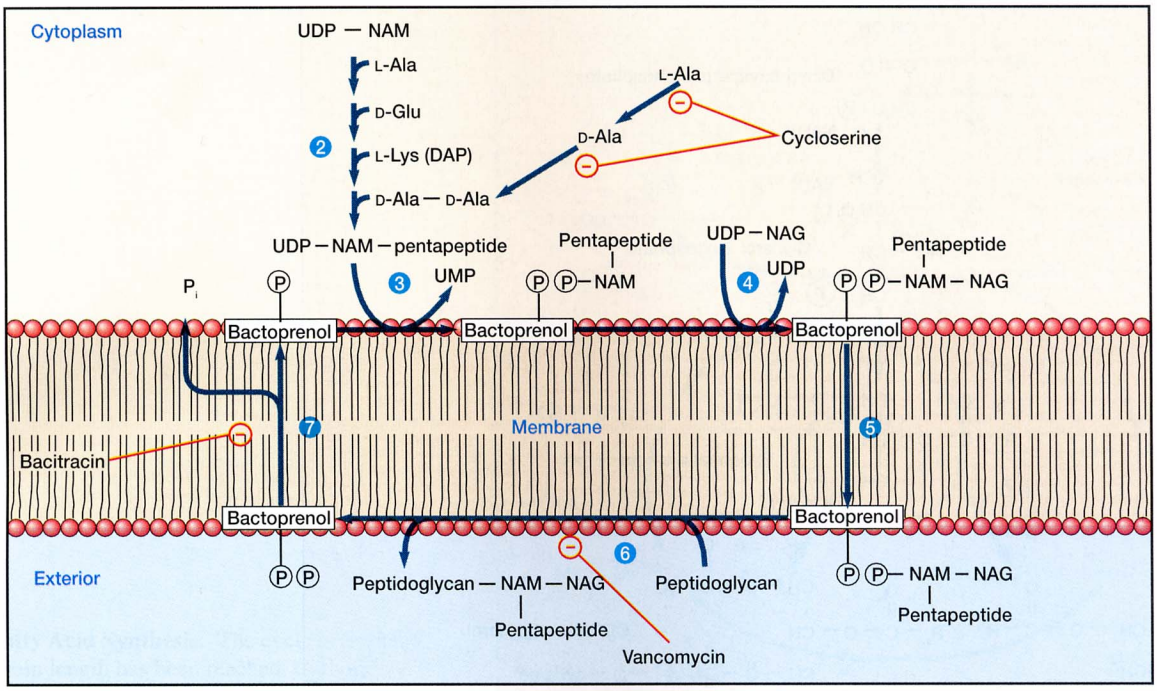

Figure 10.28 Peptidoglycan Synthesis. NAM is *N*-acetylmuramic acid and NAG is *N*-acetylglucosamine. The pentapeptide contains L-lysine in *S. aureus* peptidoglycan, and diaminopimelic acid (DAP) in *E. coli*. Inhibition by bacitracin, cycloserine, and vancomycin also is shown. The numbers correspond to six of the eight stages discussed in the text. Stage eight is depicted in figure 10.29.

The synthesis of peptidoglycan, outlined in **figures 10.28** and 10.29, occurs in eight stages.

1. UDP derivatives of N-acetylmuramic acid and N-acetylglucosamine 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.
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** (**figure 10.29**). 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 (figure 10.29), and bacitracin blocks the dephosphorylation of bactoprenol pyrophosphate (figure 10.28). Antibiotic effects on cell wall synthesis (pp. 813–15, 817)

10.10 Patterns of Cell Wall Formation

To grow and divide efficiently, a bacterial cell must add new peptidoglycan to its cell wall in a precise and well-regulated way while maintaining wall shape and integrity in the presence of high osmotic pressure. Because the cell wall peptidoglycan is essentially a single enormous network, the growing bacterium