



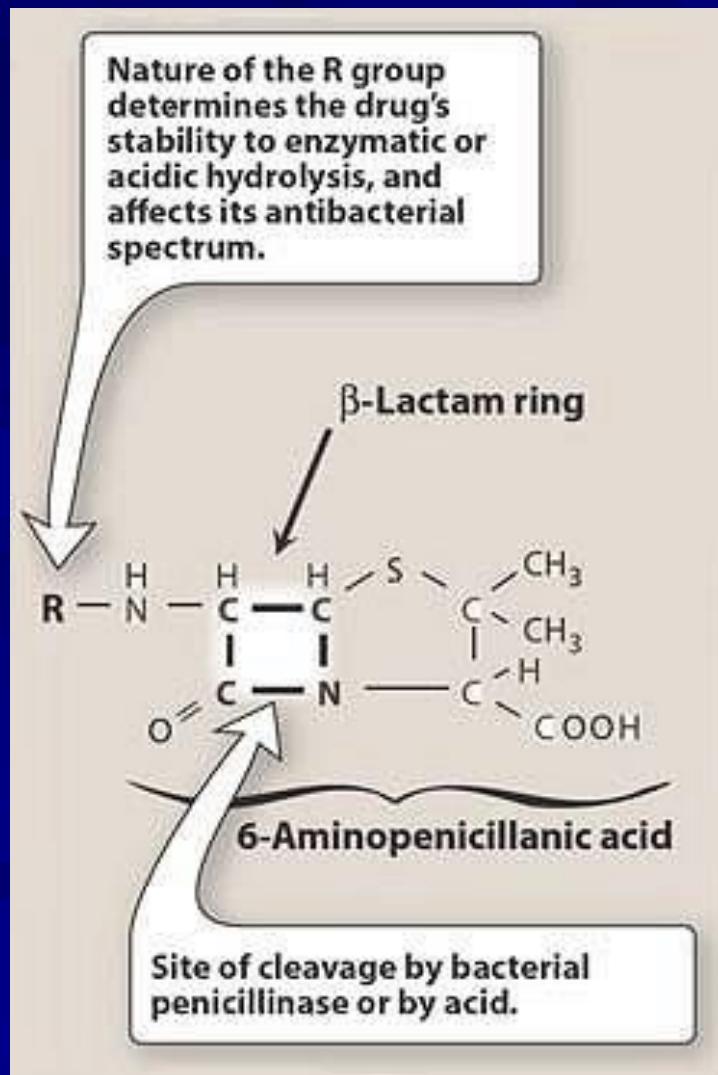
Cephalosporins

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Cephalosporin

- The cephalosporins are B-lactam antibiotics that are closely related both structurally and functionally to the penicillins. that were originally derived from the fungus *Cephalosporium acremonium*
- Most cephalosporins are produced semisynthetically by the chemical attachment of various R1 and R2 groups to 7-aminocephalosporanic acid

Structural features of β -lactam antibiotics



Mechanism of Action

- **Cephalosporins:** Inhibit cell wall synthesis in a way similar to that of penicillins

Cephalosporins	Prototypes	Other Significant Agents
1 st Gen.	Cefazolin	Cephradine, Cephalexin, Cephadroxil
2 nd Gen.	Cefamandole	Cefaclor, Cefotetan, Cefoxitin, Cefuroxim
3rd Gen.	Cefoperazone	Cefotaxime, Ceftazidime, Ceftriaxone, Cefixime
4th Gen.	Cefipime	Cefpirome
5th Gen.	Ceftopibrole	

Pharmacokinetics

- Oral & parenteral
- $t_{1/2}$ is 1 - 4h exception ceftriaxone 8 h
- Wide distribution
- Binding to plasma protein vary from one to another

Pharmacokinetics

- 3rd & 4th Gen. can penetrate CNS except (Cefoperazone & Cefixime)
- Cephalosporins are excreted unchanged in the urine
- Many are actively secreted by the renal tubule, a process which can be blocked with probenecid so the dose of Cephalosporins should be reduced in patients with poor renal function. (Probenecid slows their elimination and prolong their half-life), except, ceftazidime & cefoperazone (glomerular filtration)
- Cefoperazone & Ceftriaxone mainly excretion by bile

Clinical Uses of 1st Gen

- Active against Gram - positive cocci
- Minimal activity against Gram - negative cocci, enterococci, MRSC

Uses:

- Infection, UTI, soft tissue abscess
- Surgical prophylaxis

Clinical Uses of 2nd Gen.

- Less activity against G - positive
- Extended activity against G-negative

Uses:

- Cefotetan, Cefoxitin in abdominal and pelvic infections caused by anaerobe bacteroides fragilis
- Cefuroxim in community acquired pneumonia which caused by strep. pneumonia
- Cefemandole, Cefuroxime, Cefaclor in sinus, ear, respiratory infection caused by H infuenzae

Clinical Uses of 3rd Gen.

- Increased activity against G-negative
- Most active against β -lactamase (H influenza and neisseria)
- Less active against Enterobacter strains

Uses:

Cefoperazone, ceftazidime active against *pseudomonas aeruginosae* (used in Septicemia)

- Ceftriaxone for Meningitis
- Ceftriaxone, cefixime are the drug of choice in gonorrhea
- Ceftriaxone in acute otitis media



4th Gen

- Very good activity against Gram-positive including *s. aureus*
- More resistant to β - lactamases produced by (*Enterobacter*, *Haemophilus*, *neisseria*)
- V. good activity against Gram-negative including *p. aeruginosa*

4th Gen. Cefepime (Clinical Uses)

- Nosocomial pneumonia of Enterobacter
- Infection caused by pseudomonas aeruginosa
- Febrile neutropenia
- UTI
- Intra-abdominal infections

5th Gen. Ceftobiprole

- Ceftobiprole: broad spectrum, MRSA, penicillin resistance streptococcus pneumonia, pseudomonas aeruginosa and enterococci

5th Gen. Ceftobiprole

- Ceftobiprole
- Its new drug for treatment diabetic foot infections

Cephalosporins adverse reactions

- Allergy :Cross-allergy with penicillin (5-10%)
- Pain
- Phlebitis
- Thrombocytopenia, haemolytic anemia
- Interstitial nephritis
- Abnormal liver function test
- Infection

Cephalosporins Adverse Reactions

- Ceftriaxone can displace bilirubin from its binding to serum albumin and may lead to the development of bilirubin encephalopathy causing brain damage or death of hyperbilirubinemic neonates ,Not advised in neonates because it interferes with bilirubin metabolism. Cefotaxime preferred in neonate (does not interfere with bilirubin metabolism), as may ceftriaxone.

Cephalosporins Adverse Reactions

- Prothrombin deficiency with Cefamandole, Cefotetan, Cefoperazone
- Cefamandole may cause a disulfiram-like reaction after ingestion of alcohol

Cephalosporins adverse reactions

- With calcium–ceftriaxone precipitates in the lung and kidneys in both term and premature neonates

Cephalosporins and Alcohol Cefamandole



Do not drink alcoholic beverages when taking this medication

Cephalosporins Drug Interaction

- Cephalosporin & Aminoglycoside
- Cephalosporin & Probencid
- Cephalosporin & Anticoagulant