Antibiotic Review

Objectives

- Identify the general characteristics of antibiotics.
- Discuss the mechanism of action, pharmacokinetics, and spectrum of activity for the most common antibiotic drug classes.
- Identify commonly prescribed antibiotics within the drug classes including dosage range and indication for prescribing.
- Identify special considerations for specific antibiotics and/or drug classes.
- Practice appropriate prescribing for common bacterial infections.
- Review basic antibiotic stewardship principles.

Antibiotic Lingo

- Susceptibility \( \rightarrow \) determine which antibiotics a bacteria is sensitive to
- MIC \( \rightarrow \) lowest concentration of drug that inhibits growth of the bacteria
- Trough \( \rightarrow \) lowest concentration of drug in bloodstream
  - Collect prior to administration of drug
- Peak \( \rightarrow \) highest concentration of drug in bloodstream

General Characteristics

- Bactericidal or bacteriostatic
- Narrow or broad spectrum
- Can elicit allergic responses
- Affect normal body flora

Antibiotic Drug Classes

- Penicillins
- Cephalosporins
- Carbapenems
- Monobactam
- Macrolides
- Fluoroquinolones
- Sulfonamides
- Tetracyclines
Penicillins

- Penicillins
  - Natural penicillins
  - Aminopenicillins
  - Anti-staphylococcal penicillins
  - Anti-pseudomonal penicillins

Penicillins

- Mechanism of action ➔ bactericidal ➔ interrupts cell wall synthesis

Natural Penicillins

**Penicillin G**

**Penicillin V**

- Pharmacokinetics
  - Penicillin G ➔ mostly IM, but one variation can be given IV
    - Poorly absorbed via PO
  - Penicillin V ➔ given PO
  - Increased gastric acid stability

Natural Penicillins

**Penicillin G**

**Penicillin V**

- Spectrum of Activity
  - Gram positive organisms
    - *Streptococcus* species (e.g. *S. pyogenes*)
    - Some enterococcus species (e.g. *E. faecalis*)
    - *Staphylococcus* ➔ only minority; most are resistant
    - *Listeria monocytogenes*
  - Gram negative organisms ➔ limited
  - Anaerobes
    - *Bacteroides*
    - *Fusobacterium species*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G benzathine</td>
<td>1.2 – 2.4 MU</td>
<td>IM</td>
<td>Most commonly used to treat Group A strep (e.g. pharyngitis), and syphilis</td>
</tr>
<tr>
<td>Penicillin G procaine</td>
<td>2.4 MU x 1 dose</td>
<td>IM</td>
<td></td>
</tr>
<tr>
<td>Penicillin G (parenteral)</td>
<td>12 – 24 MU/daily</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Penicillin V</td>
<td>125-500 mg every 6-8h</td>
<td>PO</td>
<td></td>
</tr>
</tbody>
</table>

Natural Penicillins

**Penicillin G**

**Penicillin V**

- Special Considerations
  - Do not administer next to nerve or artery
  - Probenecid decreases renal clearance of penicillins.
    - Co-administration can be used to increase concentration levels
  - Decrease parental dosage when CrCl is less than 50 ml/min
  - Allergy
Beta-lactamase Inhibitors
Clavulanic acid (clavulanate)
Sulbactam
Tazobactam

Aminopenicillins
Amoxicillin
Amoxicillin/Clavulanate
Ampicillin
Ampicillin/Sulbactam

- Spectrum of Activity
  - Same activity as natural penicillins
  - Susceptible gram-positive organisms
  - Improved gram-negative coverage
    - Enterobacteriaceae
    - H. pylori used as part of multi-drug treatment
    - H. influenzae

- Pharmacokinetics
  - Amoxicillin +/- clavulanate given PO
  - Stable in gastric acid
  - Best absorbed penicillin
  - Ampicillin +/- sulbactam
  - Ampicillin can be given PO, IM, or IV
  - With the addition of the sulbactam can only be given IM or IV

Amoxicillin (Amoxil)
250-500 mg every 8h
500-875 mg BID
PO
Sinusitis, meningitis, susceptible UTIs, abscesses

Amoxicillin/Clavulanate (Augmentin)
250-500 mg every 8h
875 mg every 12h
PO
Soft skin infections related to group A strep, Otitis media, pneumonia

Ampicillin
250-500 mg every 6h
PO, IM, IV

Ampicillin/Sulbactam (Unasyn)
1.5-3 g every 6h
IM, IV

Anti-staphylococcal Penicillins
Dicloxacillin
*Methicillin
Nafcillin
Oxacillin

- Pharmacokinetics
  - Dicloxacillin given PO
  - Delayed absorption when given with meals
  - Nafcillin given IM or IV
  - Poor oral absorption
  - Primarily metabolized through the liver
  - Oxacillin given IM or IV
  - Poor oral absorption
  - Primarily metabolized through the liver

- Special Considerations
  - Of note, dosing of drugs with beta-lactamase inhibitors is based on the amoxicillin or ampicillin NOT the inhibitor.
  - Decrease parental dosage when CrCl is less than 50 ml/min
  - MSSA coverage with Amoxicillin/Clavulanate but none with Amoxicillin only
  - No pseudomonas coverage.
**Anti-staphylococcal Penicillins**

**Dicloxacillin**

**Nafcillin**

**Oxacillin**

- **Spectrum of Activity**
  - Drug class also known as the Penicillinase-Resistant Penicillins
  - Gram-positive organisms
    - Staphylococcal species
      - MSSA*
    - Streptococcal species

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<tbody>
<tr>
<td>Dicloxacillin</td>
<td>125-500 mg every 6h</td>
<td>PO</td>
<td>Drug of choice for MSSA infections → cellulitis, osteomyelitis, and bacteremia</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>0.5-2 g every 4-6h</td>
<td>IV, IM</td>
<td></td>
</tr>
<tr>
<td>Oxacillin</td>
<td>0.25-2 g every 4-6h</td>
<td>IM, IV</td>
<td></td>
</tr>
</tbody>
</table>

**Anti-staphylococcal Penicillins**

**Dicloxacillin**

**Nafcillin**

**Oxacillin**

- **Special Considerations**
  - No MRSA coverage
  - Nafcillin tends to be better tolerated
  - Oxacillin → drug-induced hepatitis
    - Usually reversible with discontinuation of the drug
  - Dose adjustments for Nafcillin and Oxacillin for patients with severe hepatic and renal dysfunction

**Anti-pseudomonal Penicillins**

**Piperacillin**

**Piperacillin/tazobactam**

**Ticarcillin**

**Ticarcillin/clavulanate potassium**

- **Spectrum of activity**
  - Typically referred to the extended-spectrum penicillins
  - Gram-positive activity
    - Staph. and Strept.
    - **NO** MRSA coverage.
  - Gram-negative activity
    - Including Pseudomonas aeruginosa
    - Also has coverage against Enterobacteriaceae.
    - Anaerobic coverage

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</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin (Pipracil)</td>
<td>3-4.9 g every 4-6h</td>
<td>IV, IM</td>
<td>intra-abdominal infections, pneumonia, severe skin and tissue infections, sepsis, etc.</td>
</tr>
<tr>
<td>Piperacillin/tazobactam (Zosyn)</td>
<td>2.25-3.75 g every 6-8h</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Ticarcillin +/-(clavulanate potassium (Timentin))</td>
<td>0.25-2 g every 4-6h</td>
<td>IV</td>
<td></td>
</tr>
</tbody>
</table>
### Anti-pseudomonal Penicillins

- **Piperacillin**
- **Piperacillin/tazobactam**
- **Ticarcillin**
- **Ticarcillin/clavulanate potassium**

**Special Considerations**
- Dosage considerations for patients with renal dysfunction
  - Elimination half-life can increase 2- to 6-fold in severe dysfunction
- Use caution with Ticarcillin in patients with HF due to the high sodium load
- High levels of Ticarcillin can increase seizure risk in patients with seizure disorders

### Cephalosporins

- **1st Generation**
  - Cefadroxil
  - Cefazolin
  - Cephalexin
  - Cephradine

**Mechanism of action**
- Bactericidal
- Interrupts cell wall synthesis

**Spectrum of Activity**
- Primarily active against gram-positive cocci.
  - Staphylococcus
  - Streptococcus
  - **NO MRSA coverage.**
- Minor gram-negative activity
  - *E. coli*
  - *H. influenzae*
  - *Klebsiella*

**Pharmacokinetics**
- Cefadroxil, Cephalexin, & Cephradine → PO
  - Rapidly absorbed from the GI tract
  - Wide distribution but do **NOT** cross the blood-brain-barrier
- Cefazolin → IM, IV
  - Widely distributed as well but poor CSF penetration

**Drug Dosage Route Indication**

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Route</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefadroxil (Duricef)</td>
<td>1-2 g/daily in two divided doses</td>
<td>PO</td>
<td>Skin and soft tissue infections, respiratory infections, some UTIs, and otitis media</td>
</tr>
<tr>
<td>Cefazolin (Ancef)</td>
<td>1-2 g every 8h</td>
<td>IM, IV</td>
<td></td>
</tr>
<tr>
<td>Cephalexin (Keflex)</td>
<td>500-1000mg every 6-12h</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Cephradine (Velosef)</td>
<td>50-100mg every 6-12h</td>
<td>PO</td>
<td></td>
</tr>
</tbody>
</table>
Penicillins: 1st Generation Cephalosporins
Cefadroxil  Cefazolin  Cephalexin  Cephradine

- Special Considerations
  - If cross-sensitivity reaction is to occur with a penicillin, it is most likely to occur with 1st generation cephalosporins.
  - Cefadroxil
  - Cefazolin can cross the blood-brain-barrier in severe renal dysfunction/failure
  - Encephalopathy
  - Seizures

Penicillins: 2nd Generation Cephalosporins
Cefaclor  Cefotetan  Cefazolin  Cefprozil  Cefuroxime

- Spectrum of Activity
  - Gram-positive coverage
    - Staphylococcus
    - Streptococcus
  - Extended gram-negative coverage
    - Same as 1st generation but ADD coverage against Neisseria, Proteus
  - Anaerobic coverage
    - Cefoxitin
    - Cefotetan

- Pharmacokinetics
  - Cefaclor & Cefprozil → PO
  - Rapidly absorbed from the GI tract
  - Cefaclor slowed absorption with food.
  - Cefprozil is not affected by food.
  - Cefotetan & Cefoxitin → IM, IV
  - Cefuroxime → PO, IM, IV
  - Rapidly absorbed from the GI tract
  - Increased absorption when taken with food (PO form)

Penicillins: 2nd Generation Cephalosporins
Cefaclor  Cefotetan  Cefazolin  Cefprozil  Cefuroxime

- Special Considerations
  - Cefotetan → possible disulfiram-like reaction with alcohol
  - Generally safe in pregnancy

Penicillins: 3rd Generation Cephalosporins
Cefdinir  Cefditoren  Cefixime
Cefotaxime  Ceftodoxime  Ceftazidime
Ceftobuten  Ceftriaxone

- Pharmacokinetics
  - Cefdinir, Cefditoren, Cefixime, Ceftodoxime, & Ceftobuten → PO
  - Rapidly absorbed from the GI tract
  - Ceftodoxime increased absorption when taken with food
  - Cefixime & Ceftobuten are not affected by food.
  - Cefotaxime, Ceftazidime, & Ceftriaxone → IM, IV
3rd Generation Cephalosporins
Cefdinir
Cefditoren
Cefixime
Cefotaxime
Cefpodoxime
Ceftazidime
Ceftibuten
Ceftriaxone

- Spectrum of Activity
  - Broader activity against gram-negative organisms
    - Some have broader gram-negative coverage compared to others.
  - Some gram-positive coverage BUT minimal
    - Streptococcus pneumoniae
    - Staphylococcus aureus
  - Minimal anaerobic coverage

• Special Considerations
  - Ceftriaxone → calcium salt precipitate in the gallbladder that can be mistaken for gallstones
  - Cholelithiasis
  - Caution when giving Cefotaxime → arrhythmias noted with IV
  - Avoid Cefditoren in patients with a milk protein allergy.

3rd Generation Cephalosporins
Cefdinir
Cefditoren
Cefixime
Cefotaxime
Cefpodoxime
Ceftazidime
Ceftibuten
Ceftriaxone

• Spectrum of Activity
  - Broader activity against gram-negative organisms
    - There are some exceptions.
  - Some have broader gram-negative coverage compared to others.
  - Some gram-positive coverage BUT minimal
    - Streptococcus pneumoniae
    - Staphylococcus aureus
  - Minimal anaerobic coverage

4th Generation Cephalosporin
Cefepime

- Spectrum of Activity
  - Good gram-positive activity
    - Staphylococcus
    - Streptococcus
  - Good gram-negative activity
    - Enterobacteriaceae
      - Escherichia
      - Klebsiella
      - Pseudomonas
      - Enterobacter
      - Proteus

4th Generation Cephalosporin
Cefepime

- Pharmacokinetics
  - Cefepime → IM, IV
    - Good penetration into fluids/tissues
    - Penetrates CSF
    - Excreted in the urine

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Route</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefdinir</td>
<td>300mg every 12h</td>
<td>PO</td>
<td>Respiratory tract infecions, skin &amp; soft tissue infections, UTIs, sepsis*, intra-abdominal infections*, CNS infections*</td>
</tr>
<tr>
<td>Cefditoren</td>
<td>200-400mg every 12h</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Cefixime</td>
<td>400mg daily</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>1-2g every 4-12h</td>
<td>IM, IV</td>
<td></td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>100-400mg every 12h</td>
<td>IM, IV</td>
<td></td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>500mg to 1g every 8h</td>
<td>IM, IV</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone (Rocephin)</td>
<td>1-2g every 12-24h</td>
<td>IM, IV</td>
<td></td>
</tr>
</tbody>
</table>
**4th Generation Cephalosporin**

Cefepime

- Special Considerations
  - Dosage needs to be adjusted for renal dysfunction
  - Neurotoxicity → seizures, encephalopathy
  - Be aware → it can cause patients to have a positive Coombs Test
  - Can cause glycosuria

**5th Generation Cephalosporin**

Ceftaroline

- Spectrum of Activity
  - Gram-positive activity
    - Staphylococcus aureus
    - Streptococcus pneumoniae
  - Gram-negative activity
    - Relatively similar coverage to other cephalosporins.
    - **NO** Pseudomonas coverage.

**5th Generation Cephalosporin**

Ceftaroline

- Special Considerations
  - Dosage adjustments in moderate to severe renal dysfunction
  - Dosage adjustments in the elderly

**Carbapenems**

- Doripenem
- Ertapenem
- Imipenem/cilastatin
- Meropenem
- Meropenem/vaborbactam

**Pharmacokinetics**

- Ceftaroline → IV only
  - Good penetration into fluids/tissues
  - Penetrates CSF
  - Excreted in the urine

**Drug Dosage Route Indication**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftaroline</td>
<td>600mg every 12h</td>
<td>IV</td>
<td>Pneumonia (CAP), skin &amp; soft tissue infection</td>
</tr>
</tbody>
</table>
Carbapenems
- Mechanism of action → bactericidal → interrupts cell wall synthesis

**Pharmacokinetics**
- All Carbapenems are → IV
- Imipenem/cilastatin inhibits dehydropeptidase I
- Doripenem, Ertapenem, and Meropenem do not require a dehydropeptidase inhibitor
- Meropenem → well distributed in body tissues/fluids including CSF
- Imipenem/cilastatin and Ertapenem → distributed in body tissues/fluids BUT low CSF concentrations

**Spectrum of Activity**
- Broad spectrum activity against gram-positive and gram-negative bacteria.
- Pseudomonas aeruginosa coverage EXCEPT Ertapenem
- ESBL (extended spectrum beta-lactamases) coverage

**Special Considerations**
- The dose must be adjusted in patients with renal disease
- Doripenem → CrCl less than 30 ml/min
- Meropenem → CrCl less than 50 ml/min
- Imipenem/cilastatin → less than 90 ml/min
- Increased seizure risk in patient with CNS/seizure disorders.

Carbapenems
- Doripenem
- Ertapenem
- Imipenem/cilastatin
- Meropenem
- Meropenem/vaborbactam

Drug | Dosage | Route | Indication
--- | --- | --- | ---
Doripenem | 500mg every 8h | IV | Skin & soft tissue infections*, intra-abdominal infections*, respiratory infections*, UTI*, sepsis*
Ertapenem | 1g daily | IM, IV | Skin & soft tissue infections*, intra-abdominal infections*, respiratory infections*, sepsis*, UTI*
Imipenem/cilastatin | 500-1000mg every 6-8h | IV | Skin & soft tissue infections*, intra-abdominal infections*, respiratory infections*, sepsis*, UTI*, sepsis*
Meropenem | 1.5 to 6g daily in 3 divided doses | IV | Skin & soft tissue infections*, intra-abdominal infections*, respiratory infections*, sepsis*, UTI*, sepsis*
Meropenem/vaborbactam | 4g every 8h | IV | Skin & soft tissue infections*, intra-abdominal infections*, respiratory infections*, sepsis*, UTI*, sepsis*

Monobactam
- Aztreonam
**Monobactam**

- **Mechanism of action**: bactericidal → interrupts cell wall synthesis

**Aztreonam**

- **Pharmacokinetics**
  - Aztreonam → IM, IV
  - IV is the preferred mode for administering
  - Inhalation version → not readily used
  - Distributed throughout tissues and fluids
  - Including CSF
  - Excreted renally

**Spectrum of Activity**

- Gram-negative organisms
  - Enterobacteriaceae (e.g. Citrobacter, Enterobacter, Proteus, Serratia, etc.)
  - Pseudomonas aeruginosa
  - Haemophilus influenzae

**Drug Dosage**

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Route</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aztreonam</td>
<td>1-2 g every 8-12h</td>
<td>IM, IV</td>
<td>UTI, respiratory tract infections, sepsis, skin &amp; soft tissue infections, intra-abdominal infections, gynecological infections</td>
</tr>
</tbody>
</table>

**Special Considerations**

- Recommend pretreating patient with bronchodilator prior to inhalation administration
- Not uncommon to use double coverage with Pseudomonas infections
- Studies has indicated tolerance in patients with penicillin and cephalosporin allergy
  - ?Cefazidime cross-allergy reaction

**Macrolides**

- Erythromycin
- Clarithromycin
- Azithromycin
- Fidaxomicin
Macrolides

- Mechanism of action: bacteriostatic* → inhibits protein synthesis

**Mechanism of action**

- Azithromycin
- Clarithromycin
- Erythromycin
- Fidaxomicin*

**Spectrum of Activity**

- Atypical bacteria
  - Chlamydia
  - Legionella
  - Mycoplasma
  - Mycobacterium
  - Neisseria
- Gram-positive bacteria
- Gram-negative bacteria
  - Neumophilus
  - Moraxella

**Pharmacokinetics**

- All the preparations can be given PO.
- Azithromycin & Clarithromycin → excellent oral absorption
- Erythromycin → variations in PO preparation dictate absorption
- Fidaxomicin → minimal systemic absorption → primarily confined to the GI tract → undetectable serum concentrations
- Good tissue distribution
- Minimum blood-brain-barrier penetration

**Drug Dosage**

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</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>PO: 250-600mg daily</td>
<td>IV: 250-500mg daily</td>
<td>COPD, CAP, MAC, skin &amp; soft tissue infections, streptococcal pharyngitis, N. gonorrhea</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>250-500mg every 12h</td>
<td>PO</td>
<td>H. pylori, CAP, MAC, skin &amp; soft tissue infections</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Varies drastically depending on the base.</td>
<td>IV, PO, ophthalmic drops, topical</td>
<td>All bacterial infections, colorectal surgical prophylaxis</td>
</tr>
<tr>
<td>Fidaxomicin</td>
<td>200mg twice daily</td>
<td>PO</td>
<td>Clostridium difficile infections</td>
</tr>
</tbody>
</table>

**Special Considerations**

- Monitor for QT prolongation
- Liver disease
  - Avoid erythromycin estolate is contraindicated 2/1 to hepatic dysfunction with or without jaundice
- Reversible deafness has occurred with Clarithromycin
- Significant drug interactions can occur with Erythromycin and Clarithromycin
  - Inhibitors of CYP3A4

**Fluroquinolones**

- Besofloxacin
- Cinocoxacin
- Ciprofloxacin*
- Delafloxacin
- Gatifloflaxin → IV form removed from market
- Gemifloxacin → no longer available in US
- Levofloxacin*
- Moxifloxacin*
- Norfloxacin → no longer available in US
- Ofloxacin*
Fluroquinolones

- **Mechanism of action**: Bactericidal, inhibits DNA synthesis

### Pharmacokinetics
- All fluroquinolones (listed here)
  - PO and ophthalmic drops
  - All PO well absorbed
  - Widely distributed throughout tissues
  - CSF
  - Excretion varies
  - Ciprofloxacin → Urine, bile, feces
  - Levofloxacin → Primarily urine
  - Moxifloxacin → Urine, feces
  - Ofloxacin → Primarily urine

**Spectrum of Activity**
- Gram positive organisms
  - Staphylococcus
- Gram negative organisms
  - Enterobacteriaceae
  - Haemophilus
  - Pseudomonas
- Atypical organisms
  - Legionella
  - Chlamydia
  - Mycoplasma
  - Mycobacterium

**Drug** | **Dosage** | **Route** | **Indication**
--- | --- | --- | ---
Ciprofloxacin | PO: 250-750mg every 12h IV: 200-400mg every 12h | PO, IV, topical, ophthalmic | UTIs*, respiratory infections, skin & soft tissue infections, intra-abdominal infections*
Levofloxacin | 250-750mg daily | PO, IV, ophthalmic, inhalation | 
Moxifloxacin | 400mg daily | PO, IV, ophthalmic | 
Ofloxacin | 200-400mg every 12h | PO, ophthalmic | 

**Special Considerations**
- Fluroquinolones are recommended for more severe infections +/- side effect profile.
- Concurrent use with NSAIDs may increase the risk of seizures.
- Can prolong QT interval
  - Ciprofloxacin, Levofloxacin, and Moxifloxacin
- Antacids decrease absorption

Sulfonamides

- **Sulfamethoxazole/trimethoprim**
**Sulfonamides**

- Mechanism of action → bacteriostatic → inhibits steps in folate synthesis

**Sulfonamides**

- Spectrum of Activity
  - Gram positive coverage
    - Staphylococcus
    - Streptococcus → some
  - Gram negative coverage
    - Enterobacteriaceae
    - Klebsiella
  - Other organisms
    - Pneumocystis → yeast-like fungus
    - Streptococcus pneumoniae → gram negative
    - Toxoplasma → parasite
    - Anacardia → gram positive

**Sulfonamides**

- Pharmacokinetics
  - Good PO absorption
  - Rapid
  - Good penetration of tissues and fluids including the CSF
  - Excreted renally

**Drug Dosage**

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</thead>
<tbody>
<tr>
<td>Sulfamethoxazole/trimethoprim</td>
<td>PO: 800/160 mg every 12-24 hours IV: 8-20 mg/kg/day</td>
<td>PO, IV</td>
<td>UTI, COPD exacerbation, PJP prophylaxis and treatment, traveler’s diarrhea, and shigellosis</td>
</tr>
</tbody>
</table>

**Sulfonamides**

- Special Considerations
  - The IV dosing is based on the trimethoprim component
  - Weight based dosing based on the trimethoprim component
  - Maximum 960 mg/day
  - Require renal-based dosing in setting of poor renal function
  - Total body clearance of trimethoprim is decreased in the elderly
  - Side effects

**Tetracyclines**

- Demeclocycline*
- Doxycycline
- Minocycline
- Tetracycline*
**Tetracyclines**

- **Mechanism of action** → bacteriostatic → inhibits protein synthesis

**Pharmacokinetics**
- Both can be given PO or IV.
- Good PO absorption
- Can be given with or without food
- Widely distributed throughout body and tissues
- Small percentage excreted in the urine as well as feces/biliary

**Spectrum of Activity**
- Gram positive organisms
  - Staphylococcus
  - Streptococcus
- Gram negative organisms
  - E. coli
  - Enterobacter
  - Klebsiella
  - Acinetobacter
  - Haemophillus
- Atypical organisms
  - Mycoplasma
  - Chlamydia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>PO: 100-200mg/daily</td>
<td>PO, IV</td>
<td>Respiratory tract infections, skin &amp; soft tissue infections, cholera, STIs, rickettsial infections, cholera, meningitis, malaria prevention</td>
</tr>
<tr>
<td></td>
<td>IV: 100mg every 12h</td>
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<tr>
<td>Minocycline</td>
<td>Initial for PO/IV → 200mg</td>
<td>PO, IV</td>
<td></td>
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<tr>
<td></td>
<td>Maintenance PO: 100mg every 12h</td>
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<tr>
<td></td>
<td>OR 50mg 4x daily</td>
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<tr>
<td></td>
<td>Maintenance IV: 100mg every 12h</td>
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</tbody>
</table>

**Special Considerations**
- Minocycline → lupus-like reaction
- Tetracyclines can increase liver enzymes.
  - Hepatitis and liver failure have been reported with Minocycline
  - Avoid in patients with hepatic insufficiency
- Okay to use doxycycline in renal failure because only small percentage excreted renally

**Other Antibiotics...**
Clindamycin

- Mechanism of action → bacteriostatic → inhibits protein synthesis
- Can be given IM, IV, or PO
  - Good and rapid PO absorption
  - Poor CSF penetration
- Active against gram positive organisms and anaerobes
- Indications → bacteremia, skin & soft tissue infections, intra-abdominal infections, respiratory tract infections, & gynecological infections
- Side effects: site reaction, GI symptoms

Metronidazole

- Mechanism of action → bactericidal → inhibits DNA synthesis & degradation
- Can be given PO or IV
  - Well absorbed PO
  - Good CNS penetration
- Active against anaerobes and protozoal parasites
- Side effects: headache, dizziness, nausea, vaginitis

Nitrofurantoin

- Mechanism of action → bactericidal → inhibits DNA, RNA, and cell wall protein synthesis
- Given PO
  - Well absorbed
- Antibiotic coverage varies slightly based on medication.
  - Macrodantin: E. Coli, Staphylococcus
  - Staphylococcus, Enterococcus, E. Coli, Klebsiella, Enterobacter
- Indications → acute uncomplicated cystitis
- Side effects: GI symptoms, headache

Vancomycin

- Mechanism of action → bactericidal → inhibits cell wall synthesis
- Can be given PO or IV
  - PO poorly absorbed
  - Widely disturbed when given IV
  - Excreted renally
- Active against gram positive organisms only
- Side effects:
  - PO: nausea, abdominal pain, & hypokalemia

Drugs to look out for...

- Lefamulin (Xeniastra)
  - FDA Approved August 2019
  - Completely new mechanism of action in last 20 years.
  - Inhibits the synthesis of a bacterial protein needed for the bacteria to grow
  - Can be given PO and IV
  - Treatment for CAP

- Imipenem/Cilastatin/Relebactam (Recarbio)
  - FDA Approved July 2019
  - Can be given IV
  - Treatment for UTI and intra-abdominal infections

Antibiotic Stewardship
**Antibiotic Resistance**
- Prescribing antibiotics when they are not needed
- Failure to narrow antibiotics
- Expanding duration of antibiotics longer than needed
- Using the wrong antibiotic and/or wrong dose

**Consequences of Antibiotics**
- Excess healthcare costs
- Preventable adverse drug events
  - Cause approximately 142,000 adult ED visits annually
- Contributes to antibiotic resistance
  - 2 million or more people acquire antibiotic resistant infections annually
  - At least 23,000 die from antibiotic-resistant infections

**Antibiotics with Resistant Bacteria**
- Penicillins
- Cephalosporins
- Carbapenems
- Monobactam
- Macrolides
- Fluoroquinolones
- Sulfonamides
- Tetracyclines
- Aminoglycosides
- Polymyxins

**Antibiotic Resistant Infections**
- *Clostridioides* (*Clostridum*) difficile
- *Streptococcus pneumoniae*
- MRSA
- *Enterobacteriaceae*
- *Pseudomonas aeruginosa*
- *Neisseria gonorrhoeae*
- Group A and B Streptococcus

**Antibiotic Stewardship Principles**
- If there are guidelines for treatment, **FOLLOW** them.
- Narrow the spectrum of the antibiotic
- Shorten the duration
- STOP treating asymptomatic bacteriuria and viral upper respiratory infections such as acute bronchitis
- Prescribe supportive care
- Hospital-based
  - De-escalate
  - Shorter durations
  - Antibiograms
  - Consult ID when appropriate

**Prescribing Case Studies**
Case Study #1

Mrs. Smith is a 70-year-old woman with past medical history of diabetes mellitus type II, stroke, chronic kidney disease stage 2, hypertension, and dementia with moderate functional impairment who resides a nursing facility. The family reports her mental status appears different and they are concerned that she may have an infection. Her baseline mental status is conversive but pleasantly confused.

The provider evaluates the patient and to appease the family runs diagnostics to rule out an infectious process as an indication for the mild change in her mental status.

Mrs. Smith has no physical complaints.

Vital signs are stable. There are no changes from her baseline.

The physical exam is unremarkable.

Diagnostics return:
- CBC à unremarkable
- CMP à unremarkable
- UA à evidence of bacteria à greater than 10^5

The patient has evidence of bacteriuria plus mild changes in her mental status.

She has no known drug allergies.

What is the next course of action for Mrs. Smith?
- Would you prescribe an antibiotic based on the findings?
  - If so, what antibiotic would you prescribe?
    a) Ciprofloxacin
    b) Macrobid
    c) Bactrim
    d) Augmentin
  - If you chose not to prescribe an antibiotic, why?

Case Study #2

Mr. Young is a 48-year-old man with past medical history of poorly controlled diabetes mellitus type II recently treated for a right lower extremity cellulitis with Clindamycin.

Now he presents with complaints of fever, abdominal tenderness, and diarrhea x 3-4 days.

He reports completing Clindamycin five days ago.

The NP has a high suspicion of C. difficile.

Culture results are positive.

He has no known drug allergies.

What antibiotic therapy would be most appropriate to prescribe?

Case Study #3

Ms. Jones is a 52-year-old woman with no significant past medical history who presents with complaints of fever, productive cough, mild chest discomfort and shortness of breath.

Vital signs of unremarkable with exception of a fever with temperature 100.1F.

On physical exam she has rales to the left lower lobe and dullness to percussion.

She has no recent history of antibiotic use.

She reports an allergy to Levofloxacin (Levaquin).

The NP diagnoses her with a community acquired pneumonia.

Common bacteria implicated are: Streptococcus pneumonia, Haemophilus influenzae, and Moraxella catarrhalis.

Based on what is known about Ms. Jones, what is the most appropriate antibiotic to prescribe?
- Augmentin 2g twice daily
- Doxycycline 100mg twice daily
- Azithromycin 500 mg x 1 dose, followed by 250 mg x 4 days
- Moxifloxacin 400 mg PO
Case Study #4

- Ms. Williams is a 62-year-old woman with past medical history of COPD who presents to the ED with fever, worsening productive cough, mild chest discomfort and moderate shortness of breath.
- Vital signs: 101.8°F – 102°F, 118/68 – 26 – 90% on RA
- On physical exam she has rales to the left lower lobe and dullness to percussion.
- She has no recent history of antibiotic use.
- She reports no known drug allergies.
- She is admitted to the hospital for community acquired pneumonia.
- What antibiotic therapy is most appropriate?

Case Study #5

- Mrs. Banks is a 68-year-old woman with past medical history of HFpEF, diabetes mellitus type II, hypertension, paroxysmal atrial fibrillation, and hyperlipidemia. She presents with complaints of urinary urgency, dysuria, and foul-smelling urine x 2 days.
- UA is consistent with a UTI.
- Home medications include: Glyburide, Lisinopril, Amlodipine, Warfarin, and Atorvastatin.
- Which antibiotic therapy is most appropriate?
  a) Sulfamethoxazole/trimethoprim (Bactrim)
  b) Nitrofurantoin (Macrobid)
  c) Levofloxacin (Levaquin)
  d) Cefaclor

Case Study #6

- Mr. Post is a 37-year-old man with no significant medical history who presents with nasal drainage, congestion, facial pain/pressure, cough, and scratchy throat x 3-4 days.
- He has no known drug allergies.
- His vital signs are unremarkable.
- The NP diagnoses an upper respiratory infection and sinusitis.
- What is the most appropriate antibiotic to prescribe for his sinusitis?

Case Study #6

- Mr. Post returns approximately 1-1.5 weeks later with resolution of the cough and scratchy throat, but now reports purulent nasal drainage, congestion, and facial pain/pressure that has failed to improve.
- He has no known drug allergies.
- His vital signs are unremarkable.
- The NP diagnoses a sinusitis.
- Common bacteria implicated are: Staphylococcus, Streptococcus, or Haemophilus influenzae.
- What is the most appropriate antibiotic to prescribe for his sinusitis?
  a) Amoxicillin
  b) Ceftriaxone
  c) Ampicillin/Sulbactam
  d) Azithromycin

Case Study #7

- Mrs. Reno is a 75-year-old woman with extensive past medical history/multiple co-morbid conditions admitted to the hospital for symptomatic atrial fibrillation with a syncopal episode prior to presentation. She has no recent hospitalizations.
- On Day 4, the plan was to discharge her; however, on evaluation, the patient has a low-grade fever, shortness of breath, and is requiring 2L oxygen to maintain sats >92%.
- On CBC presence of leukocytosis.
- CXR reveals a right lower lobe infiltrate.
- The NP diagnoses her with a hospital acquired pneumonia (HAP).
- In HAP, you want to ensure you cover for gram-negative organisms. Gram positive coverage (especially if concerned for resistance) is necessary if high gram-positive isolates or recent antibiotic therapy within 90 days.
- What is the most appropriate antibiotic therapy for Mrs. Reno?
  a) Ceftriaxone plus azithromycin
  b) Doxycycline
  c) Levofloxacin
  d) Cefepime
Case Study #8

- Mr. Andrews is a 50-year-old man with uncontrolled diabetes mellitus type II, hypertension, and chronic kidney disease, stage II who presents with redness, tenderness, edema, and erythema to his right lower extremity.
- He has no known drug allergies.
- The NP provide diagnoses him with a mild, non-purulent cellulitis.
- Common bacteria implicated are: Staphylococcus and Streptococcus.
- What is the most appropriate antibiotic therapy to prescribe?

Case Study #9

- Mr. Wright is a 61-year-old man with a past medical history of COPD, Gold Stage III on chronic home O2 2L nasal cannula. He presents with worsening dyspnea and increased sputum purulence.
- Over the last 2–3 days, he’s had to increase his O2 requirements to 4L nasal cannula.
- He is allergic to penicillins and Azithromycin → severe, diffuse rash.
- The NP diagnoses him with a COPD exacerbation.
- He’s started on supportive therapy including oral steroids. He is to return for follow-up in 3–4 days after starting treatment.
- What antibiotic is most appropriate to start?

Case Study #10

- Ms. Jewels is a 31-year-old woman with past medical history of asthma who presented to the ED with complaints of fever, chills, severe epigastric pain, and nausea/vomiting x 3–4 hours.
- On exam, the patient appears uncomfortable. There is tenderness to palpation → mostly noted to the epigastric region.
- Vital signs: 101°F – 118 – 14/90 – 26 – 96% on RA
- Labs reveal:
  - Leukocytosis with shift
  - Mild elevation of AST and ALT
  - Lipase negative
  - Pregnancy test negative
- The NP orders an ultrasound. The results indicate:
  - Pericholecystic fluid, gallbladder wall thickening, and multiple gallstones.
- The patient is admitted for cholecystitis.
- Surgery is consulted and orders are written.
- The patient has a known penicillin allergy. However, she has been prescribed other beta-lactam antibiotics in the past with no allergic response.
- Common bacteria implicated are: Klebsiella, E. Coli, and anaerobes.
- What antibiotic therapy would you prescribe?

Questions??

Thank you!