The high yeld

The major cell wall synthesis inhibitors currently in use are:

1- The beta-lactams (e.g., penicillin and cephalosporins), which block the formation of the peptidoglycan layer.

2- The glycopeptides (vancomycin and teicoplanin), which disrupt assembly of the peptidoglycan precursor lipid II.

Beta lactam antibacterial drugs

Share common structure

Share common mechanismn of action

penicillins, cephalosporins, monobactams and carbapenems

Features of beta lactam antibiotics:

1. contain the 4-membered ring (lactam).... hydrolysis (acidic or enzymatic).So it is not taken orally
2. Target: cell-wall biosynthesis
   Action: bactericidal(against growing cells)
3. have variable spectrum

bacterial cell wall consist glycopeptides linked via five peptide bridges between amino acid side chains.

penicillin binding proteins (PBP) to which transpeptidases are attached (in the peri plasmic space).

trans-peptidation reaction gives
-rigid mechanical stability
-prevent osmnotic shock.

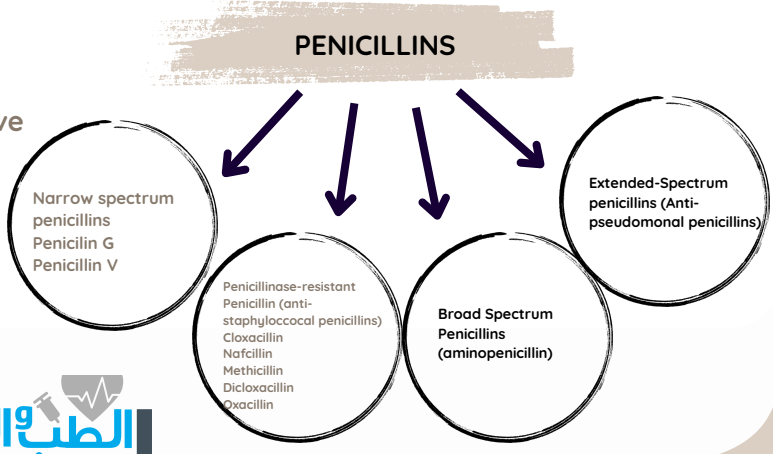
Mechanism of action (note it is very important)

Penicillins are bactericidal through inhibition of bacterial cell wall synthesis for growing bacteria.

Bind with PBP causes → Inhibition of these transpeptidases → inhibition cell wall synthesis → bacterial cell death.

Mechanism of resistance to penicillins:

1. Enzymatic hydrolysis(destroy B-lactam antibiotics.)
2. Inability of the drug to penetrate(gram negative bacteria).
3. Active efflux pumps(remove the antibiotic)
4. Alteration in PBP(decreased affinity)
5. Natural (intrinsic) resistance(no cell wall like Mycoplasma)



The high yeld

Narrow spectrum (natural) penicillins

1. Including :

penicillin G (benzyl penicillin)
-not used orally (acid labile) given by Intravenous(IV)or intramuscuar (IM) injection.

penicillin V(phenoxymethyl penicillin)
-more stable in acidic medium
-better absorbed from GIT after oral administration

2.Highly active gram-positive cocci (ineffective against most strains of Staph. aureus).

3.Some gram-negative cocci and anaerobic bacteria are susceptible to natural pehicillins.

4.short acting (t1/2 is 30 minutes) so need frequent administration

5.Penicillin G penetrates readily inflamed meninges

6.Excretion is mainly by the kidney (10% via glomerular filtration & 90% by active tubular secretion).

7.probenecid may be given as it blocks renal tubular secretion of penicillins (prolonged of action)

Long-acting penicillin
These IM. preparations release penicillin slowly from the area in which it is injected and produces relatively low but persistent concentrations of antibiotic in the blood.
Example :
-Penicillin G benzathine Once per month as a prophylaxis in rheunatic fever)
-Penicillin procaine
I.M./12 hours

Therapeutic uses of penicillin G

- Pneumococcal infection: pneumonia and meningitis
- Streptococcal infection such as pharyngitis prevents development of acute rheumatic fever, but not glomerulonephritis. Penicillin plus aminoglycoside (streptococcal endocarditis)
- Meningococcal infection: in acute meningitis , but ineffective in meningococcal carrier state or prophylaxis.
- Anthrax
- Clostridia infections: gas gangrene
- Gonococcal infection, but ceftriaxone is an effective alternative
- Anaerobic infection: e.g. brain abscess
- Diphtheria
- Chemoprophylaxis
- Syphilis

The high yeld

Penicillin G is used for Prophylaxis in the following conditions:

1. Recurrence of rheumatic fever. Benzathine penicillin G given monthly as I.M. injection.

2.Contact persons to patients suffering from syphilis.

3.Surgical or dental procedures in cardiac patients with rheumatic valve disease to guard against sub-acute bacterial endocarditisinfection (penicillin plus aminoglycoside).

Penicillins and other cell wall inhibitors facilitate the entry of aminoglycoside into bacterial cells (Synergism)

The penicillin ase resistant (anti-staphylococcal) penicillins

1.resistant fo hvdrolysis by staphylococcal penicılinases: treatment of infection caused by staphylococci

2.less effective against microorganisms susceptible to penicillin G

3.gram negative bacteria no effect on gram

4.Methicillin was withdrawn because of causing interstitial nephritis.

5.Combination of flucloxacillin and amoxicillin are available as oral or injectable preparations.
- combinations of dicloxacillin and ampicillin are available.

Forever. Flucloxacillin
No. Nafcillin,
One. Oxacilin
Can. Cloxacillin
Destroy. Dicloxacillin
Me. Methicillin

Methicillin-resistant Staph. aureus (MRSA):term applied now to all bacteria which are resistant to all penicillinase resistant penicillins like Methicillin.

MRSA is resistant to most B-lactamns because of the presence of mecA, a gene that produces a penicillin binding protein (PBP2a) with low affinity for B-lactam antibiotics

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صلو على سول الله