

Study Outline Chapter 20

Introduction (p. 531)

- An antimicrobial drug is a chemical substance that destroys pathogenic microorganisms with minimal damage to host tissues.
- Chemotherapeutic agents include chemicals that combat disease in the body.
- Antimicrobial drugs may be synthetic drugs (prepared in the laboratory) or antibiotics (produced by bacteria or fungi).

The History of Chemotherapy (pp. 531- 532)

- Paul Ehrlich developed the concept of chemotherapy to treat microbial diseases; he predicted the development of chemotherapeutic agents, which would kill pathogens without harming the host.
- Sulfa drugs came into prominence in the late 1930s.
- Alexander Fleming discovered the first antibiotic, penicillin, in 1929; its first clinical trials were done in 1940.

The Spectrum of Antimicrobial Activity (pp. 532- 533)

- Antibacterial drugs affect many targets in a prokaryotic cell.
- Fungal, protozoan, and helminthic infections are more difficult to treat because these organisms have eukaryotic cells.
- Narrow-spectrum drugs affect only a select group of microbes—gram-positive cells, for example; broad-spectrum drugs affect a large number of microbes.
- Small, hydrophilic drugs can affect gram-negative cells.
- Antimicrobial agents should not cause excessive harm to normal microbiota.
- Superinfections occur when a pathogen develops resistance to the drug being used or when normally resistant microbiota multiply excessively.

The Action of Antimicrobial Drugs (pp. 533- 536)

- General action is either by directly killing microorganisms (bactericidal) or by inhibiting their growth (bacteriostatic).
- Some agents, such as penicillin, inhibit cell wall synthesis in bacteria.
- Other agents, such as chloramphenicol, erythromycin, tetracyclines, and streptomycin, inhibit protein synthesis by acting on 70S ribosomes.
- Agents such as polymyxin B cause injury to plasma membranes.
- Rifampin and the quinolones inhibit nucleic acid synthesis.
- Agents such as sulfanilamide act as antimetabolites by competitively inhibiting enzyme activity.

A Survey of Commonly Used Antimicrobial Drugs (pp. 536- 549)

Antibacterial Antibiotics: Inhibitors of Cell Wall Synthesis (pp. 536- 540)

- All penicillins contain a β -lactam ring.
- Natural penicillins produced by *Penicillium* are effective against gram-positive cocci and spirochetes.
- Penicillinases (β -lactamases) are bacterial enzymes that destroy natural

penicillins.

- Semisynthetic penicillins are made in the laboratory by adding different side chains onto the β -lactam ring made by the fungus.
- Semisynthetic penicillins are resistant to penicillinases and have a broader spectrum of activity than natural penicillins.
- The monobactam aztreonam affects only gram-negative bacteria.
- Cephalosporins inhibit cell wall synthesis and are used against penicillin-resistant strains.
- Carbapenems are broad-spectrum antibiotics that inhibit cell wall synthesis.
- Polypeptides such as bacitracin are applied topically to treat superficial infections.
- Bacitracin inhibits cell wall synthesis primarily in gram-positive bacteria.
- Vancomycin inhibits cell wall synthesis and may be used to kill penicillinase-producing staphylococci.
- Isoniazid (INH) inhibits mycolic acid synthesis in mycobacteria. INH is administered with rifampin or ethambutol to treat tuberculosis.
- The antimetabolite ethambutol is used with other drugs to treat tuberculosis.

Inhibitors of Protein Synthesis (pp. 541- 542)

- Aminoglycosides, tetracyclines, chloramphenicol, and macrolides inhibit protein synthesis at 70S ribosomes.

Injury to the Plasma Membrane (p. 542)

- Polymyxin B and bacitracin cause damage to plasma membranes.

Type III (Immune Complex) Reactions (pp. 510- 511)

- Immune complex diseases occur when IgG antibodies and soluble antigen form small complexes that lodge in the basement membranes of cells.
- Subsequent complement fixation results in inflammation.
- Serum sickness and glomerulonephritis are immune complex diseases.

Inhibitors of Nucleic Acid (DNA/RNA) Synthesis (pp. 542- 543)

- Rifampin inhibits mRNA synthesis; it is used to treat tuberculosis.
- Quinolones and fluoroquinolones inhibit DNA gyrase for treatment of urinary tract infections.

Competitive Inhibitors of the Synthesis of Essential Metabolites (p. 543)

- Sulfonamides competitively inhibit folic acid synthesis.
- TMP-SMX competitively inhibits dihydrofolic acid synthesis for treatment of urinary tract and intestinal infections.

Antifungal Drugs (pp. 543- 545)

- Polyenes, such as nystatin and amphotericin B, combine with plasma membrane sterols and are fungicidal.
- Imidazoles and triazoles interfere with sterol synthesis and are used to treat cutaneous and systemic mycoses.
- Griseofulvin interferes with eucaryotic cell division and is used primarily to treat skin infections caused by fungi.
- The antifungal agent flucytosine is an antimetabolite of cytosine.

Antiviral Drugs (pp. 545- 547)

- Amantadine blocks the penetration or uncoating of influenza A virus.
- Nucleoside analogs such as acyclovir, AZT, ddI, and ddC inhibit DNA or RNA synthesis.
- Drugs that inhibit viral enzymes are nevirapine, which inhibits reverse transcriptase, and protease inhibitors, which block an HIV enzyme.
- Xenografts are subject to hyperacute rejection.
- Alpha-interferons inhibit the spread of viruses to new cells.

Antiprotozoan and Antihelminthic Drugs (pp. 547- 549)

- Chloroquine, quinacrine, diiodohydroxyquin, pentamidine, and metronidazole are used to treat protozoan infections.
- Antihelminthic drugs include niclosamide, mebendazole, praziquantel, and piperazine.
- Mebendazole disrupts microtubules; pyantel pamoate paralyzes intestinal roundworms.

Tests to Guide Chemotherapy (pp. 549- 550)

- These tests are used to determine which chemotherapeutic agent is most likely to combat a specific pathogen.
- These tests are used when susceptibility cannot be predicted or when drug resistance arises.

The Diffusion Methods (p. 549)

- In this test, also known as the Kirby-Bauer test, a bacterial culture is inoculated on an agar medium, and filter paper disks impregnated with chemotherapeutic agents are overlayed on the culture.
- After incubation, the absence of microbial growth around a disk is called a zone of inhibition.
- The diameter of the zone of inhibition, when compared with a standardized reference table, is used to determine whether the organism is sensitive, intermediate, or resistant to the drug.
- MIC is the lowest concentration of drug capable of preventing microbial growth; MIC can be estimated using the E test.

Broth Dilution Tests (pp. 549- 550)

- In a broth dilution test, the microorganism is grown in liquid media containing different concentrations of a chemotherapeutic agent.
- The lowest concentration of a chemotherapeutic agent that kills bacteria is called the minimum bactericidal concentration (MBC).

The Effectiveness of Chemotherapeutic Agents (pp. 550- 553)

Drug Resistance (pp. 550- 551)

- Resistance may be due to enzymatic destruction of a drug, prevention of penetration of the drug to its target site, or cellular or metabolic changes at target sites.
- Hereditary drug resistance (R) factors are carried by plasmids and transposons.
- Resistance can be minimized by the discriminating use of drugs in appropriate concentrations and dosages.

Effects of Combinations of Drugs (pp. 551- 552)

- Some combinations of drugs are synergistic; they are more effective when taken together.
- Some combinations of drugs are antagonistic; when taken together, both drugs become less effective than when taken alone.

The Future of Chemotherapeutic Agents (pp. 552- 553)

- Many bacterial diseases, previously treatable with antibiotics, have become resistant to antibiotics.
- Chemicals produced by plants and animals are providing new antimicrobial agents, including antimicrobial peptides.
- New antimicrobial drugs include DNA that is complementary to specific genes in a pathogen; the DNA will bind to the pathogen's DNA or mRNA and inhibit protein synthesis.