephrotoxicity
 - (pharmacy monitors trough levels and doses)
 - Infusion-related reaction
 - "Red Man" syndrome
 - Skin rash and hypotension
 - Not an allergy; slow infusion down & give antihistamines
- **telavancin**
 - Taste disturbances
 - Foamy urine

Cyclic Lipopeptide

- **MOA:** binds irreversibly to the cell wall and weakens it allowing essential ions to leak out eventually causing cell death
- **Coverage:**
MRSA, VRE, and gram-positive infections
- **Uses:**
Skin and skin structure infections, endocarditis
***Do not use in the treatment of MRSA pneumonia (Inactivated by lung surfactant)
- **Examples:**
Daptomycin (Cubicin®)

Nitroimidazoles

- MOA:** Reactive intermediates that disrupt bacterial DNA
- Coverage:**
Anaerobes (*Bacteroides*)
Protozoa
- Uses:**
Clostridium difficile infection
Trichomoniasis, Amebiasis
Gynecologic infections
Intra-abdominal infections
- Example:**
Metronidazole (Flagyl®)

Metronidazole (Flagyl®)

- Disulfiram reaction with alcohol consumption
– do not take with alcohol including mouthwashes, cough syrups, etc
- Causes a metallic taste
- May discolor the urine (brown, black, dark)



Fluoroquinolones

MOA: Target DNA gyrases to prevent relaxation and supercoiling, blocking nucleic acid synthesis

Coverage: broad spectrum

Uses:

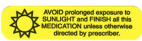
- Pneumonia
- UTI
- Skin infections

Examples:

- Ciprofloxacin (Cipro) (IV, PO)
- Levofloxacin (Levaquin) (IV, PO)
- Moxifloxacin (Avelox) (IV, PO)

Fluoroquinolones

- Interferes with cartilage development and maintenance
 - not recommended in pregnant or breastfeeding women and use with caution in children younger than 18 years old
- Avoid the sun and tanning beds due to photosensitivity
- Do not take with antacids or calcium products (i.e. vitamins. milk) 2 hours before abx or 6 hours after



Folate Antagonists

MOA: folic acid synthesis antagonist

Coverage: broad spectrum (resistance)

Uses:

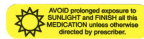
- UTI
- Skin infections
- Prophylaxis of *Pneumocystis jirovecii* pneumonia

Agent:

- Trimethoprim/Sulfamethoxazole (Bactrim, Sulfa) (IV, PO)

Sulfamethoxazole-Trimethoprim

- **Adverse reactions:** neutropenia, rash, **Steven-Johnsons syndrome**, hypersensitivity
- Drink plenty of water because drug can precipitate in the urinary tract (crystalluria)
- Avoid the sun and tanning beds due to photosensitivity



Macrolides

MOA: bind to the 50s subunit of bacterial ribosomes

Coverage: broad spectrum (resistance)

Uses:

- Upper and lower RTIs
- Traveler's diarrhea
- Gastrointestinal (GI) ulcer disease

Examples:

- Erythromycin (IV, PO)
- Azithromycin (Zithromax) (IV, PO)
- Clarithromycin (Biaxin) (PO)

Macrolides

- **Adverse reactions:**
 - GI intolerance (mostly with Erythromycin)



- metallic taste (Clarithromycin)
- QT prolongation in the heart



Lincosamides

MOA: binds to 50S ribosome preventing protein synthesis

Coverage: gram-positive bacteria and anaerobes

Uses:

- Skin & soft tissue infections (SSTIs)
- Acne
- Oral cavity infections

Examples:

- Clindamycin (Cleocin) (IV, PO)

Clindamycin

- Take with food if causes stomach pain
- May cause loose stools or diarrhea
- Superinfection of *Clostridium difficile* diarrhea or colitis
 - Could be life-threatening
 - SEVERE diarrhea and fever

Streptogramins

- **MOA:** binds to different 50S subunit of bacterial ribosome preventing protein synthesis
- **Coverage:** gram-positive organisms such as MRSA and VRE
- **Uses:**
 - MRSA & VRE infections that don't respond to other agents
- **Adverse reactions:** arthralgia, myalgias
- **Agent:**
 - Quinupristin-Dalfopristin [Synercid] (IV)

Oxazolidinones

- **MOA:** binds to the 50S subunit of the bacterial ribosome preventing translation
- **Coverage:** gram-positive infections
- **Uses:**
 - Skin and soft tissue infections (SSTIs)
 - Pneumonia
 - MRSA and VRE infections
- **Agents:**
 - Linezolid [Zyvox] (IV, PO)
 - Tedizolid [Sivextro] (IV, PO) **NEW 2014**

Aminoglycosides

- **MOA:** bind to the bacterial ribosome 30S subunit
- **Coverage:** gram-negative bacteria; synergistic gram positive activity
- **Uses:**
 - Ventilator associated pneumonia (VAP)
 - Febrile neutropenia
 - Sepsis
 - In combination with another agent for gram-positive infections
- **Adverse Effects:**
 - Nephrotoxicity (monitor drug levels with peaks and troughs)
 - Ototoxicity
- **Agents:**
 - Gentamicin (INJ)
 - Tobramycin (INJ)
 - Amikacin (INJ)

Does it matter if you are careful when preparing gentamicin, tobramycin or amikacin products? WHY?





<http://www.symbiantpd.com/userfiles/image/Safety%20Syringe-1.jpg>

Tetracyclines

- MOA: bind to the bacterial ribosome at the 30S subunit
- Coverage: gram(+), gram(-), atypical bacteria
- Uses:
 - RTIs
 - CAP
 - Tick-borne diseases
 - Acne
- Agents:
 - Minocycline (INJ, PO)
 - Doxycycline (INJ, PO)
 - Tetracycline (PO)

Tetracyclines

- **Adverse effects:**
 - photosensitivity (doxy) 
 - dizziness and vertigo (mino)
 - esophageal irritation
- Reduced absorption with iron, antacids, calcium, MVI w/ iron
- Pregnancy category D 
- Do NOT use in children less than 8 years (permanent teeth discoloration, retardation of skeletal development and reduced bone growth)

AVOID prolonged exposure to SUNLIGHT and TANNING BEDS while taking this MEDICATION unless otherwise directed by prescriber.

DO NOT TAKE WITH MILK, JUICE, OR ANTACIDS. TAKE WITH WATER.

Tetracycline-Stained Teeth



Accessed from http://www.toothmingle.com/wp-content/uploads/2009/06/tetracycline_teeth_300x78.jpg on 2/6/10

Is it safe to use antibiotics that are out of date?



<http://tummyhelp.com/wp-content/uploads/2014/03/Medicine.jpg>

Glycylcycline


- **MOA:** bind to the bacterial ribosome at the 30S subunit
- **Coverage:** gram(+), gram(-), atypical bacteria
- **Uses:**
 - Skin and soft tissue infections
 - RTIs
 - Complicated polymicrobial infections
- **Adverse reactions:** nausea, vomiting, diarrhea, photosensitivity, permanent teeth discoloration
- **Agent:**
 - Tigecycline (Tygacil) (INJ)

Miscellaneous Antibiotics

- Nitrofurantoin [Macrobid, Macrodantin] (PO)
- Rifampin [Rifadin] (INJ, PO)
- Fosfomycin [Monurol](PO)
- Colistin [colistimethate sodium](INJ)
- Chloramphenicol (INJ)

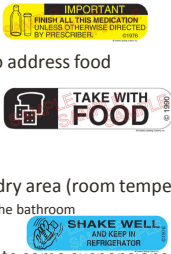
Antibiotics

- Auxiliary labels
 - Suspensions (azithromycin, cefdinir, etc.)
 - Usually can be stored up to 2 weeks
 - Cefdinir
 - Stool can appear red in color due to insoluble cefdinir-iron complex



Antibiotics

- Auxiliary Labels:
 - Finish all the antibiotics even if patient feels better
- Label to address food
 - TAKE WITH FOOD
- Storage
 - Store in dry area (room temperature)
 - Not in the bathroom
 - Refrigerate some suspensions but not all



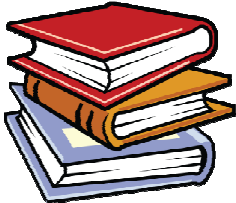
Name	Refrigeration status	Clinical Pearls
Amoxicillin	Not required but preferred for taste	Can be mixed with milk, formula, water, or other cold drinks
Amoxicillin/Clavulanate	Must refrigerate	May cause diaper rash
Azithromycin	Room temperature	May cause diaper rash
Cefaclor	Refrigerate	
Cefdinir	Room temperature	May cause red-colored stool
Cefpodoxime proxetil	Refrigerate	
Cefuroxime axetil	Refrigerate	Give with food
Cephalexin	Refrigerate	

Name	Refrigeration status	Clinical Pearls
Clarithromycin	DO NOT REFRIGERATE	Give with or without food; this medication can leave a bad taste in mouth so may want to take with food
Clindamycin	DO NOT REFRIGERATE	May cause rare form of severe diarrhea called pseudomembranous colitis
Penicillin VK	refrigerate	Give on an empty stomach

Antimicrobial Stewardship

- “involves selecting an appropriate drug and optimizing its dose and duration to cure an infection while minimizing toxicity and conditions for selection of resistant bacterial strains”
- J Med. 2006 Jun;119(6 Suppl 1):S53-61; discussion S62-70

What types of resources are available for infectious disease and antibiotic questions?



<http://www.bradleybookoutlet.com/wp-content/uploads/2013/06/bradleys-book-outlet-books-only-logo.png>

1. Which of the following agents can be very toxic to the kidney?

- A. Erythromycin, clarithromycin and azithromycin
- B. Oxacillin, nafcillin, amoxicillin and ampicillin
- C. Linezolid, tedizolid, and daptomycin
- D. **Gentamicin, tobramycin, and amikacin**

- Aminoglycosides are nephrotoxic and should be dosed according to peak and trough levels.

2. Which of the following agents is a carbapenem?

- A. Piperacillin/tazobactam
- B. Ertapenem
- C. Amikacin
- D. Linezolid
- E. Vancomycin

2. Which of the following agents is a carbapenem?

- A. Piperacillin/tazobactam
- B. **Ertapenem**
- C. Amikacin
- D. Linezolid
- E. Vancomycin

- The carbapenem antibiotics all end with the suffix "penem" and are injectable only.

3. Which of the following agents should not be given at the same as antacids or multivitamins?

- A. Levofloxacin and doxycycline
- B. Linezolid and vancomycin
- C. Amoxicillin and cephalixin
- D. Ertapenem and gentamicin

3. Which of the following agents should not be given at the same as antacids or multivitamins?

- A. **Levofloxacin and doxycycline**
 - B. Linezolid and vancomycin
 - C. Amoxicillin and cephalixin
 - D. Ertapenem and gentamicin
- Fluoroquinolone and tetracycline antibiotics bind with cations (calcium, magnesium, aluminum, iron, etc) and should not be given within 2 hours of each other

4. Which of the following classes of antibiotics are considered to be beta-lactam antibiotics and possess cross-allergenicity with each other?

- A. Glycopeptides, sulfonamides, lincosamides
- B. Aminoglycosides, macrolides, tetracyclines
- C. Penicillins, cephalosporins, carbapenems
- D. Streptogramins, fluoroquinolones, nitroimidazoles

4. Which of the following classes of antibiotics are considered to be beta-lactam antibiotics and possess cross-allergenicity with each other?

- A. Glycopeptides, sulfonamides, lincosamides
- B. Aminoglycosides, macrolides, tetracyclines
- C. Penicillins, cephalosporins, carbapenems
- D. Streptogramins, fluoroquinolones, nitroimidazoles

• Because these classes of drugs all share a beta-lactam ring, someone that is allergic to one could potentially be allergic to all of them.

5. Which of the following antibiotics should be taken with plenty of water to prevent crystalluria?

- A. Levofloxacin
- B. Clindamycin
- C. Azithromycin
- D. Trimethoprim/Sulfamethoxazole
- E. Doxycycline

5. Which of the following antibiotics should be taken with plenty of water to prevent crystalluria?

- A. Levofloxacin
- B. Clindamycin
- C. Azithromycin
- D. Trimethoprim/Sulfamethoxazole
- E. Doxycycline

• All patients should be reminded that TMP/SMX should be taken with plenty of water to prevent it from crystallizing in the urine.

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