	Aminoglycosides (cidal)	Macrolides (static) Moderate spectrum	Chloramenipheco l (Static- broad spectrum)	Clindamycin (static)	Tetracyclines (static-broad spectrum)
PDs	Irreversible binding to 30S subunit: misreading of mRNA	Binding of 50S subunit: (weak reversible binding) Increasing concentration turns the drug into cidal MW>500	Binding (weak) to 50S subunit MW<500, only 2 –OH groups, 2 Cl atoms Not used nowadays except topical for eye infections	Binding to 50 S subunit (as erythromycin) at the same binding site MW <500	Reversible (weak) binding to 30S subunit MW<500 except tigecycline (parentral) Containing –OH groups, least in minocycline
PKs	• Not absorbed orally • Parentral • Not pass BBB • Can pass placenta and breast milk • Not metabolized • Excreted unchanged in urine: active in alkaline urine • N.B. **Synergy** - The aminoglycosides synergize with β-lactam antibiotics. The β-lactams inhibit cell wall synthesis and thereby increase the permeability of the aminoglycosides.	• Poor oral absorption, affected by food (on empty stomach) • Not pass BBB • Pass placenta but not teratogenic: **safe in pregnancy: erythromycin, zithromycin** • Pass to most body fluids in good concentration (prostate) • Concentrated in macrophages and polymorphs (long biological half life) • Metabolism: liver • Excretion: bile, enterohepatic circulation • **Membres: erythromycin**, clarithromycin, azithromycin, spiramycin	• Well-absorbed, not affected by food • Pass BBB: **2nd choice in meningitis** • Widely distributed: high Vd • Pass placenta, in breast milk • Metabolized by glucorunidation in liver: glucoronyl transferase phase II • Excreted in urine: inactive metabolites	• Rapid complete oral absorption • pass BBB in small amounts **enough to treat meningitis** • Penetrates bone, tissue fluids including prostate • Pass placenta: **not teratogenic** • Metabolism: liver • Excretion: bile	• Partially absorbed • Absorption decreased with: food, milk, antacid, iron (binds to heavy metals) • Incomplete passage to BBB • Concentrated in bone, teeth • Pass placenta (teratogenic) and breast milk **(high affinity to Ca) ≠ pregnancy, lactation, children<8 y** • Metabolism: extensive in liver • Excreted in urine 80% (inactive) more than in bile (enterohepatic circulation) • N.B. doxycycline and minocycline : nearly complete oral absorption, 50% renal excretion, 50% in bile: can be used in renal impairment

All five groups are static except for aminoglycoside which is cidal

Weak reversible binding

Irreversible binding

except for microloids if given with high concentrations

Broad spectrum, the two toxins; chloramphenicol tetracycline

Macroloids are with moderate spectrum. The rest are of narrow spectrum.

AT30

A: Aminoglycoside
T: tetracycline

Aminoglycoside and tetracycline binds to 30S subunit, the rest bind for 50S.

PKs

- Molecular weight > 500; aminoglycoside, macrolides"ketolides", (Tigecycline)tetracycline.
- -Oh, in 2 groups
  - Chloramphenicol; 2- Cl and 2-Oh
  - tetracycline
    - (Oh↑↑↑, especially Tigecycline)
      - Parental only
    - Minocycline,Oh↓↓↓
      Could be given orally

PKs Aminoglycosides "Mr Nooo"

No absorption
No distribution
No metabolism
excreted unchanged

PKs Absorption

Not Absorbed Orally
Tigecycline
Aminoglycosides

Poor orally absorption
Macroloids in high dosage

Partial Orally Absorption
Tetracycline

good orally absorption
clindamycin(twin to macrolides)
chloramphenicol (only 2 Oh; which results in good absorption)

PKs

Distribution

BBB

No pass (macrolides, aminoglycosides, tetracycline(Incomplete))

Pass (The two C;Chloramphenicol, clindamycin)

treatment of meningitis

Placental Barrier

No pass Aminoglycosides

Pass All except aminoglycosides.

Teratogenic, safe for pregnancy?

Two are safe, two are non-safe.

safe during pregnancy, macrolides, and clindamycin.

Unsafe during pregnancy, teratogenic, the 2 toxic, tetracycline, and chloramphenicol, contraindicated.

Macroloids, drug of choice during pregnancy. Clindamycin is safe too, but priority to macroloids.

Breast milk

The two toxic, chloramphenicol and tetracycline.

Macrolides get intracellularly(IC), could be used for respiratory infection"Azithromycin"

Results in Increased biological half-life.

PKs Metabolism

all are metabolized by liver.

Chloramphenicol needs to get into Phase II metabolism.

Glucuronidation of chloramphenicol,chloramphenicol is conjugated with glucuronic acid,by glucuronosyltransferase

Tetracycline undergoes excessive metabolism by the liver.

Drugs enter Enterohepatic circulation :

Half life ↑↑↑ (Liver→enterohepatic circulation→liver) ; longer duration of action

As passing to the liver twice could be “hepatotoxic”

gets into Enterohepatic circulation

Macroloids? Good

Tetracycline? Hepatotoxic

PKs Execration

By bile clindamycin, macrolides, first 20% tetracycline

By urine Aminoglycoside unchanged, active in alkaline, tetracycline 80%, chloramphenicol(inactive) → Used for UTI, alkalinization is recommended as its activity will be higher.

All tetracycline are execreted 20% by bile, 80% by urine, except for minocycline and doxycycline 50%, 50%.