

Antibiotics – A Brief Overview for Team Medicine

General questions to ask:

- What is the likely source of infection?
- What is the likely organism based on the source, where the patient is from, comorbidities? *Cystic Fibrosis*
- Which antibiotics would cover the bugs I'm concerned about based on the answers to above questions?
- Will the antibiotic I prescribe reach the intended target (route of administration, penetration of organ system)?
- Are there any contraindications to the antibiotic I want to prescribe (allergies, medication interactions), do I need to adjust the dose based on renal function, and will my patient take it (compliance, cost, availability) if prescribed? *PO/IV different.*

Don't guess about the antibiotic to use --- look it up or ask for help.

Don't delay giving antibiotics if the patient needs them (ex: septic, meningitis) and ensure appropriate cultures drawn prior to administration.

Start empiric therapy and when cultures and sensitivities return, switch to more targeted therapy.

Classes of antibiotics:

β-lactams

Penicillins

- inhibit cell wall synthesis by binding to penicillin-binding proteins responsible for peptidoglycan cross-linkage

- 1st generation – Pen V (po) and Pen G (iv) – excellent gram+ve cocci activity but *S. aureus* and *Strep pneumoniae* often resistant, *syphilis*; high resistance of Staph

- 2nd generation – amoxicillin (po) and ampicillin (iv) – same coverage as 1st generation plus some gram-ve (H. flu, E. coli, Proteus) and enteric gram+ve like *enterococcus*. *only drug that covers enterococcus.*

- 3rd generation – cloxacillin (po/iv) – same coverage as 1st generation with good *S. aureus* but be wary of *MRSA*; *Anti-staphylococcal* (same as methicillin). *iv more effective.* *β-lactamase inhibitor.* *(good for MSSA).*

- 4th generation – piperacillin (iv) often combined with tazobactam (Pip/Tazo) a β-lactamase inhibitor

Anti-pseudomonal - same coverage as 3rd generation plus pseudomonas and anaerobes

- also have combination of amoxicillin + clavulanic acid (a β-lactamase inhibitor) which provides better gram-ve coverage than amox alone *(equivalent to Pip-Tazo).*

β-lactams

Cephalosporins

- inhibit cell wall synthesis

- 1st generation – cephalexin/keflex (po), cefazolin/ancef (iv) – excellent gram+ve cocci activity with some activity against gram-ve rods (*strep + staph!*) *better tissue penetration.*

- 2nd generation – cefuroxime (iv/po), cefotetan (iv) – better gram-ve coverage } *don't bother learning*

- 3rd generation – ceftriaxone (iv) - excellent gram-ve coverage with some gram+ve coverage } *learn pseudomonas, enterococcus, anaerobes*

- 3rd generation – ceftazidime (iv) – excellent gram-ve coverage and antipseudomonal coverage

- 4th generation - cefepime - better gram *(+ve)*

- 5th generation



Vancomycin *→ sits in the gut. → not a β-lactam.*

- inhibits cell wall synthesis, renal toxic, ototoxic - tinnitus.

- excellent gram+ve coverage, including MRSA, except for VRE (vancomycin resistant enterococcus) *or unresolvid.*

- if given too quickly, can cause red man syndrome (secondary to histamine release; not a true allergy); for C. (gram +ve). *diff, needs to be given orally; needs renal adjustment*

disolvent ↓ BP *histamine release & give fluids.*

avoid E test (cause vertigo + tinnitus). *ie aminoglycosides*

Carbapenems (new!)

- meropenem, imipenem (iv) – provide very broad coverage; gram+ve (Strep, Staph, Enterococcus, Listeria),

gram-ve including pseudomonas, anaerobes, ESBL: extended spectrum β-lactamases: mutated, + resistant to

- usually used exclusively in ICU *clavulin + tazobactam.*

- *meropenem* - not pseudomonas.

Pip

gram +ve

Ribosome Inhibitors

Macrolides

- interfere with protein synthesis at 50S ribosomal subunit
- erythromycin (po/iv), clarithromycin (po), azithromycin (iv/po) - most gram+ves, some gram-ves (H. flu) and atypical pneumonias (mycoplasma, legionella, Chlamydia)
- intracellular in cells → not all antibiotics, can penetrate.

Clindamycin

- inhibits protein synthesis at 50S ribosomal subunit (binds the ribosomes)
 - good for gram+ve cocci (S. aureus and S. pneumo) and anaerobes (for oral bugs; dentists love!).
 - higher incidence of C. diff complications.
 - (iv and po) essentially the same bioavailability
- Toxic Shock Syndrome: immune response from Group A Strep exotoxin.

Aminoglycosides (bad! → kill kidneys + ears)

- inhibit protein synthesis at 30S ribosomal subunit
- gentamicin, tobramycin - aerobic gram -ve and pseudomonal coverage
- can cause nephrotoxicity and ototoxicity; if long term use, should get baseline audiometry and monitor creatinine
- dose adjustment based on CrCl; once daily dosing preferred - ↓ toxicity, but ↓ effectiveness.
- not monotherapy, usually adjuncts.

Tetracyclines

- inhibit protein synthesis at 30S ribosomal subunit, good for weird + wonderful.
- tetracycline, doxycycline, minocycline - useful for lyme, brucellosis, rickettsia, mycoplasma, Chlamydia, acne

Dirty Drug

Septra (Trimethoprim/sulfamethoxazole) TMP-SMX + many side effects!

- inhibits folic acid synthesis and therefore nucleic acid synthesis, used a lot in HIV patients.
- covers gram+ve, gram-ve and atypical respiratory pathogens; used for pneumocystis, toxoplasma, nocardia
- may cause hypoglycemia. Also hyperkalemia, hemolytic anemia in G6PD, bone marrow suppression, SJS/TEN
- conversion from iv → oral complicated.

DNA

Metronidazole (Flagyl)

- interacts with bacterial DNA causing bacterial death
- good anaerobic coverage; iv and po
- used orally to treat C. diff, giardia, entamoeba, trichomonas
- don't take with alcohol - disulfiram reaction

DNA synthesis inhibitor

Fluoroquinolones (good atypical coverage. Mycoplasma, Legionella) → bacteriostatic, less stronger than Aminoglycosides.

- bind DNA gyrase and therefore inhibit DNA synthesis
- Ciprofloxacin** (iv/po) - gram-ve coverage (all including pseudomonas); only oral therapy against pseudomonas
- poor gram+ve and anaerobic coverage so not good in pneumonia (anything upper respiratory) - COPD!
- atypical coverage including legionella, mycoplasma, Chlamydia
- Levofloxacin** - 1st generation respiratory fluoroquinolone that provides gram+ve coverage for Strep, gram-ve coverage (all but only moderate activity against pseudomonas), atypicals and mycobacteria (some anti-TB activity and can sterilize cultures --- Therefore if even slight chance may be TB, don't use levo)
- Moxifloxacin** - same coverage as levofloxacin but also covers anaerobes

good for aspiration. pneumonia.

some activity against TB - however sterilizes cultures in sputum!

