Bug Busters:

A Clinician's Guide to Infectious Diseases

Shivani Patel, PharmD, BCIDP
Infectious Diseases/Antimicrobial Stewardship Pharmacist
Mount Carmel Health System
Shivani.patel002@mchs.com

CMEPRO

Disclosures

This presenter has no current or potential conflicts to report.

Objectives

- Understand the principles of infectious diseases and summarize antibacterial drugs by class
- Review antifungals, antivirals, and associated disease states
- Identify treatment and prophylaxis of specific infections

Introduction

Infectious diseases are caused by one or more pathogens (like bacteria, fungi, viruses, protozoa, parasites, or infectious proteins called prions

They are transmitted through various mechanisms such as physical contact or airborne transmission

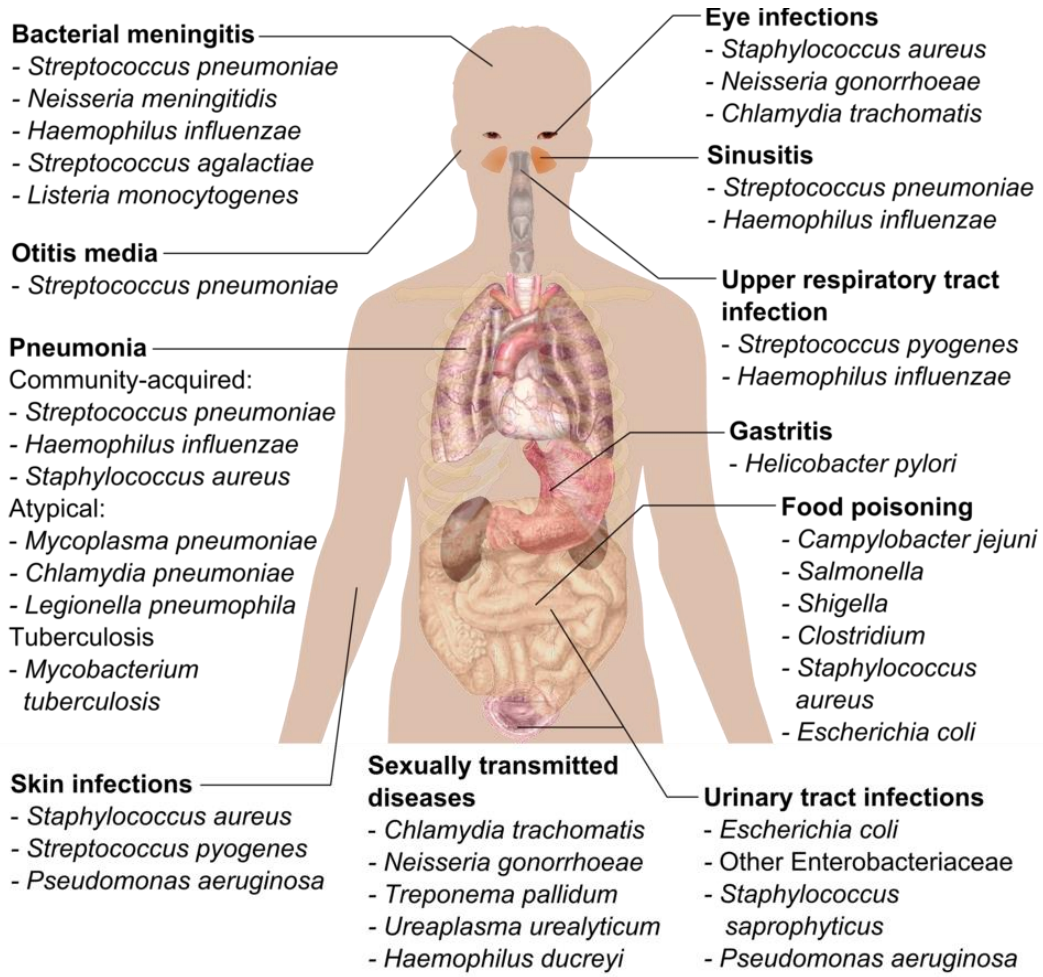
The primary factors that impact treatment decisions include the bug (pathogen), the drug (the antimicrobial), and the patient (host)

Brief Review of Bacterial Classifications

Gram Positive	Gram Negative	Atypical
Staphylococcal spp. **Streptococcal spp.** **Enterococcus spp.**	**Enterobacteriaceae** • **Ex:** Escherichia coli, Salmonella spp., Shigella, Proteus spp., Enterobacter spp., Citrobacter spp., Klebsiella spp., etc **Pseudomonas spp.** **Acinetobacter spp.** **Neisseria spp.**	***Chlamydia*** pneumoniae ***Legionella*** pneumophilae ***Mycoplasma*** pneumoniae

Note: This list is not exhaustive, and there are many other species of gram-negative, gram-positive, and atypical bacteria. Some of these bacteria are common pathogens that can cause serious infections, while others are part of the normal flora of the human body.

Bacteria Within the Human Body



Fisher, Bruce; Harvey, Richard P.; Champe, Pamela C. *Lippincott's Illustrated Reviews: Microbiology (Lippincott's Illustrated Reviews Series)*, Hagerstwon, MD: Lippincott Williams & Wilkins, pp. Chapter 33, pages 367–392

Antibiotics

Mechanisms of Action

Cell Wall Inhibitors

Beta-lactams
Monobactams
Vancomycin
Dalbavancin
Telavancin
Oritavancin

Cell Membrane Inhibitors

Polymyxin
Daptomycin
Telavancin
Oritavancin

Protein Synthesis Inhibitors

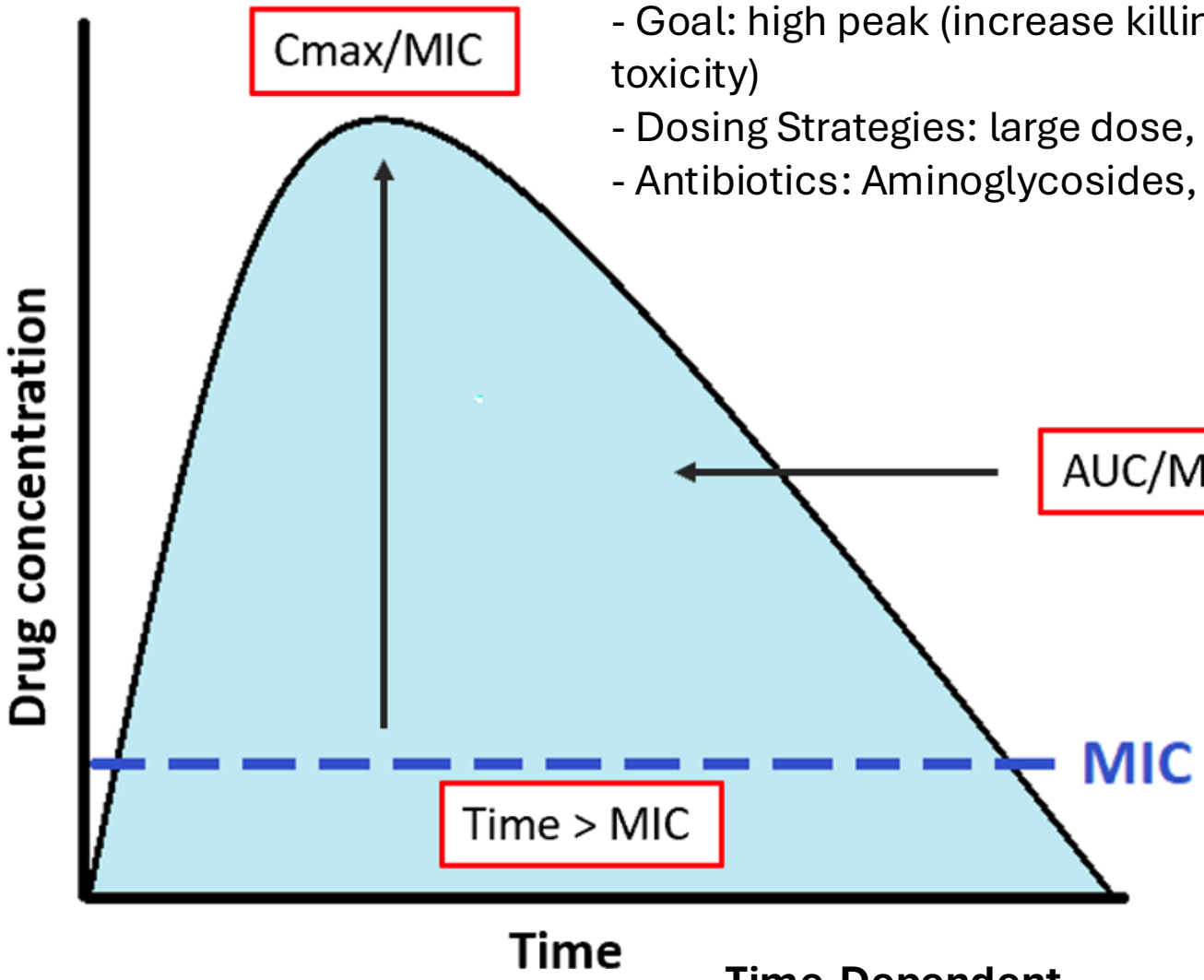
Aminoglycosides
Macrolides
Tetracyclines
Clindamycin
Linezolid

DNA/RNA Inhibitors

Quinolones
Metronidazole
Rifampin

Folic Acid Synthesis Inhibitors

Sulfonamides
Trimethoprim
Dapsone



Concentration-Dependent

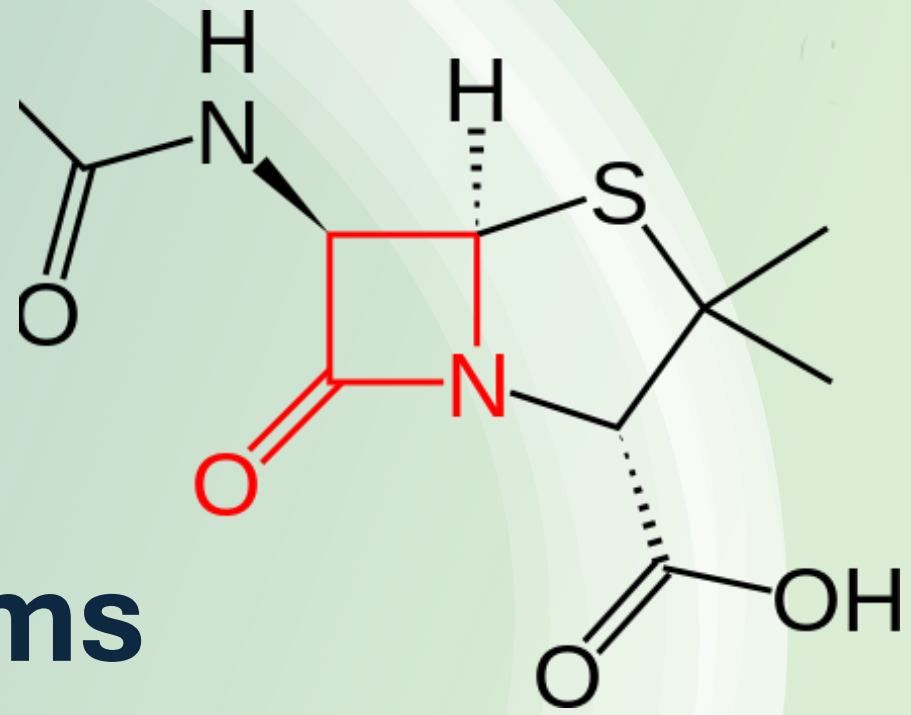
- Goal: high peak (increase killing), low trough (decrease toxicity)
- Dosing Strategies: large dose, long interval
- Antibiotics: Aminoglycosides, quinolones, daptomycin

- Goal: exposure over time
- Dosing Strategies: variable
- Antibiotics: Vancomycin, macrolides, tetracyclines, polymyxins

Time-Dependent

- Goal: maintain drug level above MIC for most of the dosing interval
- Dosing Strategies: shorter dosing interval, extended or continuous infusion
- Antibiotics: Beta Lactams (penicillins, cephalosporins, carbapenems)

Beta-lactams



Beta-lactams

- Penicillins
- Cephalosporins
- Carbapenems

  - **Should be considered first for any susceptible bacterial infection**
    - Excellent safety and efficacy data

What is a Beta-Lactamase?

- Beta lactams work by inhibiting cell wall synthesis of bacteria
- Some bacteria produce **beta-lactamases** (enzymes) that break down the beta-lactam rings, rendering the beta-lactam inactive
    - Beta-lactamases are a common resistance mechanisms of bacteria
    - Common beta-lactamases: ESBL, AmpC, OXA, KPC, etc
    - Different pathogens will produce different beta-lactamases

Beta-lactam – Beta-lactamase inhibitors

- Beta-lactamase inhibitors can be co-formulated with beta-lactams to inactivate beta-lactamase enzymes, restoring the activity of beta-lactams
- Beta-lactamase inhibitors: clavulanic acid, sulbactam, tazobactam, avibactam, vaborbactam, relebactam
- Each beta-lactamase inhibitor has different potencies and spectrums

Penicillins

PENICILLINS	Antibiotics	Coverage
Natural Penicillins	Penicillin G Penicillin VK	**- Streptococci** **- Enterococci** **Gram Positive anaerobes** - mouth flora
Aminopenicillins	Amoxicillin Ampicillin	**- Streptococci** **- Enterococci** - Gram positive anaerobes - Haemophilus - Neisseria - Proteus - E. coli
Aminopenicillins combined with beta lactamase inhibitor (clavulanate, sulbactam, tazobactam)	Amoxicillin/Clavulanate Ampicillin/Sulbactam	- **Adds activity against MSSA**, some resistant strains of gram-negative bacteria, gram negative anaerobes (B. fragilis)
Extended Spectrum Penicillins with beta lactamase inhibitor	Piperacillin/tazobactam	**Broad Spectrum** - adds expanded coverage gram negative bacteria including **pseudomonas**
Antistaphylococcal penicillins	Dicloxacillin Nafcillin Oxacillin	- Streptococci **- enhanced MSSA coverage** -NO activity against Enterococcus, Gram negative pathogens, and anaerobes

Key Features of Oral Penicillins

Oral	
Penicillin VK	First line treatment for strep throat and mild, nonpurulent skin infections (no abscess)
Amoxicillin	• First line treatment for acute otitis media (80-90 mg/kg/day) • Drug of choice for IE prophylaxis before dental procedures (2g x1 30-60 min prior to procedure)
Amoxicillin/Clavulanate (Augmentin)	First line treatment for acute otitis media (90 mg/kg/day) and for sinus infections (if antibiotics are indicated)
Dicloxacillin, oxacillin	• Cover MSSA • No renal dose adjustment needed

IE: Infective Endocarditis

Key Features of Parenteral Penicillins

Parenteral (IV, IM)	
Penicillin G Benzathine (Bicillin)	• Drug of choice for syphilis (2.4 million units IM x1) • NEVER used IV
Nafcillin	• Covers MSSA • No renal dose adjustment needed
Piperacillin/Tazobactam (Zosyn)	• Only penicillin active against pseudomonas • Extended infusions (4 hours) can be used to maximize T > MIC

IM: Intramuscular, IV: Intravenous

Cephalosporins

CEPHALOSPORINS

Generation	Agents	Pearls
First	Cefazolin (Ancef, IV, IM) Cephalexin (Keflex, PO) Cefadroxil (PO)	• Cefazolin is commonly used for **MSSA**, has good CNS penetration, and commonly used for surgical prophylaxis • Cephalexin is commonly used for skin infections and strep throat
Second	Cefuroxime (PO, IV, IM) Cefotetan (IV, IM) Cefaclor (PO) Cefoxitin (IV, IM)	• Cefuroxime is often used for acute otitis media, community acquired pneumonia (CAP), sinus infections (if antibiotics are indicated) • Cefotetan and Cefoxitin offer anaerobic coverage (B. fragilis) and are commonly used for colorectal surgical prophylaxis • Cefotetan can cause a disulfiram-like reaction with alcohol ingestion
Third (group 1)	Cefdinir (PO) Ceftriaxone (IV, IM) Cefotaxime (IV, IM) Cefixime (PO) Cefpodoxime (PO)	• **Cefdinir** is commonly used for CAP and sinus infections (if antibiotics are indicated) – cefdinir overall has poor bioavailability, poor urine penetration • Ceftriaxone and Cefotaxime are commonly used for CAP, meningitis, spontaneous bacterial peritonitis (SBP), pyelonephritis • Ceftriaxone does NOT require renal dose adjustments • Should NOT be used in neonates (can cause biliary sludging, kernicterus)
Third (group 2)	Ceftazidime Ceftazidime/Avibactam (Avycaz, IV)	• Ceftazidime is active against Pseudomonas • Ceftazidime/Avibactam is used for MDR gram-negatives (like Pseudomonas)
Fourth	Cefepime (Maxipime, IV, IM)	• Cefepime is active against Pseudomonas
Fifth	Ceftaroline fosamil (Teflaro, IV) Ceftolozane/Tazobactam (Zerbaxa, IV)	• Ceftaroline: only beta lactam active against MRSA • Ceftolozane/Tazobactam: used for MDR gram-negative organisms (including Pseudomonas)
Siderophore Cephalosporin	Cefiderocol	• Broad spectrum against gram-negative bacteria

Carbapenems

CARBAPENEMS

- Broad spectrum, reserved for MDR Gram negative infections
  - Should rarely be used empirically
- Active against most Gram positive, Gram negative (including ESBL producers), and anaerobes
- **NO activity against atypical pathogens, MRSA, VRE, C. difficle, Stenotrophomonas**

Agent	Key Features	
Doripenem (IV)	• NOT used for pneumonia	• CNS adverse effects (confusion, seizures) • **Major drug interaction with valproic acid and derivatives**
Imipenem (IV) **Imipenem/Cilastatin (IV)** **Imipenem/Cilastatin/Relebactam (Recarbio, IV)**	• Imipenem/Cilastatin/Relebactam is approved for complicated UTI/Pyelonephritis and intraabdominal infections	
Meropenem (Merrem, IV)		
Meropenem/Vaborbactam (Vabomere, IV)	Approved for complicated UTI/Pyelonephritis	
Ertapenem (Invanz, IV)	Ertapenem • No coverage for Pseudomonas, Acinetobacter, Enterococcus • Commonly used for diabetic foot infections	

Beta-Lactam Allergies

Beta-lactam allergies

- The use of broad-spectrum antibiotics in patients labeled “penicillin-allergic” is associated with:
  - higher healthcare costs
  - increased risk for antimicrobial resistance
  - suboptimal antibiotic therapy

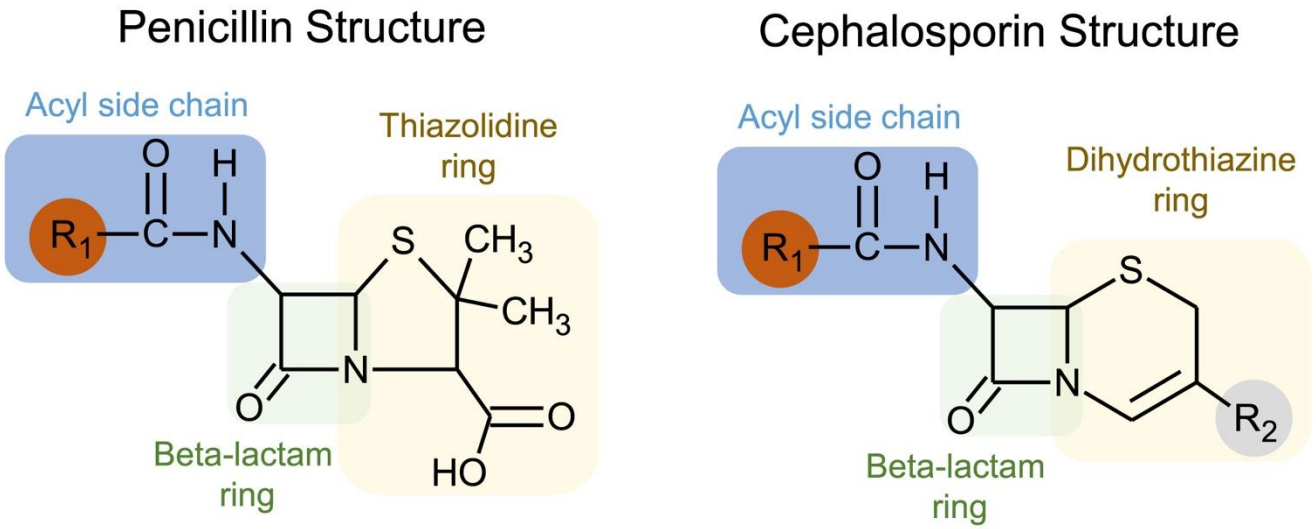
https://blogs.cdc.gov/safehealthcare/antibiotic-stewardship-and-allergy-labels/

Beta-lactam allergies

- Questions to ask:
  - **When** did the allergy occur and **to what** agent specifically?
  - What was your **reaction** to this agent?
    - This will help assess if it was an intolerance or a true anaphylactic/IgE mediated allergy
  - What other antibiotics have you taken? Did you have a reaction to any of these?
  - Are you open to trialing this type of medication again?
  - Are you open to being de-sensitized to this allergy?

Beta-lactam allergies

- Beta-lactam allergy cross-reactivity is mediated by the R1 group side chain
  - Identical R1 chains in patients with IgE-mediated allergy posing the highest risk of cross reactivity
  - Cross-reactivity through R2 side chains and the beta-lactam ring are rare



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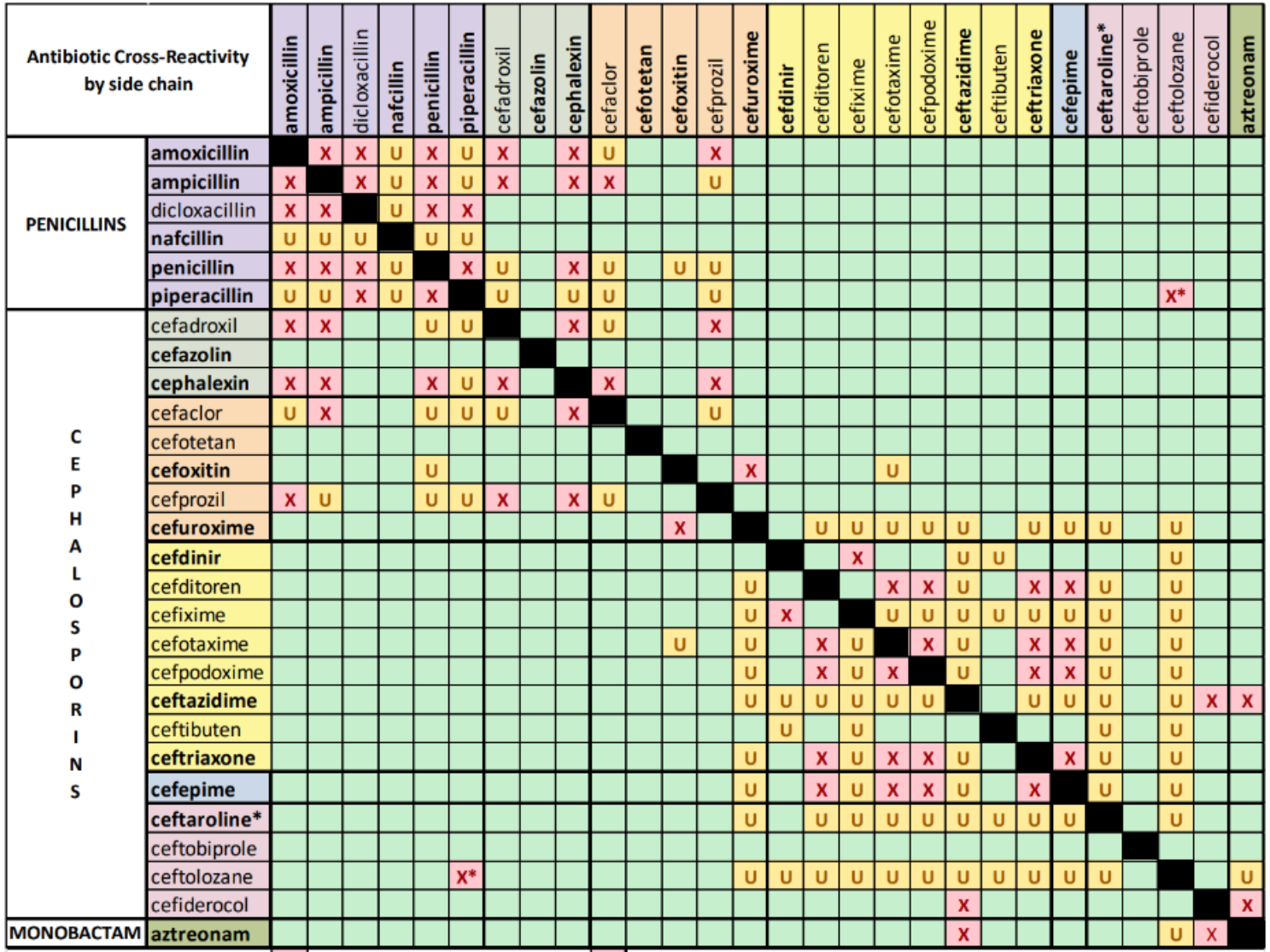
Beta-lactam allergies

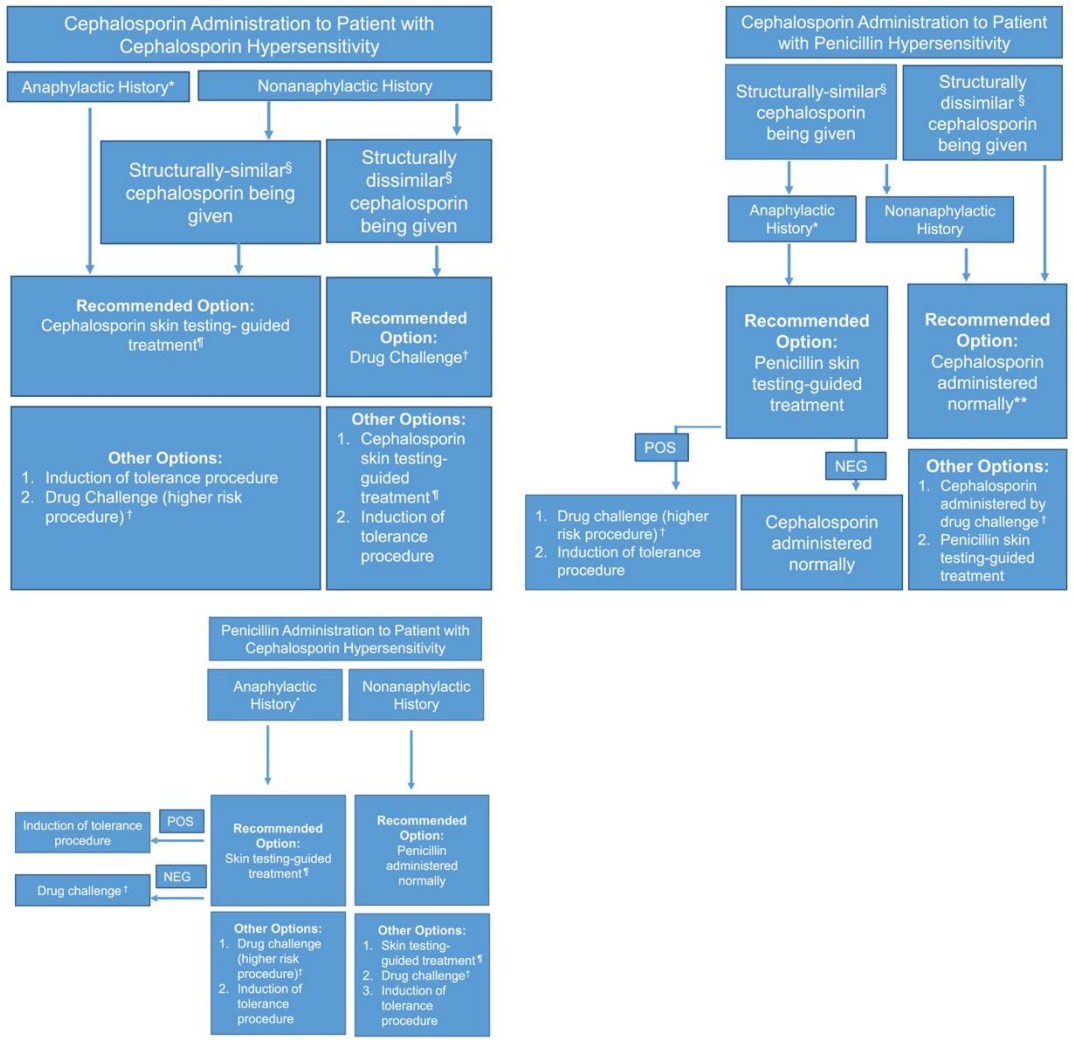


Antibiotic Cross-Reactivity by side chain		amoxicillin	ampicillin	dicloxacillin	nafcillin	penicillin	piperacillin	cefadroxil	cefazolin	cephalexin	cefaclor	cefotetan	cefoxitin	cefprozil	cefuroxime	cefdinir	cefditoren	cefixime	cefotaxime	cefpodoxime	ceftazidime	ceftibuten	ceftriaxone	cefepime	ceftaroline*	ceftobiprole	ceftolozane	cefiderocol	aztreonam
PENICILLINS	**amoxicillin**		X	X	U	X	U	X		X	U			X														
	ampicillin	X		X	U	X	U	X		X	X			U														
	dicloxacillin	X	X		U	X	X																					
	nafcillin	U	U	U		U	U																					
	penicillin	X	X	X	U		X	U		X	U		U	U														
	piperacillin	U	U	X	U	X		U		U	U			U													X*		
CEPHALOSPORINS	cefadroxil	X	X			U	U			X	U			X														
	cefazolin																											
	cephalexin	X	X			X	U	X			X			X														
	cefaclor	U	X			U	U	U		X				U														
	cefotetan																											
	cefoxitin					U									X				U									
	cefprozil	X	U			U	U	X		X	U																	
	cefuroxime												X				U	U	U	U	U		U	U	U		U	
	cefdinir																	X			U	U					U	
	cefditoren														U				X	X	U		X	X	U		U	
	cefixime														U	X			U	U	U	U	U	U	U		U	
	cefotaxime												U		U		X	U		X	U		X	X	U		U	
	cefpodoxime														U		X	U	X		U		X	X	U		U	
	ceftazidime														U	U	U	U	U	U			U	U	U		U	X	X
	ceftibuten															U		U							U		U		
	ceftriaxone														U		X	U	X	X	U			X	U		U		
	cefepime														U		X	U	X	X	U		X		U		U		
	ceftaroline*														U		U	U	U	U	U	U	U	U			U		
	ceftobiprole																												
	ceftolozane						X*								U	U	U	U	U	U	U	U	U	U	U				U
	cefiderocol																				X							X	X
MONOBACTAM	**aztreonam**										X*										X						U	X	

Bolded are formulary	X	= Identical side chain	X* Available product shares a beta-lactamase inhibitor
*Restricted use	U	= Unclear, similar side chain and/or limited data, avoid with severe reaction	

JACI The Journal of Allergy and Clinical Immunology

Drug allergy: A 2022 practice parameter update



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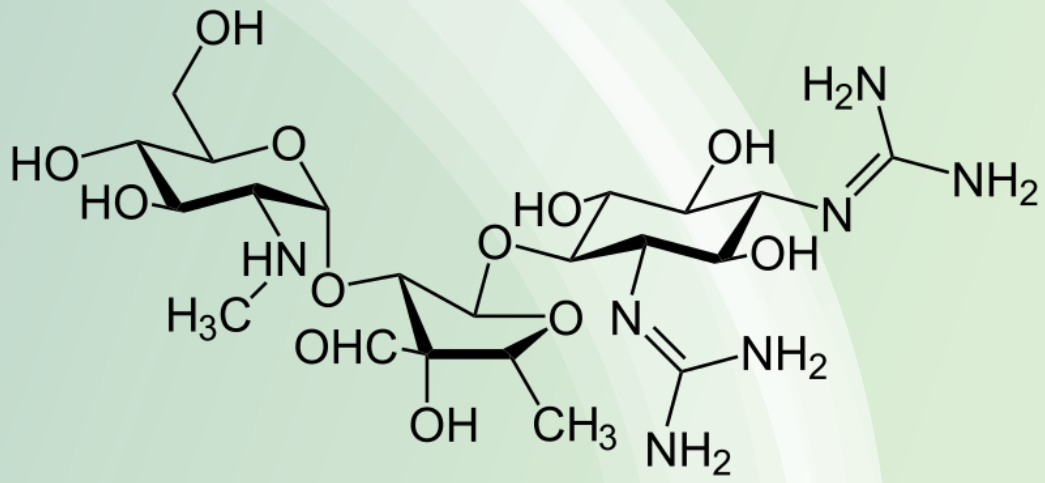
Aztreonam

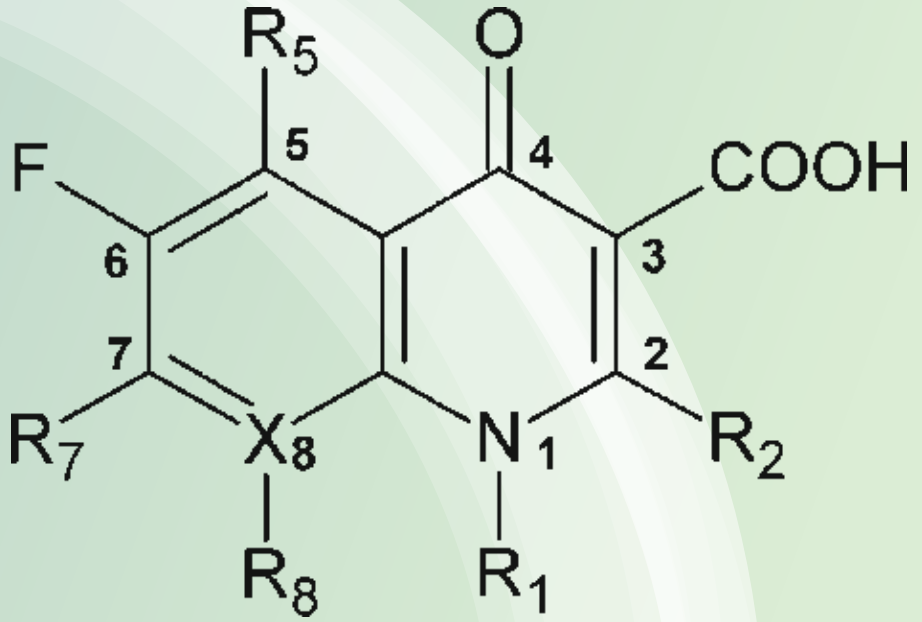
- **Monobactam**
  - **Its monobactam structure makes cross-reactivity with beta-lactam allergy unlikely**
- Should not be used empirically
  - Reserved for resistant infections, serious allergies
- Spectrum
  - Gram negative organisms (including **Pseudomonas**)
  - NO gram-positive activity
  - NO anaerobic activity



Aminoglycosides

Aminoglycosides

Agents	Pearls	Class Features
Gentamicin (IV, IM, ophthalmic, topical)	Can by synergistic with beta-lactams or vancomycin for certain gram-positive organisms	• Coverage: gram negative (including Pseudomonas – EXCEPT Gentamicin) • ADRs: renal toxicity, ototoxicity **2 Dosing Strategies** • Traditional: uses lower doses more frequently • Extended Interval: uses higher doses less frequently leading to less accumulation and less toxicity
Tobramycin (IV, IM, ophthalmic, inhaled)	Often used in cystic fibrosis	
Amikacin (IV, IM)	Second-line treatment for Mycobacterial infections	
Plazomicin (IV)	For complicated UTI; use only when there are no alternative options	



Fluoroquinolones

Fluoroquinolones

Broad spectrum → Variety of gram negative, gram positive, and atypical pathogens

- *Notably, resistance to fluoroquinolones is increasing rapidly*

AGENT		PEARLS	CLASS EFFECTS
Respiratory Fluoroquinolones Used for pneumonia, reliable activity against S. pneumoniae	Levofloxacin	**Antipseudomonal**	**Black Box Warning:** • Tendon inflammation/rupture • Peripheral Neuropathy • CNS effects • Avoid in patients with myasthenia gravis ADRs • **QTc prolongation** • Hypo- and hyperglycemia • Photosensitivity Counseling pearls: • Avoid sun exposure • Separate from cations (to optimize absorption) • Monitor blood glucose
	Moxifloxacin	• Does not reach adequate concentrations in the urine so should not be used for UTIs • No renal dose adjustments needed	
	Gemifloxacin	Rarely used	
	Ciprofloxacin	**Antipseudomonal** • Cannot put cipro suspension through NG tube • CAN crush immediate release tablets – hold tube feeds at least 1 hour before and 2 hours after the dose	

Fluoroquinolones

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	Moxifloxacin	• Does not reach adequate concentrations in the urine so should not be used for UTIs	
	Ciprofloxacin	through NG tube • CAN crush immediate release tablets – hold tube feeds at least 1 hour before and 2 hours after the dose	Counseling pearls: • Avoid sun exposure • Separate from cations (to optimize absorption) • Monitor blood glucose

AVOID IN ELDERLY IF POSSIBLE

Fluoroquinolones

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	Ciprofloxacin	• CAN crush immediate release tablets – hold tube feeds at least 1 hour before and 2 hours after the dose	• Avoid sun exposure • Separate from cations (to optimize absorption) • Monitor blood glucose

Place in therapy?

- Transitioning to PO pseudomonas therapy for outpatients
- Resistance to beta-lactams

Sulfonamides

Sulfamethoxazole/Trimethoprim (Bactrim)

Spectrum	**Staphylococci (including MRSA)** **Some broad gram-negative coverage:** • Haemophilus • Proteus • E. coli • Klebsiella • Enterobacter • Shigella • Salmonella • Stenotrophomonas	**Some opportunist infections (OI):** • Nocardia • Pneumocystis • Toxoplasmosis **NO coverage for:** • Pseudomonas • Enterococci • Atypicals • Anaerobes
Formulations	PO, IV Single Strength (SS) tablets: 400 mg SMX/80 mg TMP Double Strength (DS) tablets: 800mg SMX/160 mg TMP Often weight-based dosing	
Pearls	• **Dosed based on TMP component** • ADRs: Skin reactions (SJS/TEN), thrombotic thrombocytopenic purpura (TTP), **photosensitivity, hyperkalemia, AKI**	

Select Gram Positive agents

Brief Review of Bacterial Classifications

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Note: This list is not exhaustive, and there are many other species of gram-negative, gram-positive, and atypical bacteria. Some of these bacteria are common pathogens that can cause serious infections, while others are part of the normal flora of the human body.

Brief Review of Bacterial Classifications

Gram Positive
Staphylococcal spp. **Streptococcal spp.** **Enterococcus spp.**

Staphylococcus spp.	Streptococcus spp.	Enterococcus spp
***Staphylococcus* aureus** • **Methicillin susceptible (MSSA)** • **Methicillin resistant (MRSA)** **Coagulase Negative Staphylococcus (CoNs)** • *S. epidermidis* • *S. haemolyticus* • *S. saprophyticus* • *S. capitis* • *S. lugdunensis*	***S. pneumoniae*** ***S. agalactiae* (GBS)** ***S. pyogenes* (GAS)** ***S. anginosis*** ***S. sanguis*** ***S. mitis***	***Enterococcus* faecalis** ***Enterococcus* faecium** • Can often be vancomycin resistant (VRE)

Agent	Route	Coverage	Pearls
Vancomycin	PO (C. diff only), IV	Only gram-positive bacteria • Staphylococci (including MRSA) • Streptococci • Enterococci (not VRE) • C. difficile (PO route only)	**IV formulation only:** • Monitor for **AKI, infusion reaction** • Requires therapeutic drug monitoring • For severe MRSA infections: AUC/MIC target is 400-600, trough target is 15-20 mcg/mL
Daptomycin	IV	Only gram-positive bacteria • Staphylococci (including MRSA) • Enterococci • Streptococci	• **Deactivated by lung surfactant so not to be used in pneumonias** • Can elevate **CK** (monitor at baseline then weekly) • Can falsely elevate PT/INR but does not increase bleed risk
Linezolid	PO, IV	Only gram-positive bacteria • Staphylococci (including MRSA) • Enterococci • Streptococci	PO and IV formulations have equivalent bioavailability ADRs: • Serotonin syndrome • Myelosuppression

Linezolid	PO, IV	Only gram-positive bacteria • Staphylococci (including MRSA) • Enterococci • Streptococci	PO and IV formulations have equivalent bioavailability ADRs: • Serotonin syndrome • Myelosuppression

But what is the actual risk of serotonin syndrome with linezolid?

----------WARNINGS AND PRECAUTIONS----------

- Myelosuppression: Monitor complete blood counts weekly. Consider discontinuation in patients who develop or have worsening myelosuppression. (5.1)
- Peripheral and optic neuropathy: Reported primarily in patients treated for longer than 28 days. If patients experience symptoms of visual impairment, prompt ophthalmic evaluation is recommended. (5.2)
- Serotonin syndrome: Patients taking serotonergic antidepressants should receive ZYVOX only if no other therapies are available. Discontinue serotonergic antidepressants and monitor patients for signs and symptoms of both serotonin syndrome and antidepressant discontinuation. (5.3)
- A mortality imbalance was seen in an investigational study in linezolid-treated patients with catheter-related bloodstream infections. (5.4)
- *Clostridium difficile* associated diarrhea: Evaluate if diarrhea occurs. (5.5)
- Potential interactions producing elevation of blood pressure: monitor blood pressure (5.6)
- Hypoglycemia: Postmarketing cases of symptomatic hypoglycemia have been reported in patients with diabetes mellitus receiving insulin or oral hypoglycemic agents. (5.9)

Risk of SS with Linezolid Use

- However, post-marketing studies show that the risk is much lower than originally thought

Study	Author Conclusions
2023 systematic review PMID: 37129603	Incidence of serotonin toxicity with linezolid monotherapy at 0.0050% and linezolid combination therapy at 0.0134% → linezolid should not always be deferred due to the risk of serotonin syndrome
2023 retrospective cohort study PMID: 37160238	Even with multiple and high-dose serotonergic drugs, concomitant use of linezolid is likely safe
2022 cross-sectional analysis PMID: 35899282	Serotonin toxicity occurring during the administration of linezolid in combination with methadone and/or buprenorphine occurred rarely
2022 cohort study PMID: 36534400	Antidepressants do not increase the risk of serotonin syndrome in patients receiving linezolid treatment and that linezolid is likely safe for patients receiving antidepressants

Risk of SS with Linezolid Use

- Based on current literature, risk of SS with linezolid can be considered minimal even when used with 1 or more serotonergic agents
- Pay extra attention to:
  - Patients on multiple serotonergic agents
  - Older adults
  - Patients who have history of serotonin syndrome
- Fortunately, Serotonin Syndrome is **reversible** but is a serious condition, so linezolid **monitoring** is always encouraged
  - Typical courses should not exceed 14 days total

Atypical Pathogens and Coverage

Brief Review of Bacterial Classifications

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Atypical Coverage

Atypicals
Chlamydia pneumoniae ***Legionella*** pneumophilae ***Mycoplasma*** pneumoniae

★ considered "atypical" because they do <u>not</u> have a cell wall and do not stain like "typical" gram positive and negative bacteria

Macrolides	Tetracyclines	Fluoroquinolones
Azithromycin **ADR:** QTc prolongation	**Doxycyline** **ADR:** GI disturbances, photosensitivity • Use in children <8 years old can inhibit bone growth and cause permanent discoloration of teeth and enamel hypoplasia **Pearl:** should be separated from calcium, magnesium, and iron containing products by several hours to avoid decrease absorption	**Levofloxacin** **Black Box Warning:** • Tendon inflammation/rupture • Peripheral Neuropathy • CNS effects • Avoid in patients with myasthenia gravis ADRs • **QTc prolongation** • Hypo- and hyperglycemia • Photosensitivity

Bacterial Infections

Upper Respiratory Tract Infections

Disease State	Common Pathogens	Treatment
Acute Otitis Media (AOM)	*S. Pneumoniae* *H. Influenzae*	• Amoxicillin (80-90 mg/kg/day in 2 divided doses) • Amoxicillin/Clavulanate (90 mg/kg/day in 2 divided doses) • Ceftriaxone (50 mg/kg IM or IV for 1 or 3 days)
Influenza	**Viral** influenza strains	Oseltamivir for 5 days
Pharyngitis	*S. Pyogenes* (GAS)	• Penicillin, Amoxicillin, or 1st or 2nd generation cephalosporin for 10 days • Azithromycin x5 days
Sinusitis	Respiratory Viruses *S. Pneumoniae* *H. Influenzae* *M. catarrhalis*	• No **antibiotics** needed for respiratory **viral** infections • Amoxicillin/Clavulanate – treatment duration varies

Hersh AL, Jackson MA, Hicks LA American Academy of Pediatrics Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics*. 2013;132(6):1146-1154

Infectious Diseases Society of America. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis*. 2012;54(8):e72-e112.

Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg*. 2015;152(2 suppl):S1-S39.

Lieberthal AS, Carroll AE, Chonmaitree T, et al. The diagnosis and management of acute otitis media [published correction appears in *Pediatrics*. 2014; 133(2): 346]. *Pediatrics*. 2013;131(3):e964-e999.

Lower Respiratory Tract Infections

DISEASE STATE	COMMON PATHOGENS	EMPIRIC TREATMENT
Community Acquired Pneumonia (CAP)	*S. Pneumoniae* *H. Influenzae* *M. Catarrhalis*	Empiric coverage should include: S. pneumoniae and atypical pathogens
		Outpatient • *No co-morbidities:* Amoxicillin (high dose, 1 g 3x daily) OR doxycycline OR azithromycin • *Co-morbidities:* Beta-lactam (Amoxicillin/Clavulanate or cephalosporin) PLUS azithromycin OR monotherapy with respiratory fluoroquinolone
		Inpatient • Beta Lactam (ceftriaxone) + macrolide (azithromycin) OR doxycycline OR • Monotherapy with respiratory fluoroquinolone (levofloxacin, moxifloxacin – *NOT ciprofloxacin*) If risk factors for MRSA: add vancomycin or linezolid If risk factors for Pseudomonas: add piperacillin/tazobactam or cefepime or another antipseudomonal agent
Duration: 5 days (beta-lactam) + 3 days (atypical)		

Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med 2019; 200:e45–67.

Lower Respiratory Tract Infections

DISEASE STATE	COMMON PATHOGENS	EMPIRIC TREATMENT
Hospital Acquired and Ventilator Associated Pneumonias (HAP/VAP)	*S. Pneumoniae* *H. Influenzae* *M. Catarrhalis* MRSA Gram negative rods • *P. aeruginosa* • Acinetobacter spp. • Enterobacter spp. • *E. coli* • Klebsiella spp	**Choose 1 antibiotic to cover pseudomonas and MSSA if low risk for MRSA or MDR pathogens** *Examples:* Cefepime or piperacillin/tazobactam
		Choose 2 antibiotics, one for MRSA and one for Pseudomonas if risk for MRSA but low risk for MDR pathogens *Examples:* • Cefepime + Vancomycin OR linezolid
		Choose 3 antibiotics, one for MRSA and two for pseudomonas if risk for both MRSA and MDR pathogens *Examples:* • Piperacillin/tazobactam + ciprofloxacin + vancomycin • Cefepime + gentamicin + linezolid
Duration: 7 days (may vary depending on clinical response)		

AC Kalil, et al, Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society, *Clinical Infectious Diseases*, Volume 63, Issue 5, 1 September 2016, Pages e61–e111, https://doi.org/10.1093/cid/ciw353

Lower Respiratory Tract Infections

DISEASE STATE	COMMON PATHOGENS	EMPIRIC TREATMENT
Hospital Acq Ventilator As Pneumonias	S. Pneumoniae H. Influenzae • E. coli • Klebsiella spp	**Choose 1 antibiotic to cover pseudomonas and MSSA if low risk for MRSA or MDR pathogens** *Examples:* Cefepime or piperacillin/tazobactam **…nas if risk for** **…nas if risk for** • Piperacillin/tazobactam + ciprofloxacin + vancomycin • Cefepime + gentamicin + linezolid
Duration: 7 days (may vary depending on clinical response)		

Reminder that HCAP is no longer an IDSA recognized term/diagnosis

- Too broad of a population, not an accurate predictor of patients at risk for MDROs
- **Instead – use IDSA identified risk factors from guidelines**

AC Kalil, et al, Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society, *Clinical Infectious Diseases*, Volume 63, Issue 5, 1 September 2016, Pages e61–e111, https://doi.org/10.1093/cid/ciw353

Skin and Soft Tissue Infections (SSTI) - **Cellulitis**

CAUSES

Previous trauma to the area
Underlying lesions

PATHOGENS

S. pyogenes
S. areus
Gram negative bacilli
Anaerobes

LOCATION

Anywhere, common on the limbs and face

Stevens, et al, Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America, *Clinical Infectious Diseases*, Volume 59, Issue 2, 15 July 2014, Pages e10–e52, https://doi.org/10.1093/cid/ciu296

Skin and Soft Tissue Infections (SSTI) -**Cellulitis**

Empiric, Non-purulent		
Mild	**PO Route** Cephalexin Penicillin VK Amoxicillin Dicloxacillin	**Duration** 5-10 days
Moderate	**IV Route** Cefazolin	
Severe	Debridement with cultures **IV Route** Vancomycin + piperacillin/tazobactam	

Penicillin allergy: can use clindamycin

Stevens, et al, Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America, *Clinical Infectious Diseases*, Volume 59, Issue 2, 15 July 2014, Pages e10–e52, https://doi.org/10.1093/cid/ciu296

Skin and Soft Tissue Infections (SSTI) -**Cellulitis**

Empiric, Purulent		
Mild	Incision and drainage (I & D) only	
Moderate	Incision and drainage (I & D) and cultures **PO Route** Sulfamethoxazole/trimethoprim (Bactrim)* Doxycycline* Clindamycin* Dicloxacillin Cephalexin	**Duration** Variable
Severe	Incision and drainage (I & D) and cultures **IV Route** Vancomycin* Daptomycin* Linezolid* Dalbavancin Oritavancin	

*If community acquired MRSA suspected

Stevens, et al, Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America, *Clinical Infectious Diseases*, Volume 59, Issue 2, 15 July 2014, Pages e10–e52, https://doi.org/10.1093/cid/ciu296

Urinary Tract Infection (UTI)

DIAGNOSIS	COMMON PATHOGENS	EMPIRIC TREATMENT
Asymptomatic Bacteriuria	Any of the below	**NONE!** *Exceptions: pregnancy, endourological procedures*
Acute Uncomplicated Cystitis	*E. coli* (majority), *S. saprophyticus*, Enterococci, Proteus spp.	Nitrofurantoin 100 mg by mouth twice daily x5 days OR SMX/TMP 1 DS tablet twice daily x3 days OR Fosfomycin 3g x1 dose
Acute uncomplicated pyelonephritis	E. coli, Klebsiella, Enterobacter, Serratia, Pseudomonas, Proteus Enterococci, Staphylococci	Ceftriaxone 1-2g IV once daily OR Cipro…vice daily) OR Levof…ce daily) OR Alternative beta-lactam
Complicated UTI		
Candida in the urine	**Treatment is NOT recommended** Exceptions: symptomatic, high-risk patients include neutropenic patients, very low-birth-weight infants (<1500 g), and patients who will undergo urologic manipulation	

*category for both women AND men

Duration for cUTI: 5-7 days per updated IDSA guidelines as of 2025

Infectious Diseases Society of America. Uncomplicated Cystitis and Pyelonephritis (UTI). Clin Infect Dis 2011

Urinary Tract Infection (UTI)

DIAGNOSIS	COMMON PATHOGENS	EMPIRIC TREATMENT
Asymptomatic Bacteri	Any of the below	**NONE!** *cal procedures*
Acute Uncor Cysti		e daily x5 days lays
Acute uncor pyelonep		
Complica		e daily) daily)
Candida in the urine	**Treatment is NOT recommended** Exceptions: symptomatic, high-risk patients include neutropenic patients, very low-birth-weight infants (<1500 g), and patients who will undergo urologic manipulation	

Old Classifications

Uncomplicated UTI: Acute cystitis in afebrile nonpregnant premenopausal women with no diabetes and no urologic abnormalities

Acute Pyelonephritis: Acute kidney infection in women otherwise meeting the definition of uncomplicated UTI above

Complicated UTI: All other UTIs

New Classifications

Uncomplicated UTI: Infection confined to the bladder in afebrile women or men

Complicated UTI: infection beyond the bladder in women or men

- Pyelonephritis
- Febrile or bacteremic UTI
- Catheter-associated (CAUTI)
- Prostatitis* (*not covered by these guidelines)

Infectious Diseases Society of America. Complicated Urinary Tract Infections (cUTI): Clinical Guidelines for Treatment and Management. Clin Infect Dis 2025

Meningitis

- **Common pathogens:** *Streptococcus* pneumoniae, *Neisseria* meningitidis, and *Haemophilus* influenzae
  - Add coverage for *Listeria* monocytogenes in neonates, age >50 years and immunocompromised patients

MENINGITIS: EMPIRIC TREATMENT		
Age <1 month (neonates)	Age 1 month to 50 years	Age >50 years or immunocompromised
Ampicillin + Cefotaxime OR gentamicin	Vancomycin + Ceftriaxone OR cefotaxime	Ampicillin (for Listeria coverage) + Vancomycin + Ceftriaxone OR cefotaxime
Do not used Ceftriaxone in neonates • Can cause biliary sludging and kernicterus in neonates		

Pearls:

- If concerned for viral meningitis, acyclovir can be started to target HSV
- Dexamethasone is often started empirically then stopped when strep pneumo (adults) or Haemophilus (pediatrics) is ruled out (adults)
- Both Vancomycin and Ceftriaxone combination therapy is used to cover for penicillin-resistant strep pneumo

Infectious Diseases Society of America. Bacterial Meningitis. Clin Infect Dis 2004

Antifungals

Fungal Classifications

YEASTS	MOLDS	DIMORPHIC FUNGI
Candida spp • C. albicans • C. glabrata • C. tropicalis • C. parapsilosis • C. krusei Cryptococcus neoformans	Aspergillus spp Zygomycetes (Mucor spp)	Histoplasma capsulatum Blastomyces dermatitidis Coccidioides immitis mold in the cold yeast in the heat

Antifungals

CLASS	AGENTS	CLASS EFFECTS
Amphotericin	Amphotericin B deoxycholate (conventional) Amphotericin B Lipid Complex Liposomal Amphotericin B	ADRs: “shake and bakes:” infusion reactions, fevers, rigors hypokalemia, hypomagnesia, nephrotoxicity Monitoring: renal function, electrolytes, LFTs
Azole Antifungals*	Fluconazole (PO, IV) Itraconazole (PO) Ketoconazole (PO, topical) Voriconazole (PO, IV) Posaconazole (PO, IV) Isavuconazole (PO, IV)	• All can cause increased LFTs • All have a risk for QTc prolongation (except Isavuconazole) • All azoles are moderate-strong CYP3A4 inhibitors • Fluconazole is the only azole that requires renal dose adjustments • Itraconazole can cause heart failure • Voriconazole can cause visual changes and phototoxicity
Echinocandins	Caspofungin Micafungin Anidulafungin	ADRs: increased LFTs, (severe skin reactions with caspofungin)
Flucytosine		ADRs: dose related myelosuppression, AKI

*Note: all azole antifungals have varying spectrums of coverage

Fungal Infection – Empiric Treatment

PATHOGEN	PREFERRED REGIMEN	ALTERNATIVE REGIMEN
Candida albicans Oropharyngeal infection (thrush)	Fluconazole	Nystatin
Candida albicans Esophageal, other infections	Fluconazole	Echinocandin
Candida krusei and glabrata	Echinocandin	Amphotericin B
Aspergillus (invasive)	Voriconazole, Posaconazole	Amphotericin B, isavuconazole
Cryptococcus neoformans meningitis	Amphotericin B + flucytosine	Fluconazole +/- flucytosine (not ideal)

Reminder: do NOT treat yeast on a UA or fungal/yeast growth on a urine culture UNLESS : symptomatic, neutropenic, very low-birth-weight infants (<1500 g), or undergoing urologic manipulation

Infectious Diseases Society of America. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Clin Infect Dis 2020
Infectious Diseases Society of America. Candidiasis. Clin Infect Dis 2025

Antivirals

ANTIVIRAL	COMMON INDICATION	PEARLS
Acyclovir **Valacyclovir**	Herpes Simplex Virus (HSV) Varicella Zoster Virus (VZV)	**Warnings** • Needs renal dose adjustment • Acyclovir requires adequate hydration to reduce risk of renal tubular damage **Side Effects** • Increased LFTs • Neutropenia • Increased Scr/BUN with crystal neuropathy **Monitoring** • Renal function, LFTs, CBC
Ganciclovir **Valganciclovir**	Cytomegalovirus (CMV)	**Boxed Warnings** • Myelosuppression, carcinogenic, teratogenic **Side Effects** • Thrombocytopenia • Neutropenia • Leukopenia **Monitoring** • CBC with differential • Scr • Retinal exam (valganciclovir)

Questions