Protein Synthesis Inhibitors

Tetracyclines

* Doxycycline, Minocycline, demeclocycline, Tetracycline.

Mechanism:
bind reversibly to 30S subunit & prevent binding of tRNA to mRNA

Antibacterial spectrum:
BACTERIOSTATIC
G(+) cocci G(+) rods
G(-) cocci protozoa
spirochetes mycobacteria
Chlamydia.

*Doxycycline ⇒ chlamydia (common) & Acne.

treatment of:
Lyme Disease
Mycoplasma pneumoniae
Cholera
Chlamydial infections.
Rocky Mountain spotted fever.

*resistance to one Tetracycline doesn't confer ↑ to all ↑'s. (all 3 Mechanisms of resis.)

* pharmacokinetics:
1) Absorption: oral
Doxy & mino → also IV
Tetra → Not w/ Dairy products.
2) Distribution:
concentrate in: liver, bile, kidney, gingival fluid, skin, calcified tissue.
✓ Most body fluids.
CSF → Mino & Doxy-. / cross placental barrier.
Saliva & tears → Mino-
* meningococcal carrier state eradication
3) Elimination: Tetra → unchanged
Mino → hepatic Metabolism / urine
Doxy → bile → faeces.

*AE: Gastric discomfort, Calcified tiss. deposition, hepatotoxicity, phototoxicity, (esp tetra & demeclo.) vestibular dysfunction, pseudotumor cerebri.

Glycocyclines

* Tigecycline.

bind reversibly to 30S subunit →

*derivative of Minocycline.

Antibacterial Spectrum:
MRSA VRE
Multidrug-resistant Streptococci
Extended-spectrum-β-lactamase-producing G(-) bacteria
Acinetobacter baumanni
Anaerobics.

treatment of: cSSTI
✓ complicated skin & soft tiss. inf.
✓ complicated intraabdominal inf.

*resistance: efflux.

*AE:
Nausea & vomiting
acute pancreatitis & death.
↑ liver enzymes & serum creatinine
other AE similar to tetracyclines
↓ warfarin clearance, ↑ PT T.

pharmacokinetics:
IV
Large Vd → low [plasma]
Biliary/faecal
(No adjustment for renal impairment, dose reduction for Hepatic dysfunction).

Contraindicated in:
Pregnant/breastfeeding.
Children < 8 yo.

Aminoglycosides

* Amikacin, Gentamicin, Neomycin, Streptomycin, Tobramycin

bind to 30S subunit
1. interfere w/ Assembly of ribosome.
2. complete ribosome misreads mRNA.
* O_2-dependent system ↳ transportation *

*BACTERICIDAL (unique).

* Antibacterial spectrum:
Aerobic
G(-) Bacilli
* P. Aeruginosa
K. pneumoniae
Enterobacter.
Enterococcus faecalis & faecium (only synergy w/ β-Lactam) + G(+) cocci

* Concentration-dependent
Cmax = 8-10x MIC.

* PAE * *
Large dose, once daily (↓ Nephrotoxicity)

Tularaemia.

+NO crossresistance.
Amikacin less vulnerable to inactivating enzymes.

*Resistance: ↓uptake, efflux, enzymes.
Amikacin less vulnerable to ↑

pharmacokinetics:
1) Absorption: highly polar, parenterally,
Neomycin → orally or topically (due to Nephrotoxicity)
2) Distribution: hydrophilic, dose based on LBM, CNS → intrathecal, cross placental barrier.
3) Elimination: 90% unchanged in urine. Accumulation in Renal dysfunction.

*AE: elderly more susceptible.
1. Ototoxicity
2. Nephrotoxicity
3. Neuromuscular paralysis
4. Allergic rxns.

AE:
① gastric distress & Motility → ↓
② Ototoxicity → ↓AA
③ Cholestatic jaundice
④ prolong QTc
⑤ ↑ Digoxin.
⑥ hepatotoxicity ⇒ Telithro

Macrolides & Ketolides

* Erythromycin, Azithromycin Clarithromycin, Telithromycin

bind to 50S subunit & inhibit translocation of tRNA & transpeptidation.

*Clarithromycin → methylated deriv.
Azithromycin → larger lactone ring.
Telithromycin → semisynthetic deriv.

* BACTERIOSTATIC.
similar binding site to Clindamycin & Chloramphenicol.

* Antibacterial Spectrum:
1) Erythro → same as penicillin G
2) Clarithro → ↑ + H. Influenzae. Legionella, H. Pylori, Chlamydia, Moraxella, Ureaplasma.
3) Azithro → more active @ Moraxella, H. Influenzae, DOC for Chlamydia Trachomatis urethritis, Mycobacterium Avium * *
4) Telithro → ↑ same.
↳ Neutralize resistance mechanisms.

*resistance: efflux, ↓influx, ↓50S affinity, erythromycin esterases in G(+) ↑ in G(-).
* cross-resistance except Telithro
* Pharmacokinetics:
1) Administration: oral, E & A also IV.
C & A & T → stable to gastric Acid
E → Not stable → coated tablets/esterified.
food ⇒ ↓E & A, ↑C.
2) distribution:
E → fluids except CSF
✓ prostatic fluid, ✓ Macrophages.
CAT → tissues
A → longest t½ & larges Vd.
3) Elimination/excretion: Cyt P450, bile (E & A) urine CC)

Chloramphenicol

* only life-threatening situations w/ NO alternative

* 50S subunit → inhibit peptidyl transferase rxn.

* Antibacterial Spectrum:
Chlamydia, Rickettsia, Spirochetes, anaerobes.

*resistance:
enzymes, ↓influx, Ribosome Alteration

* pharmacokinetics:
IV, ✓ CSF,
hepatic metabolism → inactive glucuronide
elimination: urine
↓dose in cirrhosis & liver dysfunction.
secreted into breast milk.

*AE:
Haemolytic Anaemia (dose-related)
Aplastic Anaemia (non-dose-related)
Grey Baby Syndrome * *

drug interactions:
block metabolism of Warfarin & Phenytoin.