Penicillin
cephalosporins
carbapenem
monobactams

MoA:
cellwall ↓ Tranpeptidases = cell lysis

Be—lactam → Bactericidal

IV only (carbapenem)

Route of Admistration

(monobactams)
IV or IM

(cephalosporins)
most of cephalsporins should be given IV or IM because of their poor oral absorption.
Except: cephalosporins given orally:-

From generation 1	From generation 2	From generation 3
cefadroxil	Cefaclor	cefdinir
Cephalexin	cefuroxime	cefixime
	(also parenteral)	cefpodoxime
		ceftibuten

(penicillin)

oral only	IV or I m only	oral + IV + IM
penicillin V	penicillin G-X(IM)	other
Amoxicillin	Piperacillin	
ampicillin	Ticarcillin	
dicloxacilli	Tazobactam	
	Benzathine + procaine (only IM)	

B— Lactam ⟶ spectrum

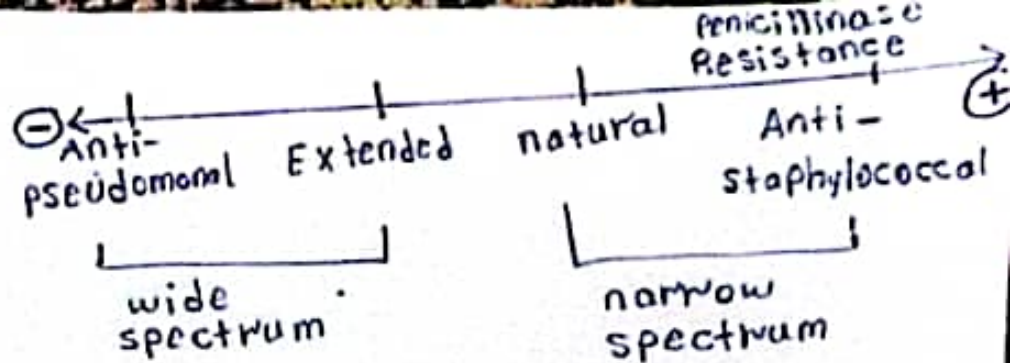
↓

pregnancy safety

↓

Penicillins and cephalosporins are the most safe

⟶ penicillin:



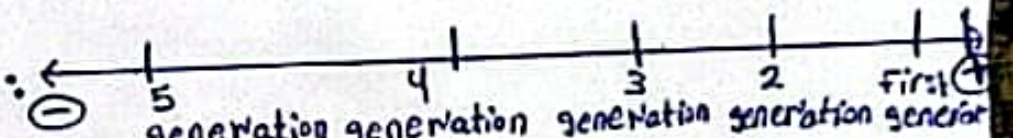
Anti-pseudomonal: (G−Ve) → wide

Extended : (G-ve)+(G+ve) → wide

natural : (G-ve)+(G+ve) → narrow

Anti-staphylococcal: (G+ve) → narrow

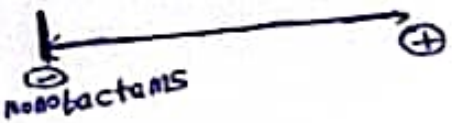
⟶ cephalosporins:



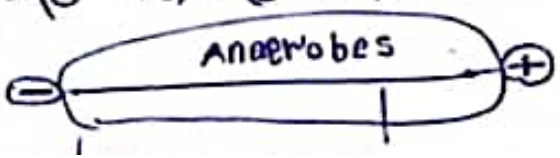
First generation : (G+ve)

الاجيال المتتالية successive generation : increase activity (G-ve) when reduce activity of (G+ve)

⟶ monobactams: only activity agonst (G-ve).



⟶ carbapenems: (G−Ve)+ (G+ve)+ (anaerobes)



B-Lactam → Side effect → peniciline

① Hypersensitivity → Rashes
→ anaphylactic → (Rare) Shock

② gastrointestinal upset → nousea, vomiting, diarrhea, pseudomembranous colitis

③ Nephritis (التهاب الكلى) → particularly → methicillin ← now it not use clinically

④ Neurotoxicity → seizures

* imipenem + cilastatin
= protects the drug + prevents toxic metabolits

*cilastatin = dehydropeptidase inhibitor

cephalosporins → Hypersensitivity

carbapenems → (imipenem) → Nephrotoxic

*If patient have history of anaphylaxis to penicillins?
- should not give patient first and second generation of cephalosporiens
- we can give patient third and fourth generation of cephalosporins with → caution. → monitored setting.

* Transpeptidase enzyme = penicillin Binding protein (PBP)

* MRSA = Methicillin [redacted] Resistant staphylococcus

aureus

→ Tranpeptidases enzyme penicilline — تعمل [redacted] على تغيير شكل كوسيلة لمقاومة ال

* Penicillin :
- → Excretion → kidney
- → have sensitivity to B-Lactamase
- → (B-Lactamase inhibitors) — لهيك صنعوه ال* [redacted]
- → B-Lactamase inhibitors
  - → clovulonic acid
  - → sulbactam
  - → tazobactam
  - → it have B-Lactam ring, but don't have antibacterial activity.
  - → B-Lactamase Inhibitor + B-Lactamase sensitive = Fixed combonation
  - → Clavulonic acid + Amoxicillin
  - → sulbactam + Ampicillin
  - → tazobactam + piperacillin

* penicillin = PNs
* cephalosporins = cPNs

* Penicillin: → classification → natural
→ Antistaphylococcal
→ Extended-spectrum
→ Anti-pseudomonal

* natural PNs: → penicillin G → Benzylpenicillin → prototype
→ penicillin V → Phenoxymethyl penicillin.

* Anti-staphylococcal penicillin: → Methicillin
→ oxacillin
→ cloxacillin
→ Dicloxacillin
→ Nafcillin

is the only type that is not susceptible (Resistant) to B-lactamase → so, it don't need B-Lactamase inhibitor.

*natural + Anti-staphylococcal = narrow spectrum

* who produces beta Lactamase? staphylococcus aureus

* Extended-spectrum PNs: → Amino PNs → Amoxicillin
→ Ampicillin (semi-synthetic)

* Anti-pseudomonal PNs: → Piperacillin
→ Ticarcillin

* Extended spectrum PNs + Anti-pseudomonal PNs = wide spectrum

* Antimicrobial therapy: The selective toxicity is relative rather than absolute, so, should be controlled in concentration of the drug.

* Natural penicillin ⟶ from Fungi penicillium chrysogenum

* Penicillin (active) —B-Lactamase→ penicilloic acid (not active)

* B-Lactamases: is bacterial degradative enzymes

* Natural penicillin: ⟶ spectrum → (G+ve), (G-ve) (Little activity), (anaerobes)

* Penicillin G: used for treatment: → syphilis, meningitis, Endocarditis, Pneumonia, septicemia in children.

* penicillin V: → activity against (G+ve) is similar to the PG
→ Less activity than PG against (G-ve)
→ used for treat infection caused by Streptococcus pyogenes: → Tonisilitis, Pharyngitis, skin infections

* Antistaphylococcal PNS: → active → MSSA
→ inactive → MRSA + streptococci
→ inactive → enterococci
→ anaerobic
→ (G-ve)

* Extended-spectrum PNS: → active (G-ve) > (G+ve)
→ For Respiratory infections

* Amoxicillin: used for treat: → urinary tract infections
→ sinusitis
→ otitis
→ Lower Respiratory tract infection.

* Ampicillin: used for treat: → shigellosis (G-ve)
→ with or without gentomicin
Listeria monocytogenes (G+ve)

* ciprofloxacin: → for Shigellosis → in adults

* Azithromycin: → for shigellosis → in children

* Piperacillin or Ticarcillin + clavulanic acid or tazobactam = for penicillinase producing organisms

* oral penicillin (Exception amoxicillin) should be given at least 1-2 hours before or after meal.

* Prodrug of ampicillin: → Pivaloyloxymethyl → greater Lipophilicity

Resistance to penicillins and other B-lactams

- Resistance to penicillins and other β-lactams is due to one of four general mechanisms:

1. Inactivation of antibiotic **by B-lactamase (the most common mechanism)**
2. Modification of target PBPs.
   - low affinity for binding B-lactam antibiotics
   - basis of methicillin resistance in staphylococci (**MRSA, use Vancomycin).**
3. Impaired penetration of drug to target PBPs.
   - only in G- (impermeable outer cell wall)
   - Absence or down-regulation of porins.
4. Efflux.
   - Gram-negative organisms also may produce an efflux pump, which transport B-lactam antibiotics from the periplasm back across the outer membrane.

*Penicillin :

- Dose must be adjusted according to renal function
- Nafcillin → cleared by → biliary
- dicloxacillin + cloxacillin + oxacillin → eliminated by kidney + biliary
- (Nafcillin + dicloxacillin + cloxacillin + oxacillin): these drug no dosage adjustment in renal failure
- penicillins + probenecid = ↑ blood levels of all penicillin

* cephalosporins → ceph (كل ادويتها فيها مقطع)
→ have five generation

* First generation: zorro ⇒ cefazolin → longer duration, penetrates well into bone
Excel ⇒ cefadroxil
flexibility ⇒ cephalexin → prototype, for pharyngitis
⇒ cephradine

→ are Resistant to staphylococcal penicillinase → cover MSSA, not cover MRSA
→ (G+ve)

* second generation: color ⇒ cefaclor
ox ⇒ cefuroxime

→ (G+ve) + (G-ve) + anaerobic

→ cefuroxime sodium: → prototype
→ has longer half life
→ it cross (BBB)
→ for → bronchitis, pneumonia
in elderly and patient who are immunocompromised

→ cefuroxime axetil: → active against B-Lactamase producing organisms

* Third generation: → (G-ve)

→ Taxi ⇒ cefotaxime → This penetrates well into CSF

→ (3 in 1) ceftriaxone → for Neisseria gonorrhoeae

→ Dinner ⇒ cef DIN IR

→ Taz ⇒ ceftazidime → active pseudomonas aeruginosa

[CSF: cerebrospinal fluid]

* 4 generation: → cefepime → active pseudomonas aeruginosa

* 5 generation: → caroline ⇒ ceftaroline

→ ↑ binding to penicillin-binding protein 2a

→ for treat → MRSA skin
→ soft tissue infections
→ pneumonia.

* CPNs: → distribute very well into body fluids, but not to CSF

→ cefazolin → for treat → surgical prophylaxis.
→ orthopedic surgery.

→ ceftriaxone + cefotaxime → for CSF -
→ for meningitis.

→ ceftriaxone → excreted by bile.
→ (سؤال) used for renal insufficiency

→ more Resistant than Penicillin to certain B-lactomas

→ cephalosporin C → prototype

→ from (Acremonium chrysogenum)

* Monobactams :
- aztreonam
- active
  - (G - ve)
  - P. aeruginosa
  - Enterobacteriaceae
- inactive
  - (G + ve)
  - anaerobic
- used for treat:
  - pneumonia
  - meningitis
  - sepsis caused by susceptible G-
- nontoxic → safe alternative For patient who have allergic to PNs and cPNs .
- Resistant to the action most B-Lactamases , exception (ESBLs)
- pentarates well into CSF.

* carbapenems:
- active:
  - (G-ve)
  - (G +ve)
  - anaerobes
  - P. Aeruginose
- So, plays role in empiric therapy.
- Excreted by → glomerular filteration (kidny)
- penem — الأدوية فيها مقطع
- imipenem:
  - for ~~meningitis~~ meningitis
  - not resists to metallo B-Lactamases (carbapenemases)