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

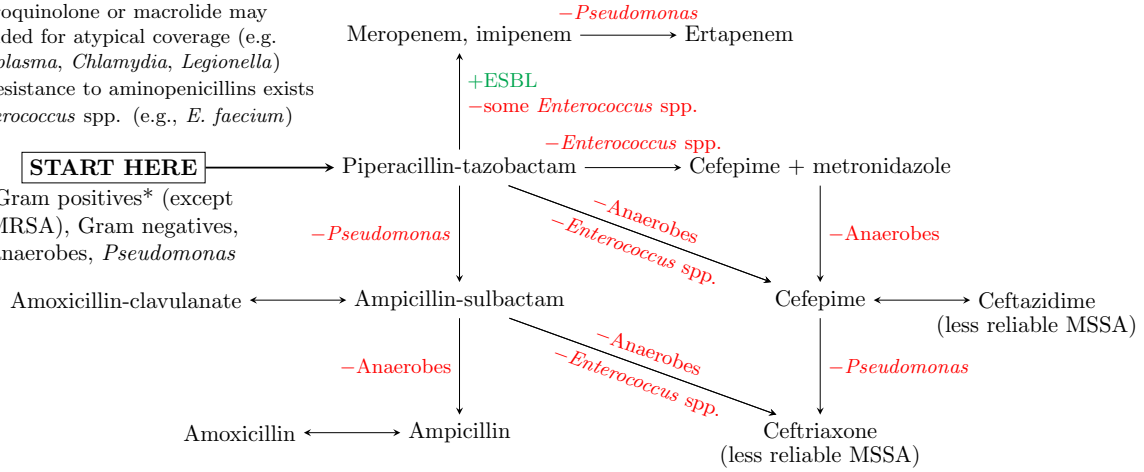
Key

- * – 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

For coverage of β-lactam resistant Gram positives (e.g. MRSA), empirically use vancomycin. For pneumonia, a fluoroquinolone or macrolide may be added for atypical coverage (e.g. *Mycoplasma*, *Chlamydia*, *Legionella*)

* Some resistance to aminopenicillins exists in *Enterococcus* spp. (e.g., *E. faecium*)



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

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

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 (C) [CW] – ceftaroline*

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

Penicillin Allergy

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

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

Monobactams (C) [CW] β Conc

- No immunologic cross-reactivity with β-lactams!

Aztreonam (C) [CW]

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

Aminoglycosides (C) [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 (C) [Prot], tobramycin (C) [Prot] → community-acquired infections

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

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)

Quinolones (C) [NA]

Ciprofloxacin (C) [NA]

- ⊕ Gm− rods
- ⊕ *Pseudomonas*

Levofloxacin (C) [NA]

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

Moxifloxacin (C) [NA]

- ⊕ Gm+
- ⊖ Gm−

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

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]