Antibiotic Basics for the Pharmacy Technician

Arkansas Association of Health-System Pharmacists Fall Seminar
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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

- The body can also raise its temperature to help kill the organisms

- Common signs of infection:
  - fever
  - pain
  - heat
  - redness
  - swelling
Some organisms are not harmful and some are helpful such as bacteria that live in the gut.

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
Basic Types of Bacteria

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
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 “-azole”
    - Oxazolidinones – end in “zolid”
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)

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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)

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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

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

<table>
<thead>
<tr>
<th>Beta Lactam Antibiotics</th>
<th>PCN Allergy Cross Reactivity</th>
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<tbody>
<tr>
<td>Cephalosporin</td>
<td>Yes (less than 10%)</td>
</tr>
<tr>
<td>Carbapenem</td>
<td>Yes (up to 50%)</td>
</tr>
<tr>
<td>Monobactam</td>
<td>No, except ceftazidime</td>
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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%)

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®, Ceftin) (IV, PO)
  - Cefoxitin (Mefoxin®) (IV)
  - Cefotetan (Cefotan®) (IV)
  - Cefaclor (Ceclor®) (PO)

Third-generation Cephalosporins

Uses:
- Lower RTIs, intra-abdominal
- urinary tract uncomplcated 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
Fourth-generation Cephalosporin

**Coverage:** broad spectrum

**Uses:**
- Nosocomial infections
- UTIs
- Febrile neutropenia
- Pneumonia
- Complicated intra-abdominal infections

**Examples:**
- Cefepime (Maxipime®)(IV)

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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 dose
  - Infusion-related reaction
    - “Red Man” syndrome
  - Skin rash and hypertension
    - 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
- **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 gyrase 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 jiroveci 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?

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)

**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)

**Tetracycline-Stained Teeth**

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

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

• 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/Clavulanic Acid | 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 |
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”

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

Questions for Discussion

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
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   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

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

- Lexicomp online edition, accessed 8/2014