Cell Wall Attackers

Beta Lactams

MoA: binds penicillin binding protein

Concentration increased by probenecid

All can cause neutropenia, LFT derangement, N&V

Penicillins

Benzylpenicillin / phenoxymethylpenicillin
- Spectrum: streptococci, most *Enterococcus faecalis*, oral anaerobes, spirochetes

Aminopenicillins (amoxicillin, ampicillin)
- Spectrum: improved Gram-negative cover, slightly better for *Enterococcus faecalis*

Anti-staphylococcal penicillins (flucloxacillin)
- Resistant to staphylococcal penicillinases
- Spectrum: MSSA, streptococci. No enterococcus or Gram-negative cover
- AEs: cholestatic hepatitis (flu- > di-), AIN (di- > flu-)

Penicillin / BLI Combinations

Amoxicillin-clavulanic acid
- Spectrum: broad Gram-negative and Gram-positive cover

Piperacillin-tazobactam
- Spectrum: broad including *Pseudomonas aeruginosa*

Cephalosporins

1st generation (cefazolin, cefalexin)
- Spectrum: GPCs (not *Enterococcus* spp.), some Gram-positive anaerobes, most *E. coli* and *K. pneumoniae*
- Used as first-line surgical prophylaxis, generally

2nd generation (cefoxitin, cefuroxime)
- Spectrum: adds *H. influenzae* and some more Gram-negatives. Cefoxitin has good anaerobic cover.
- Cefuroxime often used as a PO step-down from CRO

3rd generation (ceftriaxone, ceftazidime)
- Spectrum: less Gram-positive activity, but better Gram-negative cover. Ceftazidime has no gram-positive coverage, but kills *Pseudomonas aeruginosa*
- AEs: hepatitis, pancreatitis

4th generation (cefepime)
- Spectrum: like ceftazidime + cefazolin

5th generation
Ceftolozane-tazobactam
- Spectrum: very broad including *Pseudomonas* sp.
- AEs: hypokalaemia, abdominal pain, VTE

Ceftaroline
- Spectrum: Gram-negatives, broad Gram-positive cover (including MRSA/VISA/hVISA/VRSA)
- AEs: neutropenia

Carbapenems

Overview
- Inactive against MRSE, VRE, *E. faecium*, *Stenotrophomonas maltophilia*, *Burkholderia cepacia,* atypicals
- AEs: decreases valproate concentration, neurotoxicity

Ertapenem
- Spectrum: inactive against *Pseudomonas* sp. and *Acinetobacter* sp.
- Poor penetration into intraabdominal abscesses

Imipenem-cilastatin
- Spectrum: active against *Enterococcus faecalis*

Meropenem
- Good CNS penetration

Monobactams

Aztreonam
- Spectrum: aerobic Gram-negatives (including *Pseudomonas aeruginosa*)
- AEs: rash, taste disturbance, thrombophlebitis

Glycopeptides

Vancomycin, teicoplanin
- MoA: Prevents formation of peptidoglycan polymers by binding to D-Ala-D-Ala terminus of precursors
- Spectrum: virtually all Gram-positive bacteria
- Requires TDM
- AEs: immune-mediated thrombocytopenia, ototoxicity, nephrotoxicity, Red-man syndrome, neutropenia

Lipopeptides

Daptomycin
- MoA: forms transmembrane channels
- Spectrum: virtually all Gram-positive bacteria
- Inactivated by lung surfactant, poor CNS penetration
- AEs: rhabdomyolysis (monitor CK), PN

Fosfomycin

MoA: inactivates MurA -> inhibits cell wall biogenesis

Spectrum: very broad aerobic cover, resistance develops rapidly

(Usually) only used for urinary tract infections

Ribosome Inhibitors

30S Subunit Inhibitors

Aminoglycosides

Gentamicin, amikacin, tobramycin
- Spectrum: most aerobic Gram-negatives
- AEs: ototoxicity, nephrotoxicity
- Requires monitoring of AEs if on prolonged therapy

Tetracyclines

Doxycycline, minocycline
- Spectrum: Rickettsia, atypicals, some typical cover (both Gram-positive and Gram-negative), NTM
- AEs: dental staining, only salfe in first 18 weeks of pregnancy, photosensitivity

Glycyclines

Tigecycline
- Spectrum: NTM, MRSA, VRE, VISA, gram-negatives
- Studies have shown increased mortality when compared with other antimicrobials for non-NTM infections
- AEs: severe N&V, diarrhoea, LFT derangement.

50S Subunit Inhibitors

Lincosamides

Clindamycin, lincomycin
- Spectrum: most Gram-positives (except *Enterococcus* sp.), most anaerobes
- High bioavailability
- Highest rates of *C. difficile* among all antibiotics
- Often used for anti-toxin effect with GAS infections
- AEs: diarrhoea, N&V, abdominal pain

Macrolides

Azithromycin, clarithromycin, roxithromycin
- Spectrum: Gram-positives (not enterococci), some gram-negatives, atypicals
- Immunomodulatory / anti-inflammatory effects
- Reduces biofilm production in mucoid *P. aeruginosa*
- AEs: QT prolongation, N&V, abdominal pain

Oxazolidinones

Linezolid
- Spectrum: “all” Gram-positives
- 100% bioavailable
- AEs: mitochondrial toxicity, serotonin syndrome

Nucleic Acid Inhibitors

Quinolones

MoA: blocks DNA gyrase and topoisomerase IV
Highly bioavailable
Separate from supplements/antacids/feeds
AEs: connective tissue inflammation, PN, worsens myasthenia gravis, N&V

Ciprofloxacin

Spectrum: Gram-negatives including *P. aeruginosa*

Moxifloxacin

Spectrum: Gram-negatives (not *P. aeruginosa*), Gram-positives (particularly streptococci), respiratory anaerobes

Nitroimidazoles (metronidazole)

Spectrum: anaerobes, protozoa | 100% bioavailable
AEs: neurotoxicity particularly PN, increaseas 5-FU toxicity, metallic taste in mouth

Enzyme Inhibitors

Sulfonamides

Competitive inhibitor of bacterial folate production

Trimethoprim-sulfamethoxazole

Spectrum: Gram-positives, Gram-negatives (including *Stenotrophomonas maltophila*), Amp-C-producers
100% bioavailable
AEs: haemolysis if G6PD deficient, avoid in pregnancy, renal

Quick Reference

MRSA Cover

Oral: doxycycline, clindamycin, trimethoprim-sulfamethoxazole, linezolid, some combination therapies (rifampicin-fusidin, rifampicin-ciprofloxacin)
IV: vancomycin, teicoplanin, daptomycin, ceftaroline

Pseudomonas sp. Cover

Remember that ‘I’ means sensitive to increased dose!
Oral: ciprofloxacin
IV: piperacillin-tazobactam, ceftazidime, cefepime, meropenem, imipenem, ceftolozane-tazobactam, aztreonam