

β - lactam antibiotics

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β - lactam antibiotics

- Antibiotics that have a β - lactam ring in their molecular structure
- Act by inhibiting bacterial cell wall synthesis
- Bactericidal

β - lactam antibiotics

Penicillins

Cephalosporins

Monobactams

Carbapenems

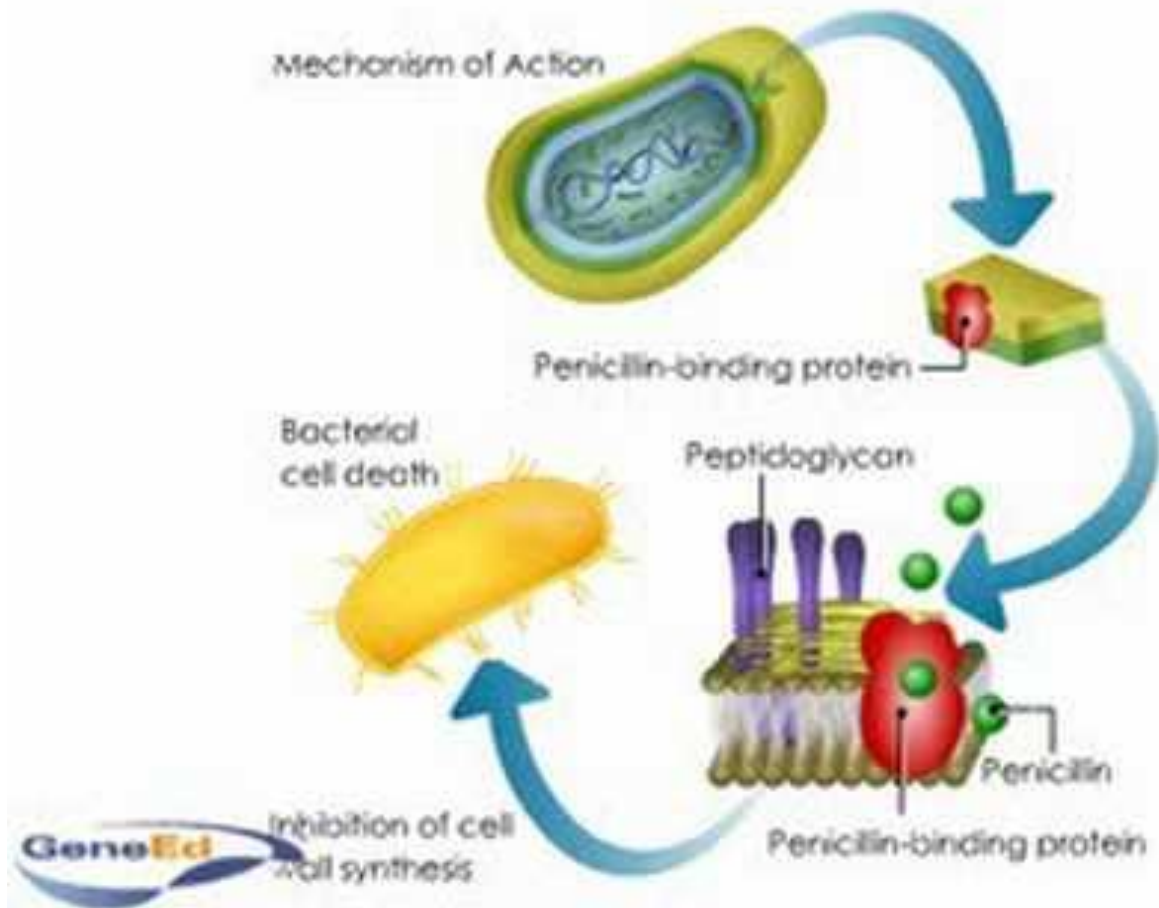
Penicillins

- History
- Mechanism of action
- Classification
- Indications/spectrum
- Adverse effects
- Resistance

Mechanism of action

- Act by inhibiting the synthesis of the peptidoglycan layer of bacterial cell walls
- Peptidoglycan layer is important for cell wall structural integrity
- The final transpeptidation step in the synthesis of the peptidoglycan is facilitated by penicillin binding proteins(PBP)
- The β -lactam nucleus of the molecule irreversibly binds to the PBP active site.
- This irreversible inhibition of the PBPs prevents the final cross linking (transpeptidation) of the peptidoglycan layer, disrupting cell wall synthesis
- Bacteria become incapable of withstanding the osmotic gradient between its environment and interior and cells swell and rupture.

Mechanism of action



Penicillins

- Bactericidal
- Effective only against multiplying organisms
- Time dependant killing
- Not effective against organisms like mycoplasma which do not have cell wall
- High safety and high therapeutic index

Classification

Natural penicillins	Benzylpenicillin(Penicillin G) Phynoxymethylpenicillin(Penicillin V)
Antistaphylococcal penicillins	Cloxacillin Flucloxacillin
Aminopenicillins	Amphicillin Amoxicillin
Antipseudomonal penicillins	Ticarcillin Piperacillin
Penicillin- beta lactamase inhibitor combinations	Pieracillin-tazobactam Co-amoxyclav

Resistance –mechanisms

1.Production of penicillinase (B lactamase)

- this enzyme cause hydrolysis of the B lactam ring
- ex-staphylococcus aureus

2.Presence of lipopolysaccharide outer layer

- gram negative bacteria have this layer,which some penicillins cant penetrate(but aminopenicillins and antipseudomonal penicillins are able to penetrate this layer

Pharmacokinetics

Absorption

- Depends on the type of penicillin

Ex- amoxicillin is well absorbed /penicillin G cant be administered orally

Pharmacokinetics

Distribution

- Bound to plasma proteins
- Widely distributed
- Do not cross the BBB significantly when not inflammed
- Only about 20% cross the BBB when meningies inflamed
so need high doses for meningitis

Ex- amoxicillin is well absorbed /penicillin G cant be administered orally

- Crosses placenta
- Excreted in breast milk

Pharmacokinetics

Elimination

- Short half life (30-60 min)
- Can be given in large doses every 4-8h as therapeutic index high

Renal elimination

- 10% glomerular filtration
- 90% tubular secretion

Probenecid-inhibits tubular secretion and increases penicillin levels in blood (not commonly used currently)

Repository forms

1. Benzathine penicillin

- Combination of 2 benzylpenicillin and 1 ammonium base molecule
- Given IM for rheumatic fever prophylaxis once in 3 weeks

2. Procaine penicillin

- Procaine (an anesthetic agent) combined with benzyl penicillin
- Given as injections every 12 to 24h
- Used in the treatment of syphilis

Penicillin V and Penicillin G

- Similar spectrum-penicillin V has lesser activity against gram negative cocci and anaerobes
- Indications
 - streptococcal infections /staphylococcal infections
 - anaerobic infections
 - meningococcal and gonococcal infections
 - syphilis
 - actinomycosis
 - anthrax
 - tetanus
 - leptospirosis
 - lyme disease
 - prophylactic use -----rheumatic fever/streptococcal infections

Cloxacillin/Flucloxacillin

- Act against penicillinase producing staphylococci only
- Resistant to the β lactamase activity of the organism
- V. narrow spectrum
- Methicillin –toxic/not used now

Amoxicillin/Amphicillin

- Broad spectrum
- Penicillin G sensitive gram + organisms (however activity less against gram +ves than natural penicillins)
- Gram negative cover-E coli, Salmonella, Shigella, H.influenzae
- Not active against –Klebsiella ,pseudomonas

Adverse effects

- Allergic reactions-urticaria ,rashes, anaphylaxis
- Diarrhea
- Cation toxicity
- Liver
- Renal

