Antibiotics

Sources

- Keith Armitage, MD, MACP: https://www.youtube.com/watch?v=3XhBMg499_w
- http://stritch.luc.edu/lumen/meded/therapy/pharm1_blockiv_2011.pdf
- David C. Nguyen, MD
- Clinical Utility Of Oral Cephalosporins – Anthony Vecchione, PharmD
- Antibiotics Review for Students, Interns, and Residents – MGH Internal Medicine

Key

* – Important to know (for non-ID docs)

(C) – Bactericidal

(S) – Bacteriostatic

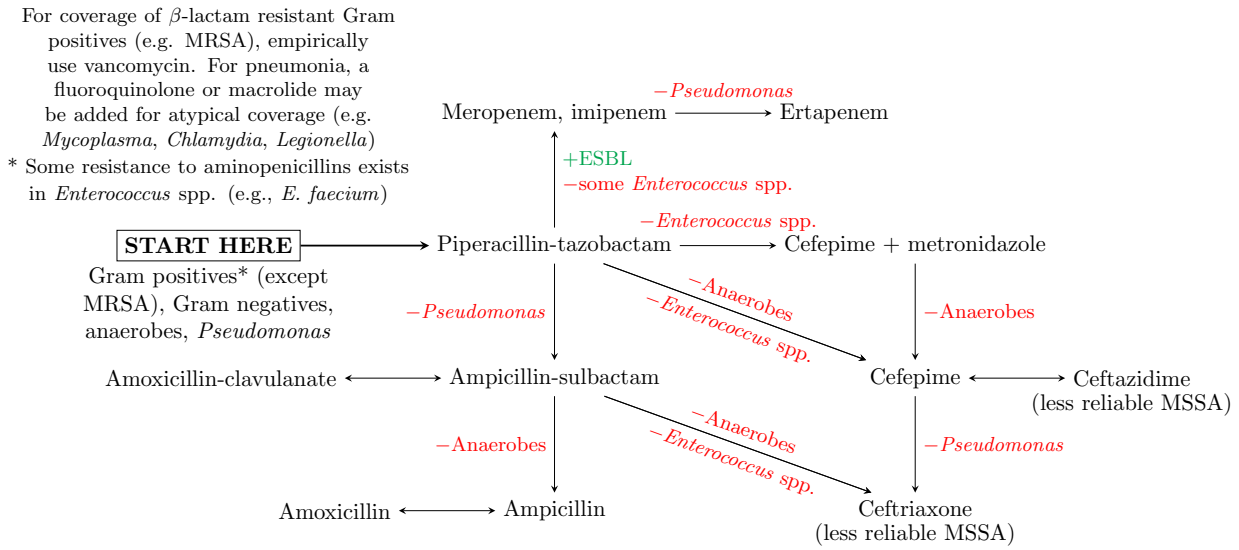
⊕ – Good coverage

⊘ – Iffy coverage

⊖ – Bad coverage

- **Mechanism of action:**
  - [CW] – Cell wall synthesis inhibitor
  - [Prot] – Protein synthesis inhibitor
  - [NA] – Nucleic acid synthesis inhibitor
  - [Met] – Metabolic inhibitor
- **Mechanism of resistance:**
  - (Enz) – Enzymatic degradation of drug
    - (β) – β-lactamase
  - (PBP) – Mutation of penicillin binding protein
  - (Mut) – Mutation of the target
  - (Conc) – Decrease in intracellular concentration (e.g., mutation in porins, development of efflux pumps)
  - (Seq) – Sequestration of drug by proteins

Overview



Not a comprehensive understanding of antibiotics but allows basic moves for empiric coverage with the major organisms in mind.

V1.5
David C. Nguyen, 2019

Drugs

Penicillins C CW β PBP Conc

Penicillin C CW
- Still good against non-pneumococcal *Strep* (e.g., GAS, GCS) due to lack of resistance
- Resistance is mediated by PBPs, *not* β-lactamases, so resistance is overcome by increasing the dose, not by using β-lactamase inhibitors

Ampicillin C CW

Anti-staphylococcal:
- Methicillin C CW
- Nafcillin C CW
- Oxacillin C CW
- Dicloxacillin C CW

Anti-pseudomonal:
- Piperacillin/tazobactam C CW
- Ticarcillin/clavulanate C CW

	Gram positive					Gram negative				
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*	Anaerobe	Atypical	Comments
Penicillin	+++	⌀	⌀	+	+	+	⌀	++(mouth)	+++ syphilis, *Leptospira*	GAS, syphilis
Amox/amp	++	⌀	⌀	+++	+++	++	⌀	+	+Lyme	UTI, *Listeria*, *Enterococcus*
Augmentin/Unasyn	++	++	⌀	+++	+++	+++	⌀	+++	⌀	Sinusitis, asp. PNA, bites, cholangitis
Nafcillin/oxacillin	+	++++	⌀	⌀	⌀	⌀	⌀	⌀	⌀	Invasive MSSA
Zosyn	++	++	⌀	+	+	++++	++++	++++	⌀	*Pseudomonas*, GI, HCAP

Drug of choice

Cephalosporins (C) [CW] (β) PBP Conc

- Not susceptible to β-lactamase

Generation 1 (C) [CW] – cefazolin*

- ⊕ *Staph* (MSSA)
- ⊕ *Strep*
- ⊘ Gm− (*E. coli*, *Proteus*, *Klebsiella*)
- ⊖ Respiratory pathogens (*Moraxella*, *H. influenzae*, *S. pneumoniae*)
- ⊖ Anaerobes
- Bad CSF penetration

Generation 2 (C) [CW] (not important for non-ID docs) – cefuroxime, cefoxitin, cefotetan

- ⊕ *Staph* (MSSA)
- ⊕ *Strep*
- ⊕ Respiratory pathogens (*Moraxella*, *H. influenzae*, *S. pneumoniae*)
- ⊕ Anaerobes
- ⊘ Gm−
- ⊖ *Pseudomonas*
- ⊖ Enterococcus
- Good CSF penetration

Generation 3 (C) [CW] – ceftriaxone*

- ⊕ *Staph* (MSSA)
- ⊕ *Strep*
- ⊕ Respiratory pathogens (*Moraxella*, *H. influenzae*, *S. pneumoniae*)
- ⊕ Anaerobes
- ⊕ Gm−
- ⊘ *Pseudomonas*
- ⊖ Enterococcus
- Good CSF penetration

Generation 3.5 (C) [CW] – ceftazidime

- ⊕ Gm−
- ⊕ *Pseudomonas*
- ⊖ Gm+

Generation 4 (C) [CW] – cefepime*

- ⊕ Gm−
- ⊕ *Pseudomonas*
- ⊕ *Enterobacter*
- ⊕ Gm+

- "Nosocomial cephalosporin"
- Neurotoxic (encephalopathy)

Generation 5 Ⓒ CW – ceftaroline*

- ⊕ MRSA
- ⊕ Enterococcus
- ⊖ *Pseudomonas*
- ⊖ Healthcare-associated Gm−

Penicillin Allergy

- If immediate type I hypersensitivity (IgE) → not safe to give cephalosporin
- Otherwise (other allergy or no allergy) → safe

	Gram positive					Gram negative				
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*	Anaerobe	Atypical	Comments
1 Cefazolin/cephalexin	+++	++++	∅	∅	∅	+	∅	∅	∅	Skin, cellulitis
2 Cefotetan	++	++	∅	∅	∅	++	∅	++	∅	Abdominal/pelvic infections
3 Ceftriaxone	++	++	∅	∅	∅	+++	∅	∅	CNS or cardiac Lyme	q24h dosing convenient; UTIs; CAP w/ azithro
3 Cefpodoxime	++	++	∅	∅	∅	++	∅	∅	∅	PO, similar spectrum as ceftriaxone
3 Ceftazidime	+	+	∅	∅	∅	+++	+++	∅	∅	Febrile neutropenia
4 Cefipime	++	++	∅	∅	∅	++++	+++	∅	∅	Broad GNR coverage
5 Ceftaroline	++	+++	++++	∅	∅	+++	∅	∅	∅	MRSA

Carbapenems (C) [CW] Conc Enz PBP

- Not what they *do* cover, but what *don't* they cover?

Imipenem (C) [CW]

- ⊘ some Gm− rods
- ⊖ MRSA, VRE

Meropenem (C) [CW]

- Safer than imipenem (esp., for people with seizure disorder)

Doripenem (C) [CW]

- Same as meropenem

Ertapenem (C) [CW]

- ⊖ *Pseudomonas*
- ⊖ *Enterococcus*
- Narrower than other carbapenems
- The once a day carbapenem

	Gram positive					Gram negative				
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*	Anaerobe	Atypical	Comments
Meropenem	+++	+++	∅	+	∅	++++	+++	++++	+	Use for ESBL
Ertapenem	+++	+++	∅	∅	∅	++++	∅	++++	+	No *Pseudomonas*, but convenient dosing

Monobactams C CW β Conc

- No immunologic cross-reactivity with β-lactams!

Aztreonam C CW

- ⊕ Aerobic Gm− rods
- ⊖ Gm+
- ⊖ Anaerobic

	Gram positive				Gram negative		Anaerobe	Atypical	Comments
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*			
Aztreonam	∅	∅	∅	∅	∅	+++	++	∅	∅	Ok in severe penicillin allergy

Aminoglycosides Ⓒ [Prot] Conc Enz Mut

- Most dangerous of the commonly used antibiotics; safe for a few days, not for >10–14
  1. Nephrotoxicity

  2a. Ototoxicity

  2b. Vestibular* (the least reversible of the toxicities)

  3. Neuromuscular
- Toxicities usually temporary (if medication stopped early enough)
- Dosing: once per day
  - ▷ Except in neuropenic fever (controversial)

⊕ Gm− aerobes

⊖ Anaerobes

Gentamicin Ⓒ [Prot], tobramycin Ⓒ [Prot] → community-acquired infections

Amikacin Ⓒ [Prot] → nosocomial infections, resistant to aminoglycosidases

	Gram positive					Gram negative				
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*	Anaerobe	Atypical	Comments
Gemtamicin	++	++	++	∅	∅	+++	++	∅	Plague, *F. tularensis*	*Strep* or *Enterococcus* endocarditis (in combination)
Tobramycin	+	+	+	∅	∅	+++	+++	∅	∅	VAP (in combination)
Amikacin	+	+	+	∅	∅	++++	++	∅	∅	Tough UTIs

Gm+ agents

Vancomycin (C) [CW] (Mut)

- Red man syndrome is an administration error, not an allergy

Linezolid (S) [Prot] (Mut)

- Toxicities if used $>$ 2 weeks

Daptomycin (C) [CW] (Conc)

- Inactivated by surfactant (cannot be used for lung infections)

Tigecycline (S) [Prot] (Conc) (Seq) (Enz)

- ⊖ *Pseudomonas*
- ⊖ *Proteus*

Doxycycline (S) [Prot] (Conc) (Seq) (Enz)

Trimethoprim/sulfamethoxazole (TMP/SMX) (C) [Met] (Mut)

- ⊕ MRSA
- ⊕ Gm−
- ⊖ *Strep pneumoniae*
- ⊖ GAS
- Allergic toxicity (sulfa → SJS/TEN)

Rifampin (C) [Prot] (Mut)

- ⊕ Biofilm-associated infection
- High resistance rates with monotherapy; should be paired with another drug
- Revs up CYPs

Clindamycin (S) [Prot] (Mut)

- ⊕ *Staph*
- ⊕ *Strep*
- ⊕ Anaerobes
- ⊘ MRSA
- ⊖ Oral infections (high resistance)

Metronidazole (C) [NA]

- ⊕ Obligate anaerobes
- ⊕ Protozoa
- Can be paired with ceftriaxone (which covers facultative anaerobes)

	Gram positive					Gram negative				
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*	Anaerobe	Atypical	Comments
Vancomycin	+++	++	++++	+++	∅	∅	∅	*C. diff* if PO	∅	Measure troughs
Linezolid	+++	+++	++++	+++	+++	∅	∅	∅	∅	MRSA, VRE. Marrow toxicity
Daptomycin	+++	+++	++++	+++	+++	∅	∅	∅	∅	MRSA, VRE. Don't use for lung infection
Tigecycline	+++	+++	+++	+++	+++	+++	∅	+++	∅	3rd line, may increase mortality
Doxycycline	++	++	++	+	+	∅	∅	∅	++++	CAP, atypical infections
TMP-SMX	+	+++	++	∅	∅	++	∅	∅	*P. jirovecii*, *Nocardia*	Elevates K^+ and Cr
Clindamycin	+++	∅	++	∅	∅	∅	∅	+++	*Babesia*	GI side effects common
Nitrofurantoin	+	∅	∅	+	+	++	∅	∅	∅	Uncomplicated UTI
Metronidazole	∅	∅	∅	∅	∅	∅	∅	++++, including *C. diff*	Some protozoa	Good anaerobe coverage
Colistin (polymixin E)	∅	∅	∅	∅	∅	++++	++++	∅	∅	GNR coverage of last resort
Rifaximin	∅	∅	∅	∅	∅	++	∅	∅	∅	Hepatic encephalopathy

Quinolones (C) [NA]

Ciprofloxacin (C) [NA]

- ⊕ Gm− rods
- ⊕ *Pseudomonas*

Levofloxacin (C) [NA]

- ⊕ Gm− rods
- ⊕ *Pseudomonas*
- ⊕ *Strep pneumoniae*

Moxifloxacin (C) [NA]

- ⊕ Gm+
- ⊖ Gm−

	Gram positive					Gram negative				
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*	Anaerobe	Atypical	Comments
Ciprofloxacin	∅	+	+	∅	∅	+++	++	∅	∅	GI, GU infections
Levofloxacin	++	++	+	∅	∅	+++	++	∅	+++	Pneumonia, expensive

Macrolides (S) [Prot] Conc Mut

Erythromycin (S) [Prot] → GI motility disorders

Clarithromycin (S) [Prot]

- ⊕ *Strep pneumoniae*

Azithromycin (S) [Prot]

- ⊕ *Chlamydia* (intracellular pathogen)
  - High intracellular concentration, low serum concentration

	Gram positive					Gram negative				
	Strep	MSSA	MRSA	VSE	VRE	Normal	*Pseudomonas*	Anaerobe	Atypical	Comments
Azithromycin	++	+	∅	∅	∅	+	∅	∅	+++	CAP, chlamydia

Anti-fungals

Azoles CW

Ketoconazole CW

Fluconazole CW

- ⊕ *Candida*

Itraconazole CW

Voriconazole CW

- ⊕ *Aspergillus*
- ⊖ Molds

Posaconazole CW

Isavuconazole CW

Amphotericin B CW

- For ID, BMT docs

Echinocandins CW

Micafungin CW

Diseases

UTI

Bugs

- *E. coli*
- *Klebsiella* spp.
- *Proteus mirabilis*

Drugs

- AAP + IDSA guidelines
  - ▷ Cephalexin (1st)
  - ▷ Cefpodoxime (3rd)
- AAP guidelines
  - ▷ Cefprozil (2nd)
  - ▷ Cefuroxime (2nd)
  - ▷ Cefixime (3rd)
- IDSA guidelines
  - ▷ Cefdinir (3rd)

- AAP guidelines, 2-24 months old (2011)
  - ▷ Cefixime 8 mg/kg daily
  - ▷ Cefpodoxime 10 mg/kg/day divided BID
  - ▷ Cefprozil 30 mg/kg/day divided BID
  - ▷ Cefuroxime 20-30 mg/kg/day divided BID
  - ▷ Cephalexin 50-100 mg/kg/day divided QID
  - ▷ *Not* cefdinir

Community-acquired Pneumonia

Bugs

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Moraxella catarrhalis*
- *Staphylococcus aureus*

Drugs

-

	Penicillin-sensitive *S. pneumoniae*	Penicillin-intermediate *S. pneumoniae*	*H. influenzae*	*M. catarrhalis*
Cefdinir	⊘	⊖	⊕	⊕
Amoxicillin	⊕	⊕	⊘	⊖
Amox-clav	⊕	⊕	⊕	⊕
Ceftriaxone	⊕	⊕	⊕	⊕

- Amoxicillin/amoxicillin-clavulanate 90 mg/kg/day divided TID mimics ceftriaxone (*S. pneumoniae*, *H. influenzae*, *M. catarrhalis*)
  - ▷ Oral cephalosporins are inferior
- If PCN-allergic (IDSA)
  - ▷ Trial cephalosporin with good *S. pneumoniae* coverage (e.g., cefpodoxime, cefprozil, cefuroxime)
  - ▷ Cefdinir *only* for *H. influenzae*

Osteomyelitis

Bugs

- *S. aureus*
- *Kingella kingae* (toddler, preschool)
- *S. pyogenes*

Drugs

	MRSA	MSSA	*Kingella kingae*	*S. pyogenes*	Bone penetration
Cephalexin	⊖	⊕	⊖	⊕	Excellent
Cefprozol	⊖	⊕	⊕	⊕	?
Cefuroxime	⊖	⊕	⊖	⊕	Good
Cefdinir	⊖	⊕	⊕	⊕	?
Cefpodoxime	⊖	⊕	⊕	⊕	Excellent
Cefixime	⊖	⊖	⊕	⊕	?
Ceftibuten	⊖	⊖	⊕	⊕	?
TMP-SMX	⊕	⊕	⊕	⊕	Excellent
Clindamycin	⊕	⊕	⊖	⊕	Excellent
Amoxicillin	⊖	⊖	⊕	⊕	Excellent
Amox-clav	⊖	⊕	⊕	⊕	Good

Thabit, A. International Journal of Infectious Diseases. 4/2019.

Pseudomonas

- PO
  - Fluoroquinolones
- IV
  - Piperacillin-tazobactam
  - Ceftazidime
  - Cefepime
  - Ceftolozane-tazobactam
  - Aztreonam
  - Aminoglycosides
  - Carbapenems (not ertapenem)
  - Colistin (polymixin E)