13.1C: Antibiotics and Selective Toxicity

Antibiotics are able to selectively target specific types of bacteria without harming the infected host.

Learning Objectives

• Describe selective toxicity

Key Points

• Their mechanism of action, chemical structure, or spectrum of activity are ways in which antibiotics are classified.
• Broad spectrum antibiotics affect a wide range of bacteria, while narrow spectrum antibiotics are able to target specific types.
• Antibiotics must go through a screening process, where they are isolated, cultured, and then tested for production of diffusible products that inhibit the growth of specific test organisms.
• Due to potential adverse side effects, antibiotics must also be tested for their selective toxicities.

Key Terms

• antibacterial: A drug having the effect of killing or inhibiting bacteria.
• bactericidal: An agent that kills bacteria.
• bacteriostatic: A drug that prevents bacterial growth and reproduction but does not necessarily kill them. When it is removed from the environment the bacteria start growing again.
Selective Toxicity in Antibiotics

Synthetic antibiotic chemotherapy as a science and development of antibacterials began in Germany with Paul Ehrlich in the late 1880s. Ehrlich noted that certain dyes would color human, animal, or bacterial cells, while others did not. He then proposed the idea that it might be possible to create chemicals that would act as a selective drug that would bind to and kill bacteria without harming the human host. After screening hundreds of dyes against various organisms, he discovered a medicinally useful drug, the synthetic antibacterial Salvarsan now called arsphenamine.

Antibiotics are commonly classified based on their mechanism of action, chemical structure, or spectrum of activity. More specifically, narrow spectrum antibiotics target specific types of bacteria, such as Gram-negative or Gram-positive bacteria, whereas broad spectrum antibiotics affect a wide range of bacteria. Following a 40-year hiatus in discovering new classes of antibacterial compounds, three new classes of antibacterial antibiotics have been brought into clinical use: cyclic lipopeptides (such as daptomycin), glycyclines (such as tigecycline), and oxazolidinones (such as linezolid).

Figure: **Bacterial Cultures**: In antibacterial production, microorganisms must be isolated, cultured, and tested for growth inhibition of target organisms and for their selective toxicity.

Some antibacterials have been associated with a range of adverse effects. Side-effects range from mild to very serious depending on the antibiotics used, the microbial organisms targeted, and the individual patient. Safety profiles of newer drugs are often not as well established as for those that have a long history of use. Adverse effects range from fever and nausea to major allergic reactions, including photodermatitis and anaphylaxis. Common side-effects include diarrhea, resulting from disruption of the species composition in the intestinal flora, resulting, for example, in overgrowth of pathogenic bacteria, such as *Clostridium difficile*. Antibacterials can also affect the vaginal flora, and may lead to
overgrowth of yeast species of the genus *Candida* in the vulvo-vaginal area. Additional side-effects can result from interaction with other drugs, such as elevated risk of tendon damage from administration of a quinolone antibiotic with a systemic corticosteroid.

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**Antibacterial Production**

Despite the wide variety of known antibiotics, less than 1% of antimicrobial agents have medical or commercial value. For example, whereas penicillin has a high therapeutic index as it does not generally affect human cells, this is not so for many antibiotics. Other antibiotics simply lack advantage over those already in use, or have no other practical applications. Useful antibiotics are often discovered using a screening process. To conduct such a screen, isolates of many different microorganisms are cultured and then tested for production of diffusible products that inhibit the growth of test organisms. Most antibiotics identified in such a screen are already known and must therefore be disregarded. The remainder must be tested for their selective toxicities and therapeutic activities, and the best candidates can be examined and possibly modified. A more modern version of this approach is a rational design program. This involves screening directed towards finding new natural products that inhibit a specific target, such as an enzyme only found in the target pathogen, rather than tests to show general inhibition of a culture.