



- What is the mechanism of action of cephalosporins?

- Binding to penicillin Binding Protein (PBP) present in the bacterial wall.
- Inhibiting cell wall synthesis by blocking transpeptidase step.
- Activating autolytic enzymes.

Notice that cephalosporins are bactericidal (killing the bacteria directly).

- Cephalosporins generations according to activity → as you progress from 1st to 4th generation:

- Activity against gram (+) bacteria decreases.
- Activity against gram (-) bacteria increases.
- Resistance to β-lactamase increases.
- CNS penetration increases.

- How are cephalosporins excreted?

- Urinary excretion.
- Bile (for 3rd generation. Example: cephatrioxin).

- Cephalosporin generations:

1st generation (cefazolin and cephalexin)	<ul style="list-style-type: none"> • Notice that cefazolin is used for prophylaxis in surgery. • They are very active against gram (+) bacteria. • They are active against some gram (-) bacteria such as: klebsilla pneumonia and Proteus. • They cannot penetrate CNS, so they are not used for meningitis. • They are not effective against bacteroid fragilis.
2nd generation (cefotetan and cefoxitin)	<ul style="list-style-type: none"> • They are more active against gram (-) bacteria when compared with 1st generation. • They cannot penetrate CNS. • They have more resistance to β-lactamase. • They are effective against B.fragillus.
3rd generation (cefoperazone and cefotaxmin)	<ul style="list-style-type: none"> • They have extended range of activity against gram (-) bacteria. • They penetrate CNS. Therefore, they are used for treatment of meningitis. • They are effective against B.fragilius and P.aeruginosa.
4th generation (cefepime and ceftazidime)	<ul style="list-style-type: none"> • Most effective against gram (-) bacteria as well as gram (+) bacteria. • Used for treatment of meningitis. • Works on bacteria which are resistant to 3rd generation cephalosporins. • Have greatest resistance against: Eneterobacter, Citrobacter and Pseudomonas.
5th generation (ceftazidime and ceftazidime)	<ul style="list-style-type: none"> • Broad spectrum anti MRSA (Methicillin Resistant S.Aureus) and CAP. • Used to treat S.aureus and skin infections.

- Adverse effects of cephalosporins:

- **Hypersensitivity reaction** (10% cross reaction with penicillin), patients who had anaphylactic shock before should not be taking it!
- **Superinfection:** bacteria + fungi.
- **Nephrotoxicity:** especially with 3rd generation cephalosporins.
- **Hypoprothrombinemia.**

- Cefazolin is used for prophylaxis:

- Low cost.
- Well tolerated (IM and IV).
- Long half-life.
- Good penetration (high tissue levels).
- Give 30-60 minutes before incision to reach blood and tissues at time of incision.
- Give a 2nd dose if the operation will last more than 3 hours.
- Post-surgical: 2 or 3 doses.