

# Penicillins

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# Therapeutic uses/ anti-bacterial spectrum

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- Penicillin G is effective in infections (meningitis and pneumonia) caused by sensitive strains of Streptococci.
- Penicillin G effective in primary, secondary and latent syphilis caused by *Spirochete treponema pallidum*.
- Diphtheria, Anthrax (*Bacillus anthracis*), clostridial infections and rat bite fever (*Spirillum minor*) are treated with penicillin G.
- Penicillin G + Aminoglycosides used for synergistic effect to treat enterococcal endocarditis.



# Penicillins.....

- A single injection of Benzathine penicillin is satisfactory for treatment of  $\beta$ -hemolytic streptococcal pharyngitis.

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- Cloxacillin or Dicloxacillin is suitable for treatment of mild localized staphylococcal infections. For serious systemic Staphylococcal infections, Oxacillin or Nafcillin can be given through intravenous infusion.
- Ampicillin and Amoxicillin have greater activity against gram negative bacteria infections like UTI, Sinusitis, Otitis and lower respiratory tract infections.
- Amoxicillin, Ampicillin, Ticarcillin and Piperacillin are also available in combination with  $\beta$ -lactamase inhibitors (Clavulanic acid, Sulbactam or Tazobactam). Combination is effective against  $\beta$ -lactamase producing strains of *Staphylococcus aureus*.

# Penicillins/adverse effects

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Hypersensitivity reactions

Acute anaphylactic shock

Serum sickness

Neurotoxicity

Diarrhea

Nephritis

# Resistance to Penicillins

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- 1. Production of  $\beta$ -lactamase enzymes
- 2. Reduction in permeability of outer membrane
- 3. Occurrence of modified PBPs
- 4. Lack of activation of autolytic enzymes



# Cephalosporins

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- Cephalosporins were first obtained from a fungus *Cephalosporium acremonium*.
- The basic structure present in all is 7-aminocephalosporanic acid which is composed of Dihydrothiazine ring and  $\beta$ -lactam ring (determine anti-bacterial activity).
- Depending upon antibacterial spectrum, Cephalosporins are classified into following four generations.
- As we move from First to four generation antibacterial activity against gram (-) bacteria increases and activity against (+) bacteria decreases.

# Cephalosporins

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graph TD; A[Cephalosporins] --- B[First Generation Cephalosporins]; A --- C[Second Generation Cephalosporins]; A --- D[Third Generation Cephalosporins]; A --- E[Fourth Generation Cephalosporins];
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## First Generation Cephalosporins

Cephalexin,  
Cephradine,  
Cephalothin,  
Cefazolin,  
Cefadroxil,  
Cephapirin

## Second Generation Cephalosporins

Cefaclor,  
Cefprozil,  
Cefuroxime,  
Cefpodoxime,  
Loracarbef

## Third Generation Cephalosporins

Cefixime,  
Cefotaxime,  
Ceftriaxone,  
Cefoperazone,  
Ceftazidime,  
Moxalactam

## Fourth Generation Cephalosporins

Cefepime

# Pharmacokinetic

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- Oral absorption vary among different Cephalosporins. Cephadrine, Cephalexine, cefaclor, cefixime etc. are effective orally. Cefoperazone, ceftriaxone are effective parentally.
- Cephalosporins widely distributed. Concentration of Cefoperazone is high in bile.
- Some Cephalosporins like Cephapirin, cefotaxime etc, are deacetylated in vivo and converted into less active metabolite.
- Excretion mainly through kidney, largely through tubular secretion.



# Clinical uses

- Drugs of choice for surgical prophylaxis.

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- Effective in infections caused by Klebsiella, Enterobacter, Proteus, Serratia and Haemophilus species.
- First and second generation Cephalosporins are effective in upper respiratory tract infection and soft tissue infections.
- Ceftriaxone, cefixime, cefoperazone are drug of first choice in Gonorrhoea, typhoid fever (*Salmonella typhi*) and late lyme disease.
- Third generation are effective in meningitis caused by *H. influenza*, *Strep. Pneumoniae*, *Neisseria meningitides* etc. as they cross BBB.

# Adverse effects

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- Hypersensitivity reactions
- Nephrotoxicity
- Serious bleeding due to thrombocytopenia, hypoprothrombinemia or platelet dysfunction with Cefoperazone.
- Super infection
- Disulfiram like effects (Nausea, vomiting, dizziness, headache, abdominal discomfort) in alcoholic patients due to blockade of alcohol oxidation that result in accumulation of acetaldehyde.



# Carbapenam

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- Examples are Imipenem, Meropenem
- Active against both gram (-) and (+) bacteria.
- Effective in surgical prophylaxis.
- Hospital acquired pneumonia.
- Imipenem is inactivated by dehydropeptidases in renal tubules. Administer together with Cilastatin (inhibitor of this enzyme). Meropenem not degraded by this enzyme.
- ADRs- skin rashes, diarrhea, nausea and vomiting

# Monobactam

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- MOA same as that of Penicillins
- Example is Aztreonam
- Active against gram (-) bacteria particularly *Pseudomonas aeruginosa*, *Haemophilus influenza* and *Neisseria meningitides*.