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Bugs & Drugs: The Antibiotic Review for Nurse Practitioners

Disclosure

E. Monee' Reed, DNP, MA, RN, ACNP-BC has no financial relationships with commercial interests to disclose. Any unlabeled and/or unapproved uses of drugs or products will be disclosed.

Objectives

- Discuss the mechanism of action, spectrum of activity, and special considerations for the most common antibiotic drug classes.
- Identify commonly prescribed antibiotics within the drug classes and indication for prescribing.
- Practice appropriate prescribing for common bacterial infections

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

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

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

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*

Drug	Dosage	Route	Indication
Amoxicillin (Amoxil)	250-500 mg every 8h 500-875 mg BID	PO	Sinusitis, meningitis, susceptible UTIs, Soft skin infections related to group A strep, Otitis media, pneumonia
Amoxicillin/Clavulanate (Augmentin)	250-500 mg every 8h 875 mg every 12h	PO	
Ampicillin	250-500 mg every 6h	PO, IM, IV	
Ampicillin/Sulbactam (Unasyn)	1.5-3 g every 6h	IM, IV	

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

Drug	Dosage	Route	Indication
Dicloxacillin	125-500 mg every 6h	PO	Drug of choice for MSSA infections → cellulitis, endocarditis, osteomyelitis, and bacteremia
Nafcillin	0.5-2 g every 4-6h	IV	
	0.5 g every 4-6h	IM	
Oxacillin	0.25-2 g every 4-6h	IM, IV	

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 Strep.
 - **NO** MRSA coverage.
 - Gram-negative activity
 - Including *Pseudomonas aeruginosa*
 - Also has coverage against Enterobacteriaceae.
- Anaerobic coverage

Drug	Dosage	Route	Indication
Piperacillin (Pipracil)	3-4 g every 4-6h	IV, IM	Intra-abdominal infections, pneumonia, severe soft/skin and tissue infections, sepsis, etc.
Piperacillin/tazobactam (Zosyn)	3.375-4.5 g every 6-8h	IV	
Ticarcillin +/- clavulanate potassium (Timentin)	0.25-2 g every 4-6h	IV	

Penicillins

- Special Considerations
 - Dosage considerations for patients with renal dysfunction
 - Probenecid decreases renal clearance of penicillins
 - MSSA coverage with Amoxicillin/Clavulanate but **none** with Amoxicillin only
 - No MRSA coverage
 - Allergy

Cephalosporins

- Cephalosporins
 - 1st Generation
 - 2nd Generation
 - 3rd Generation
 - 4th Generation
 - 5th Generation

Cephalosporins

- Mechanism of action → bactericidal → interrupts cell wall synthesis

1st Generation Cephalosporins

Cefadroxil
Cefazolin
Cephalexin
Cephadrine

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

Drug	Dosage	Route	Indication
Cefadroxil (Duricef)	1-2 g/daily in two divided doses	PO	Skin and soft tissue infections, respiratory infections, some UTIs, and otitis media
Cefazolin (Ancef)	1-2g every 8h	IM, IV	
Cephalexin (Keflex)	250-1000mg every 6-12h	PO	
Cephradine (Velosef)	250-500mg every 6-12h	PO	

2nd Generation Cephalosporins

Cefaclor
Cefotetan
Cefoxitin
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

Drug	Dosage	Route	Indication
Cefaclor	250-500mg every 8h	PO	Skin & soft tissue infections, UTIs, respiratory tract infections
Cefotetan	1-2g every 12h	IM, IV	
Cefoxitin	1-2g every 6-8h	IM, IV	
Cefprozil	250-500mg every 12-24h	PO	
Cefuroxime	PO: 250-500mg every 12h IM, IV: 0.5-1g every 6-8h	PO, IM, IV	

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

Drug	Dosage	Route	Indication
Cefdinir	300mg every 12h 600mg every 24h	PO	Respiratory tract infections, skin & soft tissue infections, UTIs, sepsis*, intra-abdominal infections*, CNS infections*
Cefditoren	200-400mg every 12h	PO	
Cefixime	400mg daily	PO	
Cefotaxime	1-2g every 4-12h	IM, IV	
Cefpodoxime	100-400mg every 12h	PO	
Ceftazidime	500mg to 1g every 8h	IM, IV	
Ceftibuten	400mg/daily	PO	
Ceftriaxone (Rocephin)	1-2g every 12-24h	IM, IV	

4th Generation Cephalosporin

Cefepime

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

Drug	Dosage	Route	Indication
Cefepime	IM: 0.5-1g every 12h IV: 1-2g every 8-12h	IM, IV	Pneumonia, intra-abdominal infections, UTI, and skin & soft tissue infections

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.

Drug	Dosage	Route	Indication
Ceftaroline	600mg every 12h	IV	Pneumonia (CAP), skin & soft tissue infection

Cephalosporins

- Special Considerations
 - If cross-sensitivity reaction is to occur with a penicillin, most likely to occur with 1st generation.
 - Cefazolin and Cefepime can cross the blood-brain-barrier in severe renal dysfunction/failure → neurotoxicity → encephalopathy, seizures
 - Encephalopathy
 - Seizures
 - Cefotetan → possible disulfiram-like reaction with alcohol
 - Ceftriaxone → calcium salt precipitate in the gallbladder that can be mistaken for gallstones
 - Cholelithiasis

Carbapenems

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

Carbapenems

- Mechanism of action → bactericidal → interrupts cell wall synthesis

Carbapenems

Doripenem
Ertapenem
Imipenem/cilastatin
Meropenem
Meropenem/vaborbactam

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

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	
Imipenem/cilastatin	500-1000mg every 6-8h	IV	
Meropenem	1.5 to 6g daily in 3 divided doses	IV	
Meropenem/vaborbactam	4g every 8h	IV	

Carbapenems

Doripenem
Ertapenem
Imipenem/cilastatin
Meropenem
Meropenem/vaborbactam

- Special Considerations
 - The dose must be adjusted in patients with renal disease
 - Ertapenem → 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.

Monobactam

- Aztreonam

Monobactam

- Mechanism of action → bactericidal → interrupts cell wall synthesis

Monobactam

Aztreonam

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

Drug	Dosage	Route	Indication
Aztreonam	1-2g every 8-12h	IM, IV	UTI, respiratory tract infections, sepsis, skin & soft tissue infections, intra-abdominal infections, gynecological infections

Monobactam
Aztreonam

- 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
 - ?Ceftazidime cross-allergy reaction

Macrolides

- Erythromycin
- Clarithromycin
- Azithromycin
- Fidaxomicin

Macrolides

- Mechanism of action → bacteriostatic* → inhibits protein synthesis

Macrolides
Azithromycin
Clarithromycin
Erythromycin
*Fidaxomicin**

- Spectrum of Activity
 - Atypical bacteria
 - *Chlamydia*
 - *Legionella*
 - *Mycoplasma*
 - *Mycobacterium*
 - *Neisseria*
 - Gram-positive bacteria
 - Gram-negative bacteria
 - *Haemophilus*
 - *Moraxella*

Drug	Dosage	Route	Indication
Azithromycin	PO: 250-600mg daily IV: 250-500mg daily	IV, PO, ophthalmic drops	COPD, CAP, MAC, skin & soft tissue infections, streptococcal pharyngitis, <i>N. gonorrhoea</i>
Clarithromycin	250-500mg every 12h	PO	<i>H. pylori</i> , CAP, MAC, skin & soft tissue infections
Erythromycin	Varies drastically depending on the base.	IV, PO, ophthalmic drops, topical	All bacterial infections, colorectal surgical prophylaxis
Fidaxomicin	200mg twice daily	PO	<i>Clostridium difficile</i> infections

Macrolides

Azithromycin
Clarithromycin
Erythromycin
*Fidaxomicin**

- Special Considerations
 - Monitor for QT prolongation
 - Liver disease
 - Avoid erythromycin estolate is contraindicated 2/2 to hepatic dysfunction with or without jaundice
 - Reversible deafness has occurred with Clarithromycin
 - Significant drug interactions can occur with Erythromycin and Clarithromycin
 - Inhibitors of CYP_{3A4}

Fluroquinolones

- Besofloxacin
- Cinoxacin
- Ciprofloxacin*
- Delafloxacin
- Gatifloxacin → 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

Fluroquinolones

Ciprofloxacin
Levofloxacin
Moxifloxacin
Ofloxacin

- 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	

Fluroquinolones

Ciprofloxacin
Levofloxacin
Moxifloxacin
Ofloxacin

- Special Considerations
 - Fluroquinolones are recommended for more severe infections 2/2 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

*Sulfamethoxazole/
trimethoprim*

- Spectrum of Activity
 - Gram positive coverage
 - *Staphylococcus*
 - *Streptococcus* → some
 - Gram negative coverage
 - *Enterobacteriaceae*
 - *Haemophilus*
 - Other organisms
 - *Pneumocystis* → yeast-like fungus
 - *Stenotrophomonas* → gram negative
 - *Toxoplasma* → parasite
 - *Nocardia* → gram positive

Drug	Dosage	Route	Indication
Sulfamethoxazole/ trimethoprim (Bactrim)	PO: 800/160 mg every 12-24 hours IV: 8-20 mg/kg/day	PO, IV	UTI, COPD exacerbation, PJP prophylaxis and treatment, traveler's diarrhea, and shigellosis

Sulfonamides

*Sulfamethoxazole/
trimethoprim*

- 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

Tetracyclines

Doxycycline
Minocycline

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

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

Tetracyclines

Doxycycline
Minocycline

- 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...



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Clindamycin

- Mechanism of action → bacteriostatic → inhibits protein synthesis
- Can be given IM, IV, or PO
- 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

<i>Metronidazole</i>	<ul style="list-style-type: none">• Mechanism of action → bactericidal → inhibits DNA synthesis & degradation• Can be given PO or IV• Active against anaerobes and protozoal parasites• Side effects: headache, dizziness, nausea, vaginitis
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<i>Nitrofurantoin</i>	<ul style="list-style-type: none">• Mechanism of action → bactericidal → inhibits DNA, RNA, and cell wall protein synthesis• Given PO• Antibiotic coverage varies slightly based on medication.<ul style="list-style-type: none">– Macrobid → <i>E. Coli</i> and <i>Staphylococcus</i>– Macrochantin → <i>Enterococcus</i>, <i>Staphylococcus</i>, <i>E. Coli</i>, <i>Klebsiella</i>, <i>Enterobacter</i>• Indications → acute uncomplicated cystitis• Side effects: GI symptoms, headache
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<i>Vancomycin</i>	<ul style="list-style-type: none">• Mechanism of action → bactericidal → inhibits cell wall synthesis• Can be given PO or IV• Active against gram positive organisms only• Side effects:<ul style="list-style-type: none">– PO: nausea, abdominal pain, & hypokalemia
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	<i>Prescribing Case Studies</i>
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<i>Case Study #1</i>	<ul style="list-style-type: none">• 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.
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<i>Case Study #1</i>	<ul style="list-style-type: none">• Common bacteria implicated are: <i>Streptococcus pneumoniae</i>, <i>Haemophilus influenzae</i>, and <i>Moraxella catarrhalis</i>.• Based on what is known about Ms. Jones, what is the most appropriate antibiotic to prescribe?<ol style="list-style-type: none">a) Augmentin 2g twice dailyb) Doxycycline 100mg twice dailyc) Azithromycin 500 mg x 1 dose, followed by 250 mg x 4 daysd) Moxifloxacin 400 mg PO
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Case Study #2

- 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?

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Case Study #2

- 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

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Case Study #3

- 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).

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Case Study #3

- 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

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Questions??

Thank you!