Anti-bacterials/Bacterial cell wall synthesis inhibitors

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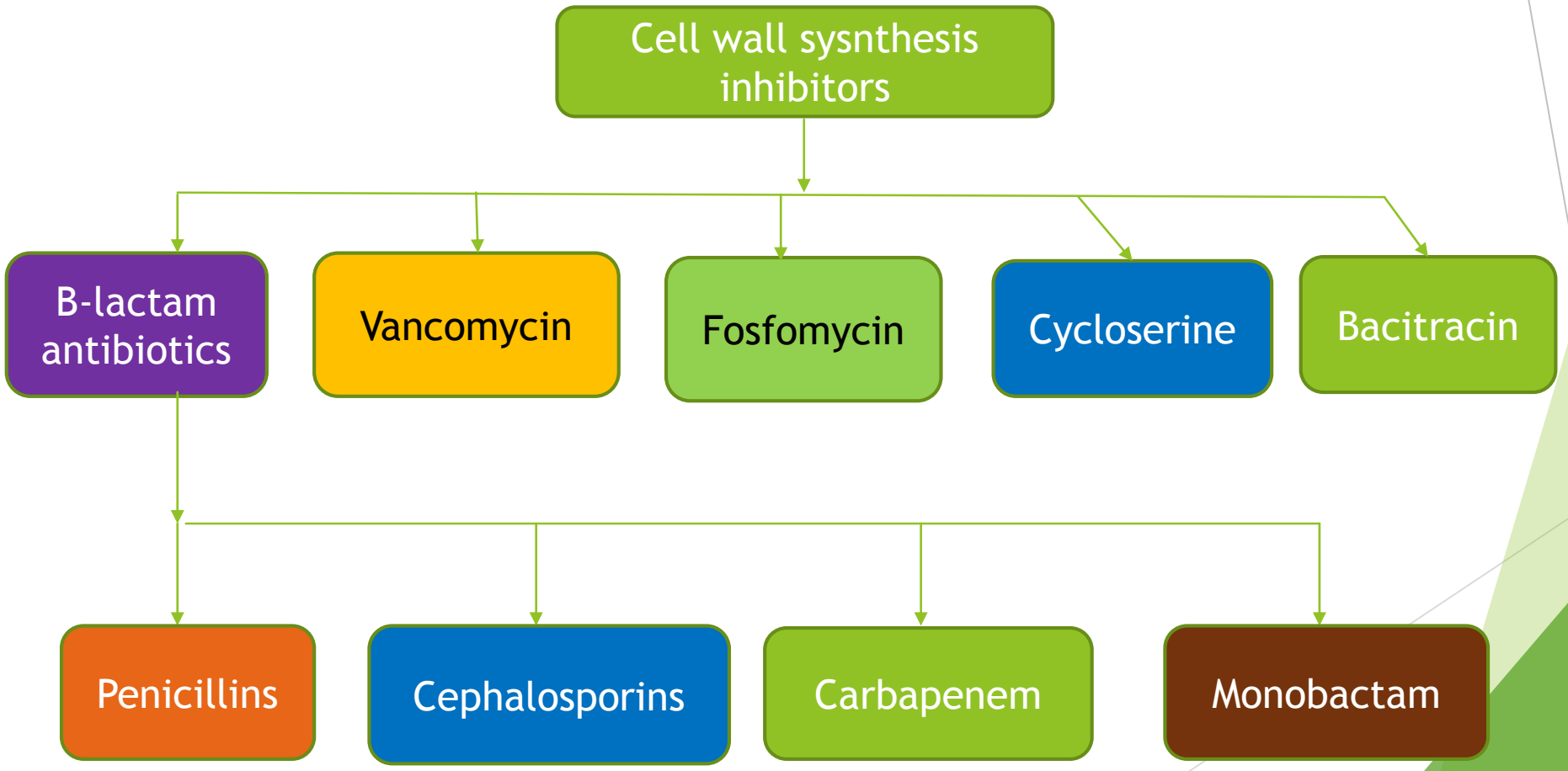
Anti-bacterials

- Anti-bacterials are classified into:
- 1. Cell wall synthesis inhibitors
- 2. Protein synthesis inhibitors
- 3. Nucleic acid synthesis inhibitors
- 4. Drugs that alter cell membrane functions

Cell wall synthesis inhibitors



B-lactam antibiotics-Penicillins

- **Classification**
- **1. Narrow spectrum penicillins**
- a. Short acting
  - Penicillin G (Benzyl Penicillin)
  - Penicillin V (Phenoxy methyl penicillins)
- b. Long acting Penicillins
  - Procain penicillin
  - Benzathine penicillin
- c. Penicillinase resistant penicillin/anti-staphylococcal penicillins
  - Dicloxacillin
  - Nafcillin
  - Methicillin
  - Cloxacillin
- **2. Extended Spectrum /broad spectrum Penicillins**
  - Ampicillin
  - Becampicillin
  - Amoxicillin
  - Aminopenicillins
  - Carbenecillins
  - Piperacillin
  - Ticarcillins
- **3. ß-lactamase inhibitors**
  - Clavulanic acid
  - Tazobactam
  - Sulbactam

Penicillins

- First penicillin was extracted from mould *Penicillium notatum* in 1940.
- Benzyl penicillin (Penicillin G) was the first natural penicillin available for clinical use.
- The basic structure of penicillin consists of Thiazolidine ring attached to ß-lactam ring known as 6-amino penicillanic acid.
- The structural integrity of 6-aminopenicillanic acid nucleus is essential for the biological activity of the molecule.
- If b-lactam ring is enzymatically cleaved by ß-lactamase, the resultant product (penicilloic acid) is completely lack of antibacterial activity.

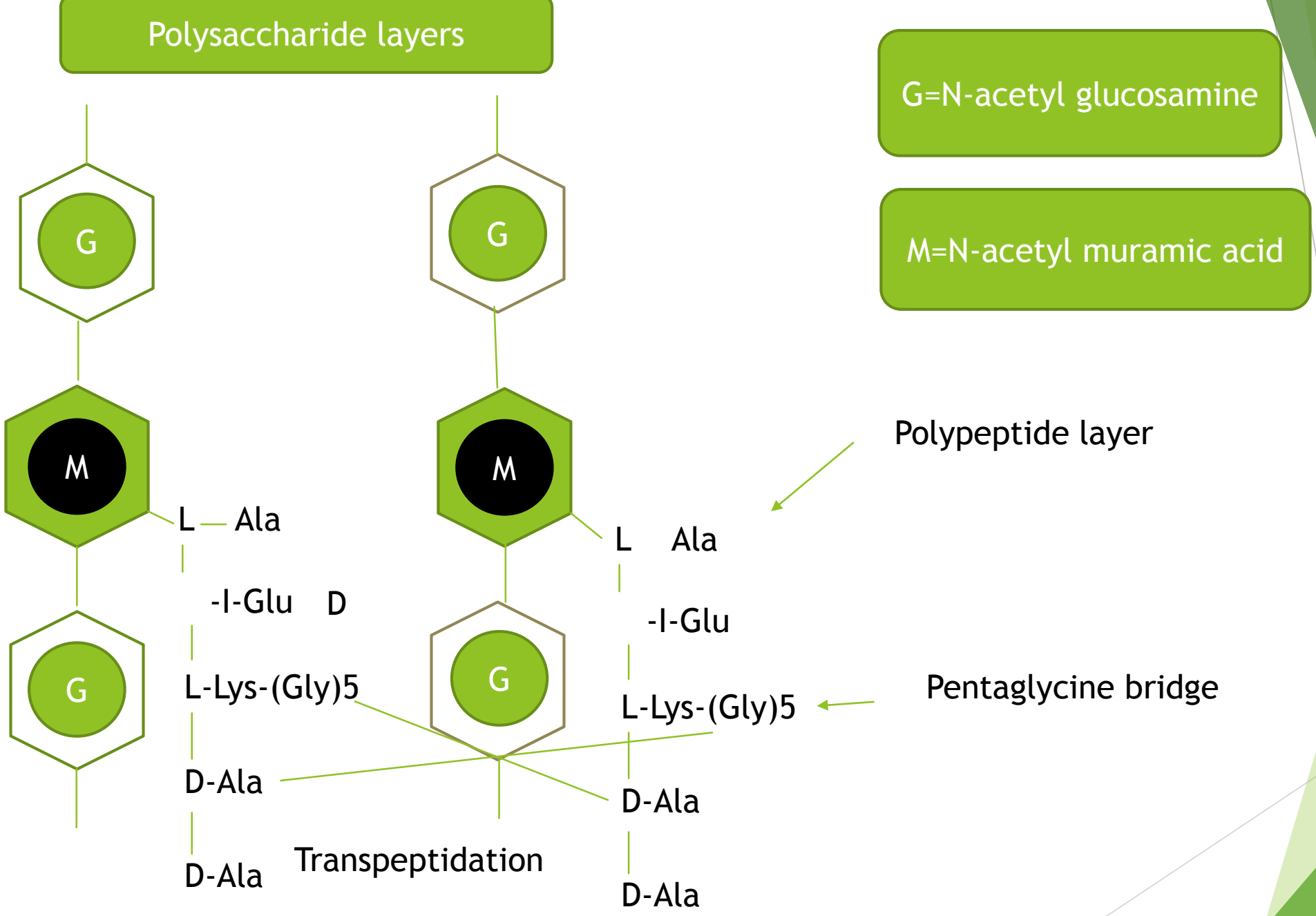
Penicillins.....

Penicillin Unit

- The activity of penicillin G was originally defined in units.
- “The one international unit of Penicillin is the specific penicillin activity contained in 0.6µg of crystalline penicillin G”.
- Semisynthetic penicillins are prescribed by weight rather than units.

Biosynthesis of cell wall

- Biosynthesis of peptidoglycan layer of cell wall is a three stage process.
- First and second stage involve synthesis reaction while third stage is of transpeptidation.
- This process involves almost 30 bacterial enzymes.
- The peptidoglycan layer of the cell wall consists of polysaccharide layer and polypeptide layers



G=N-acetyl glucosamine

M=N-acetyl muramic acid

Polypeptide layer

Pentaglycine bridge

Penicillin-mechanism of action

- Penicillins are selective inhibitors of bacterial cell wall synthesis.
- Penicillins bind to bacterial cell receptors called penicillin binding proteins (PBPs). The no. of PBPs vary in different bacteria and every penicillin has different affinity with different PBPs.
- After binding of penicillins with PBPs, the transpeptidation reaction is inhibited and synthesis of peptidoglycan is stopped.
- Autolytic enzymes are activated that cause the lysis of bacteria.

Pharmacokinetics……

- Penicillin oral absorption depends upon the acid stability and presence of food in the stomach. Preferred time 1-2 hour before or after meal.
- Dicloxacillin, Ampicillin and Amoxicillin are well absorbed orally as these are acid stable drugs.
- Penicillin G is acid labile administered parenterally.
- Maximum upto 95% bound to plasma protein.
- Well distributed to all body fluids, also appeared in milk and sputum.
- Penicillin G T1/2 half life is 30 minutes, extended spectrum have upto 1 hour.
- Penicillin excretion through kidney, 10% GFR and 90% through tubular secretion.
- Nafcillin excreted through bile.