13.2A: Inhibiting Cell Wall Synthesis

β-Lactam (beta-lactam) and glycopeptide antibiotics work by inhibiting or interfering with cell wall synthesis of the target bacteria.

Learning Objectives

• Describe the two types of antimicrobial drugs that inhibit cell wall synthesis: beta-lactam and glycopeptide antibiotics

Key Points

• The peptidoglycan layer is important for cell wall structural integrity, being the outermost and primary component of the wall.
• β-Lactam antibiotics are a broad class of antibiotics that includes penicillin derivatives (penams), cephalosporins (cephems), monobactams, and carbapenems.
• β-Lactam antibiotics are bacteriocidal and act by inhibiting the synthesis of the peptidoglycan layer of bacterial cell walls.
• Glycopeptide antibiotics include vancomycin, teicoplanin, telavancin, bleomycin, ramoplanin, and decaplanin.
• Glycopeptide antibiotics inhibit the synthesis of cell walls in susceptible microbes by inhibiting peptidoglycan synthesis.

Key Terms

• beta-lactam antibiotic: A broad class of antibiotics that inhibit cell wall synthesis, consisting of all antibiotic
agents that contains a β-lactam nucleus in their molecular structures. This includes penicillin derivatives (penams), cephalosporins (cephems), monobactams, and carbapenems.

- **Glycopeptide antibiotic**: Glycopeptide antibiotics are composed of glycosylated cyclic or polycyclic nonribosomal peptides. Significant glycopeptide antibiotics include vancomycin, teicoplanin, telavancin, bleomycin, ramoplanin, and decaplanin. This class of drugs inhibit the synthesis of cell walls in susceptible microbes by inhibiting peptidoglycan synthesis.

- **peptidoglycan**: A polymer of glycan and peptides found in bacterial cell walls.

Two types of antimicrobial drugs work by inhibiting or interfering with cell wall synthesis of the target bacteria. Antibiotics commonly target bacterial cell wall formation (of which peptidoglycan is an important component) because animal cells do not have cell walls. The peptidoglycan layer is important for cell wall structural integrity, being the outermost and primary component of the wall.

The first class of antimicrobial drugs that interfere with cell wall synthesis are the β-Lactam antibiotics (beta-lactam antibiotics), consisting of all antibiotic agents that contains a β-lactam nucleus in their molecular structures. This includes penicillin derivatives (penams), cephalosporins (cephems), monobactams, and carbapenems. β-Lactam antibiotics are bacteriocidal and act by inhibiting the synthesis of the peptidoglycan layer of bacterial cell walls. The final step in the synthesis of the peptidoglycan is facilitated by penicillin-binding proteins (PBPs). PBPs vary in their affinity for binding penicillin or other β-lactam antibiotics.
Figure: **Penicillin spheroplast generation**: Diagram depicting the failure of bacterial cell division in the presence of a cell wall synthesis inhibitor (e.g. penicillin, vancomycin). 1- Penicillin (or other cell wall synthesis inhibitor) is added to the growth medium with a dividing bacterium. 2- The cell begins to grow, but is unable to synthesize new cell wall to accommodate the expanding cell. 3- As cellular growth continues, cytoplasm covered by plasma membrane begins to squeeze out through the gap(s) in the cell wall. 4- Cell wall integrity is further violated. The cell continues to increase in size, but is unable to “pinch off” the extra cytoplasmic material into two daughter cells because the formation of a
division furrow depends on the ability to synthesize new cell wall. The cell wall is shed entirely, forming a spheroplast, which is extremely vulnerable relative to the original cell. The loss of the cell wall also causes the cell to lose control over its shape, so even if the original bacterium were rod-shaped, the spheroplast is generally spherical. Finally, the fact that the cell has now doubled much of its genetic and metabolic material further disrupts homeostasis, which usually leads to the cell’s death.

Bacteria often develop resistance to β-lactam antibiotics by synthesizing a β-lactamase, an enzyme that attacks the β-lactam ring. To overcome this resistance, β-lactam antibiotics are often given with β-lactamase inhibitors such as clavulanic acid.

The second class of antimicrobial drugs that interfere with cell wall synthesis are the glycopeptide antibiotics, which are composed of glycosylated cyclic or polycyclic nonribosomal peptides. Significant glycopeptide antibiotics include vancomycin, teicoplanin, telavancin, bleomycin, ramoplanin, and decaplanin. This class of drugs inhibit the synthesis of cell walls in susceptible microbes by inhibiting peptidoglycan synthesis. They bind to the amino acids within the cell wall preventing the addition of new units to the peptidoglycan.