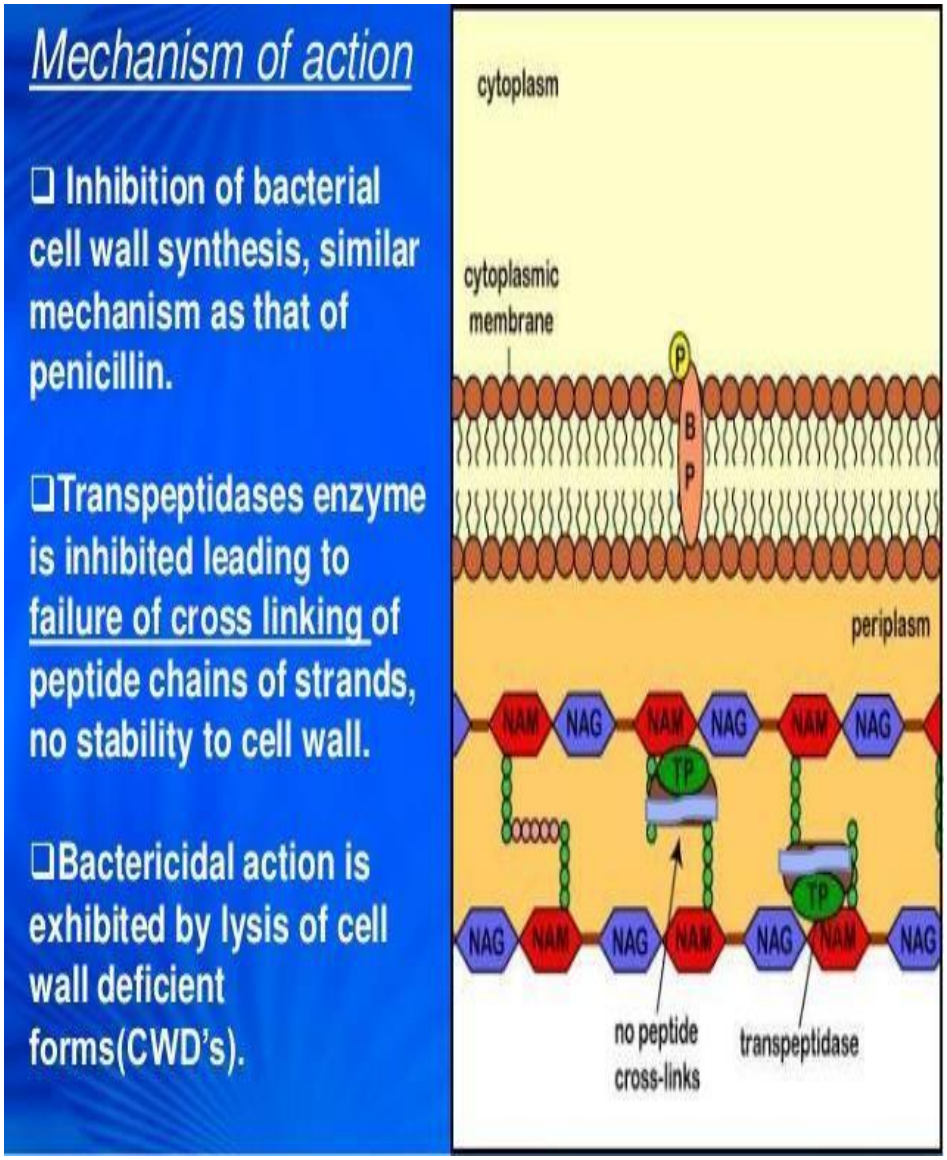
CEPHALOSPORINS

These are a group of semisynthetic antibiotics derived from 'cephalosporin-C' obtained from a fungus Cephalosporium. They are chemically related to penicillins; the nucleus consists of a P-lactam ring fused to a dihydrothiazine ring, (7-aminocephalosporanic acid). By addition of different side chains at position 7 of [3-lactam ring (altering spectrum of activity) and at position 3 of dihydrothiazine ring (affecting pharmacokinetics), a large number of semisynthetic comp ounds have been produced.

Generations of Cephalosporin

Oral	Parentral
1st generation	
Cephalexin	Cephalothin
Cephradine	Cefazolin
Cefadroxil	
2nd generation	
Cefaclor	Cefuroxime
Cefuroxime axetil	Cefoxitin
3rd generation	
Cefixime	Cefotaxime
Cefdinir	Ceftizoxime
Ceftibuten	Ceftriaxone
Ceftamer pivoxil	Ceftazidime
4th generation	
	Cefepime
	Cefpirome

First generation: The first-generation cephalosporins act as *penicillin G* substitutes. They are resistant to the staphylococcal penicillinase and also have activity against Proteus mirabilis, E. coli, and Klebsiella pneumonia



Second generation: The second-generation cephalosporins display greater activity against three additional gram-negative organisms: H. influenzae, Enterobacter aerogenes, and some Neisseria species, whereas activity against gram-positive organisms is weaker [Note: The exception to this generalization is the structurally related cephamycin, *cefoxitin* which has little activity against H. influenzae yet is effective against the anaerobe Bacteroides fragilis

Third generation: These cephalosporins have assumed an important role in the treatment of infectious disease. Although inferior to first-generation cephalosporins in regard to their activity against gram-positive cocci, the third-generation cephalosporins have enhanced activity against gram-negative bacilli, including those mentioned above, as well as most other enteric organisms plus Serratia marcescens. *Ceftriaxone* [sef-trye-AKS-own] or *cefotaxime* [sef-oh-TAKS-eem] have become agents of choice in the treatment of meningitis. *Ceftazidime* [sef-TA-zi-deem] has activity against P. aeruginosa.

Fourth generation: *Cefepime* is classified as a fourth-generation cephalosporin and must be administered parenterally. *Cefepime* has a wide antibacterial spectrum, being active against streptococci and staphylococci (but only those that are *methicillin*-susceptible). *Cefepime* is also effective against aerobic gram-negative organisms, such as enterobacter, E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa.

C. Pharmacokinetics

Administration: Many of the cephalosporins must be administered IV or IM. because of their poor oral absorption.

1. **Distribution:** All cephalosporins distribute very well into body fluids. However, adequate therapeutic levels in the CSF, regardless of inflammation, are achieved only with the third-generation cephalosporins. For example, *ceftriaxone* or *cefotaxime* are effective in the treatment of neonatal and childhood meningitis caused by H. influenzae. *Cefazolin* [se-FA- zo-lin] finds application as a single prophylaxis dose prior to surgery because of its 1.8-hour half-life and its activity against penicillinase-producing S. aureus. However, additional

intraoperative *cefazolin* doses may be required if the surgical procedure lasts longer than 3 hours. *Cefazolin* is effective for most surgical procedures, including orthopedic surgery because of its ability to penetrate bone. All cephalosporins cross the placenta.

2. **Fate:** Biotransformation of cephalosporins by the host is not clinically important. Elimination occurs through tubular secretion and/or glomerular filtration). Therefore doses must be adjusted in cases of severe renal failure to guard against accumulation and toxicity. *Ceftriaxone* is excreted through the bile into the feces and, therefore, is frequently employed in patients with renal insufficiency

Adverse effects

Cephalosporins are generally well tolerated, but
are more toxic than penicillin.

1. Pain after i.m. injection occurs with many. This is so severe with cephalothin as to interdict i.m. route, but many others can be injected i.m. (seeindividual compounds). Thrombophlebitis of injected vein can occur.

2. Diarrhoea due to alteration of gut ecology or irritative effect is more common with oral cephradine and parenteral cefoperazone (it is significantly excreted in bile).

3. Hypersensitivity reactions caused by cephalosporins are similar to penicillin, but incidence is lower. Rashes are the most frequent manifestation, but anaphylaxis, angioedema, asthma and urticaria have also occurred. About 10% patients allergic to penicillin show cross reactivity with cephalosporins. Those with a history of immediate type of reactions to penicillin should better not be given a cephalosporin. Skin tests for sensitivity to cephalosporins are unreliable. A positive Coombs' test occurs in many, but haemolysis is rare.

4. Nephrotoxicity is highest with cephaloridine, which consequently has been withdrawn.

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5. Bleeding common inpatients with cancer, intra-abdominal infection or renal failure.

6. Neutropenia and thrombocytopenia are rareadverse effects reported with ceftazidime and some others.

7. A disulfiram-like interaction with alcohol hasbeen reported with cefoperazone.

Uses

1 . As alternatives to PnG;

2. Respiratory, urinary and soft tissue infections

3. Penicillinase producing staphylococcal infections.

4. Septicaemias

5. Surgical prophylaxis:

6. Meningitis:

7. Gonorrhoea

8. Typhoid:

9. Mixed aerobic-anaerobic infections in cancer Patients.