Biosynthesis of Bacterial Cell Wall

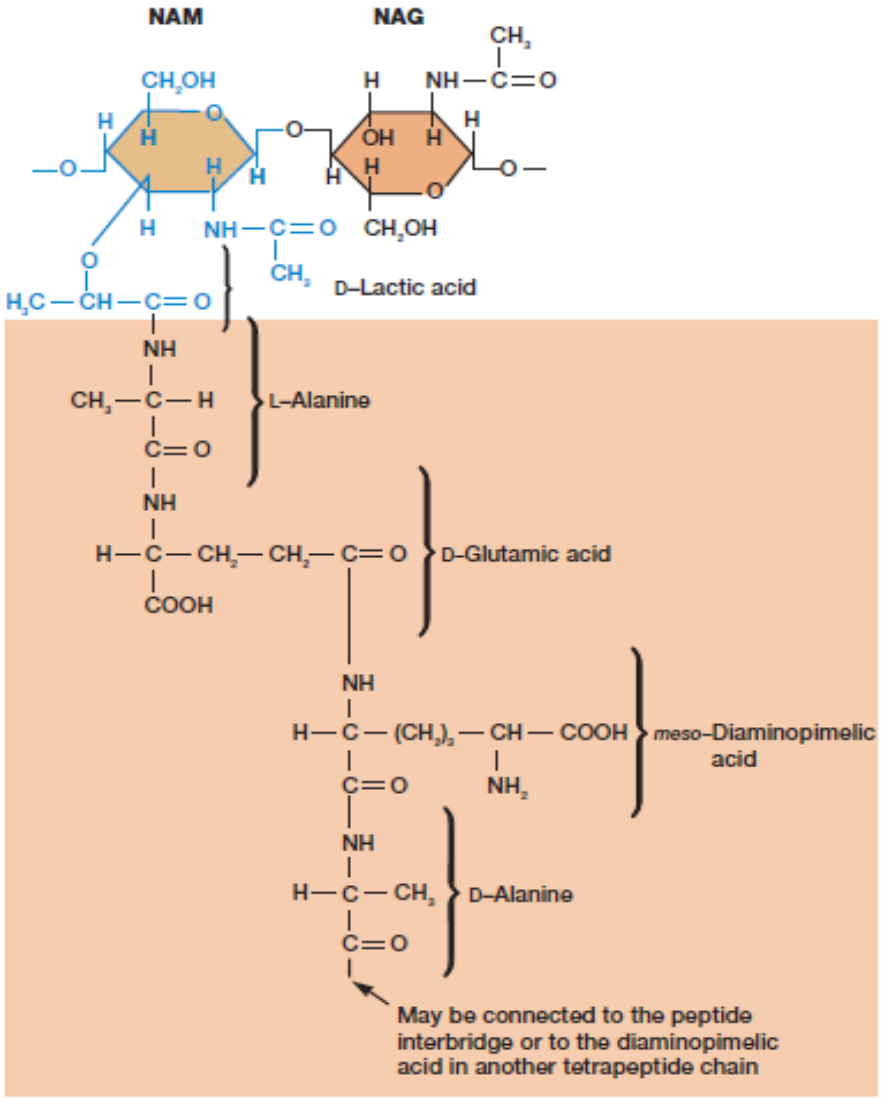
By- Dr. Ekta Khare

Department of Microbiology,

Chhatrapati Shahu Ji Maharaj University, Kanpur

Peptidoglycan Synthesis

- Bacterial cell walls contain a large, complex peptidoglycan molecule consisting of long polysaccharide chains made of alternating N-acetylmuramic acid (NAM) and N-acetylglucosamine (NAG) residues.
- Pentapeptide chains are attached to the NAM groups.
- The polysaccharide chains are connected through their pentapeptides or by interbridges



… Peptidoglycan Synthesis

- Such an intricate structure requires an equally intricate biosynthetic process, especially because the synthetic reactions occur both inside and outside the cell membrane.
- Peptidoglycan synthesis is a multistep process that has been best studied in the gram-positive bacterium *Staphylococcus aureus.*
- Two carriers participate:
  - uridine diphosphate (UDP) and
  - bactoprenol
- Bactoprenol is a 55-carbon alcohol that attaches to NAM by a pyrophosphate group and moves peptidoglycan components through the hydrophobic membrane.

… Peptidoglycan Synthesis

- **The synthesis of peptidoglycan, occurs in eight stages:**

1. UDP derivatives of N-acetylmuramic acid and Nacetylglucosamine are synthesized in the cytoplasm.
2. Amino acids are sequentially added to UDP-NAM to form the pentapeptide chain (the two terminal D-alanines are added as a dipeptide).

- ATP energy is used to make the peptide bonds, but tRNA and ribosomes are not involved.

3. The NAM-pentapeptide is transferred from UDP to a bactoprenol phosphate at the membrane surface.
4. UDP-NAG adds NAG to the NAM-pentapeptide to form the peptidoglycan repeat unit.

- If a pentaglycine interbridge is required, the glycines are added using special glycyl tRNA molecules, not ribosomes.

5. The completed NAM-NAG peptidoglycan repeat unit is transported across the membrane to its outer surface by the bactoprenol pyrophosphate carrier.
6. The peptidoglycan unit is attached to the growing end of a peptidoglycan chain to lengthen it by one repeat unit.

… Peptidoglycan Synthesis

7. The bactoprenol carrier returns to the inside of the membrane.

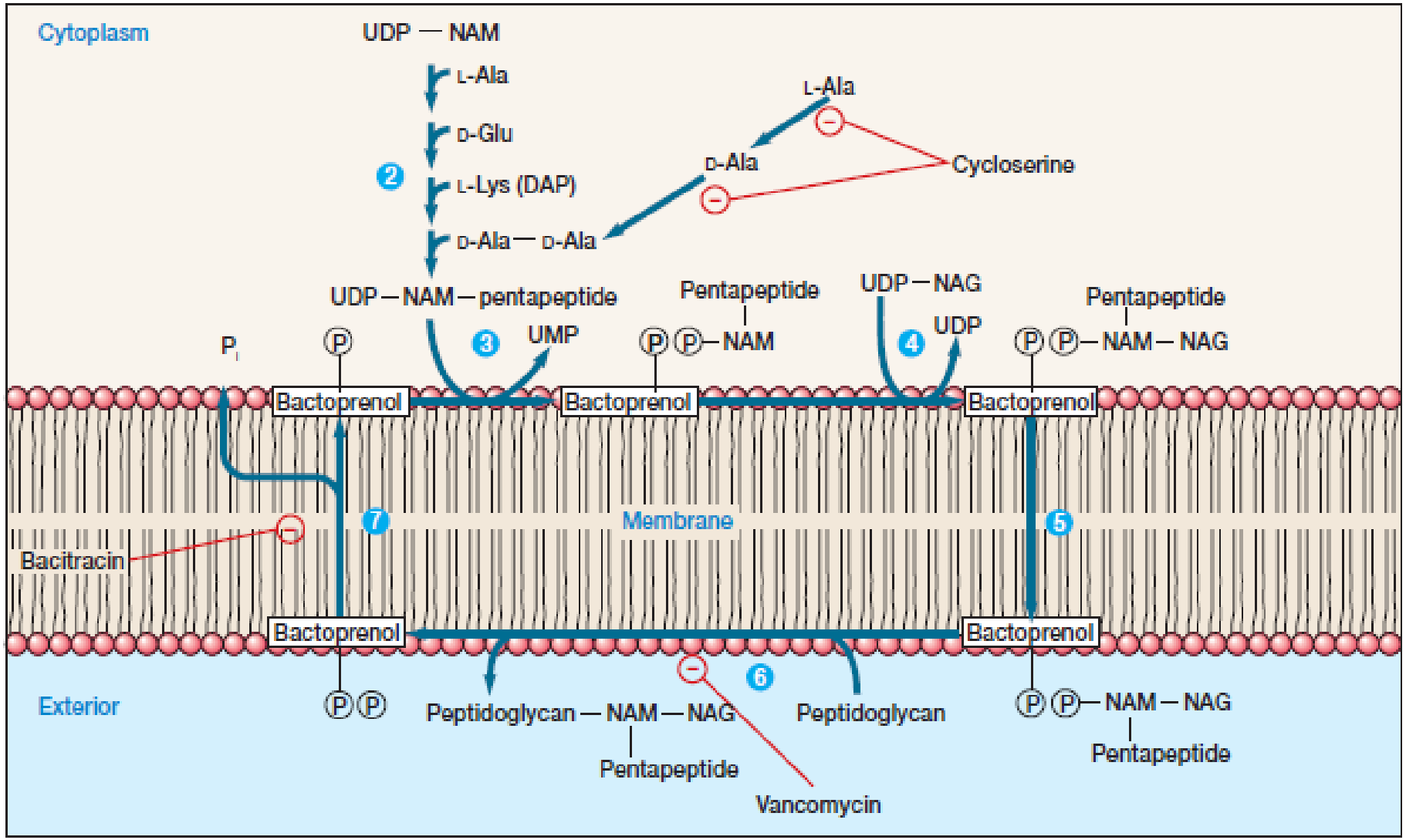
- A phosphate is released during this process to give bactoprenol phosphate, which can now accept another NAM-pentapeptide.

8. Finally, peptide cross-links between the peptidoglycan chains are formed by transpeptidation**.**

- In *E.* coli the free amino group of diaminopimelic acid attacks the subterminal D-alanine, releasing the terminal D-alanine residue.
- ATP is used to form the terminal peptide bond inside the membrane. No more ATP energy is required when transpeptidation takes place on the outside.
- The same process occurs when an interbridge is involved; only the group reacting with the subterminal D-alanine differs.
- Peptidoglycan synthesis is particularly vulnerable to disruption by antimicrobial agents. Inhibition of any stage of synthesis weakens the cell wall and can lead to osmotic lysis.
- Many antibiotics interfere with peptidoglycan synthesis. For example, penicillin inhibits the transpeptidation reaction, and bacitracin blocks the dephosphorylation of bactoprenol pyrophosphate.

Peptidoglycan Synthesis.

NAM is N-acetylmuramic acid and NAG is N-acetylglucosamine. The pentapeptide contains L-lysine in *S. aureus* peptidoglycan, and diaminopimelic acid (DAP) in *E. coli.*
Inhibition by bacitracin, cycloserine, and vancomycin also is shown.



Transpeptidation.

The transpeptidation reactions in the formation of the peptidoglycans of *Escherichia coli* and *Staphylococcus aureus*.