20 Antimicrobial Drugs

Chemotherapy is the treatment of disease with chemicals (drugs) taken into the body. The class of chemotherapeutic agents used to treat infectious diseases is **antimicrobial drugs;** unlike disinfectants, they must act within the host, where they kill the harmful organism without damaging the host, called **selective toxicity. Antibiotics** are produced by microorganisms and, in small amounts, inbibit another microorganism.

THE HISTORY OF CHEMOTHERAPY

During the early part of the twentieth century, Dr. Paul Ehrlich of Germany speculated about a "magic bullet" that would destroy pathogens but not harm the host. Eventually, he found an arsenic derivative, *salvarsan,* that was useful against syphilis. Prior to this discovery, the only chemotherapeutic agent available was *quinine,* for the treatment of malaria. *Sulfa drugs* were discovered during the 1930s. The drugs are wholly synthetic and technically are not antibiotics. *Penicillin,* an antibiotic, was first discovered in 1928 but was not available in a useful form until after 1940. Today, most antibiotics are discovered by so-called *high-throughput methods* that screen very high numbers of microbes, generally from soil or aquatic samples.

THE SPECTRUM OF ANTIMICROBIAL ACTIVITY

It is comparatively easy to find antimicrobials against prokaryotes (bacteria) because prokaryotes differ substantially from the eukaryotic cells of humans. Fungi, protozoa, and helminths are eukaryotic, which makes selective toxicity for the pathogen (without affecting the host) more difficult. It is difficult to find antimicrobials against viruses, which exist inside a host cell and interact with the host cell to synthesize new viruses.

If an antimicrobial drug affects relatively few bacteria, it has a narrow **spectrum of microbial activity,** as opposed to **broad-spectrum antibiotics.** Antibiotics may eliminate normal microbiota and allow opportunistic pathogens to flourish (**superinfection**).

THE ACTION OF ANTIMICROBIAL DRUGS

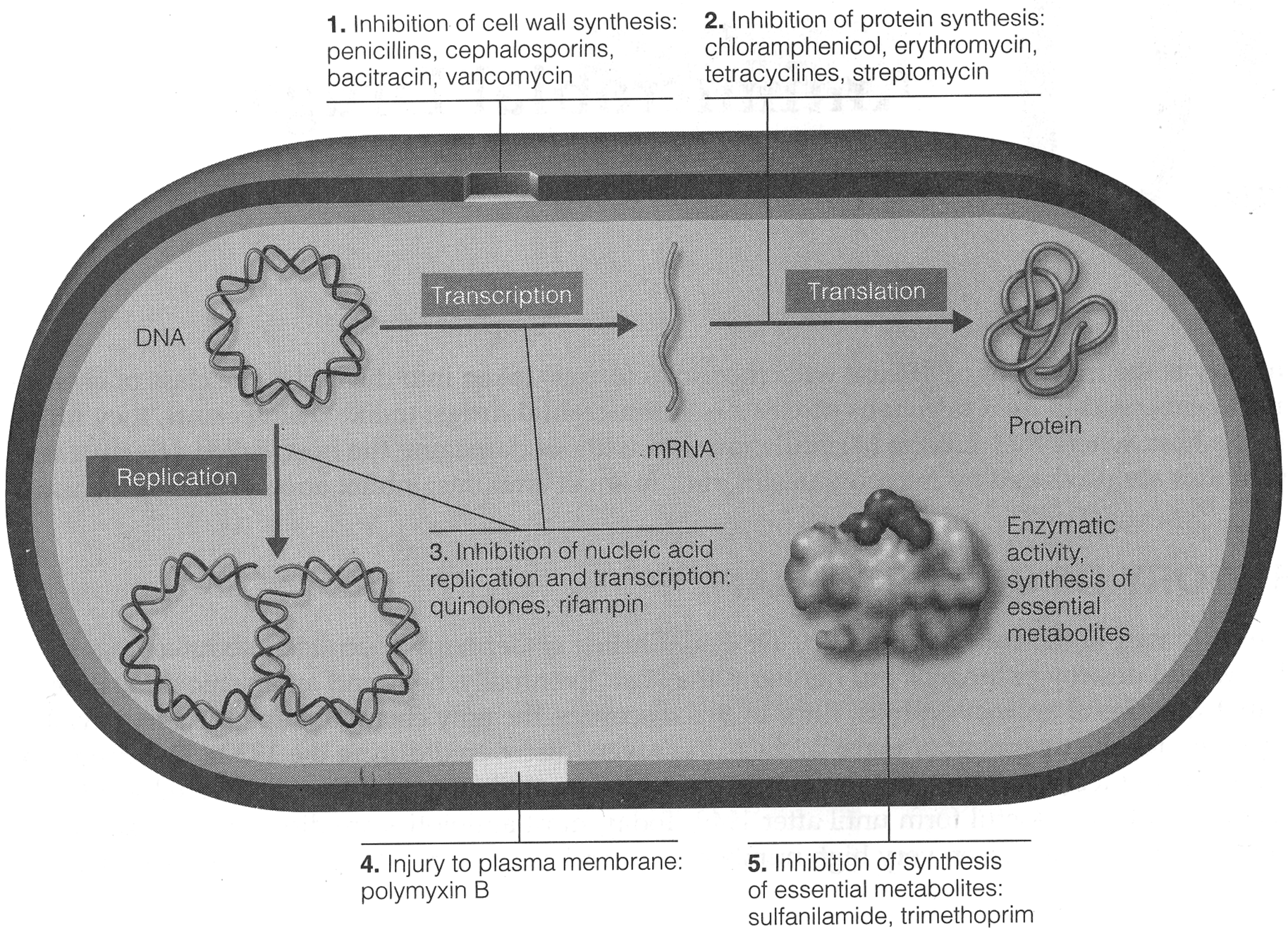
See the summary in Figure 20.1. Antimicrobial drugs are either **bactericidal** (they kill microbes directly) or **bacteriostatic** (they prevent microbes from growing).

Inhibiting Cell Wall Synthesis

The cell walls of bacteria consist of a layer of peptidoglycan, which is found only in bacterial cells. Therefore, interference with the synthesis of bacterial cell walls usually does not harm the host. Antibiotics using this mode of action include penicillins, cephalosporins, bacitracin, and vancomycin. Because the peptidoglycan layer of gram-positive bacteria is more accessible than that of gram-negative ones, these bacteria are the most susceptible to such agents.

Inhibiting Protein Synthesis

Ribosome structure differs greatly between prokaryotic and eukaryotic cells. Many antibiotics such as chloramphenicol, gentamicin, erythromycin, tetracyclines, and streptomycin interfere with protein synthesis by reacting with the ribosomes of bacteria.



Key Concept

Antimicrobial drugs function in one of the following five ways: inhibiting cell wall synthesis, inhibiting protein synthesis, inhibiting nucleic acid synthesis, injuring the plasma membrane, or inhibiting synthesis of essential metabolites.

Figure 20.1 A summary of the major modes of action of antimicrobial drugs. This illustration shows these actions as they might affect a highly diagrammatic representation of a bacterial cell.

Injuring the Plasma Membrane

Antibiotics, especially such polypeptides as polymyxin B, can adversely affect the membrane permeability of microbial cells. Loss of important metabolites occurs from these changes in permeability. Similarly, the effectiveness of nystatin, miconazole, ketoconazole, and amphotericin B against fungi is based on their combining with sterols to disrupt fungal plasma membranes.

Inhibiting Nucleic Acid Synthesis

Similarities between microbial and host cell DNA and RNA are so close that drugs that act by interfering with the nucleic acid synthesis of microbial cells have only limited clinical application. Drugs acting on this principle are rifampin and the quinolones.

Inhibiting the Synthesis of Essential Metabolites

Sulfa drugs, for example, competitively inhibit the synthesis of folic acid, which is a vitamin that is synthesized by bacteria but not humans. The drug resembles the metabolite **para-aminobenzoic acid,** which is required to synthesize folic acid.

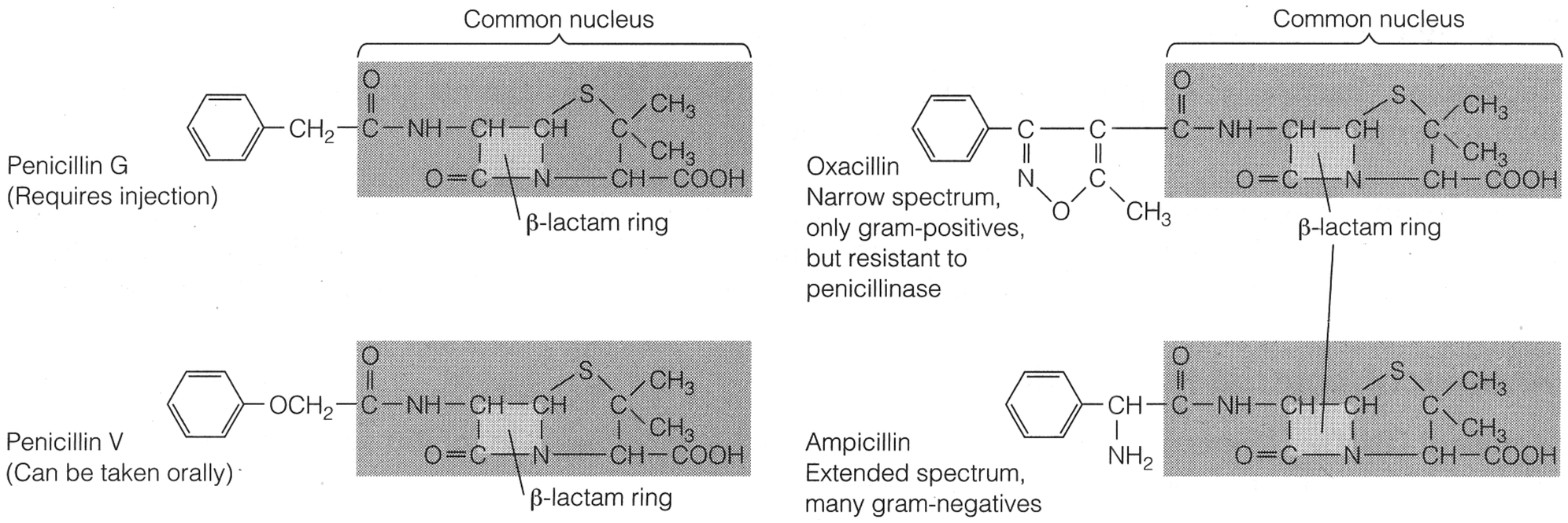


Figure 20.2 The structure of penicillins, antibacterial antibiotics. The portion that all penicillins have in common—which contains the β-lactam ring—is shaded. The unshaded portions represent the side chains that distinguish one penicillin from another.

A SURVEY OF COMMONLY USED ANTIMICROBIAL DRUGS

Antibacterial Antibiotics: Inhibitors of Cell Wall Synthesis

Penicillins. The term **penicillin** refers to a group of related antibiotics (Figure 20.2).

Natural Penicillins. **Natural penicillins,** such as *penicillin G* or *V,* are products of *Penicillium* mold growth. *Procaine penicillin* and *benzathine penicillin* combine penicillin G with other drugs to prolong the antibiotic's retention in the body. **Penicillinases** (*β-lactamases*) are enzymes that cleave the *β-lactam* ring of penicillins, causing resistance.

Semisynthetic Penicillins. A large number of **semisynthetic penicillins** have been developed to overcome the disadvantages of natural penicillins. Side chains of natural penicillins are removed and other side chains added to extend their spectrum or make them resistant to penicillinases.

Penicillinase-Resistant Penicillins. The first semisynthetic penicillin designed to evade the action of penicillinases was *methicillin.* Eventually, so many staphylococcal strains became resistant that the abbreviation **MRSA (methicillin-resistant *Staphylococcus aureus*)** made its appearance. Methicillin has been discontinued; however, *oxacillin* and *nafcillin* are still in use.

Extended-Spectrum Penicillins. Certain semisynthetic penicillins, such as *ampicillin, amoxicillin* (both **aminopenicillins**), *carbenicillin,* and *ticarcillin* (both **carboxypenicillins**), have a broader spectrum of activity than do natural penicillins. Semisynthetics such as the **ureidopenicillins,** which include *mezlocillin* and *azlocillin,* also have a broader spectrum of activity.

Penicillins Plus β-Lactamase Inhibitors. Another approach to penicillinase resistance is to combine penicillins with *potassium clavulanate (clavulanic acid),* which is a noncompetitive inhibitor of penicillinase. Augmentin is the trade name of such a combination.

Carbapenems. The **carbapenems** are a class of β-lactam antibiotics that have an extremely broad spectrum of activity. An example is Primaxin, a combination of *imipenem* and *cilastin.*

Monobactams. Another penicillin variant, **monobactams** have only a single-ring structure. One of these, *aztreonam,* affects only gram-negative bacteria.

Cephalosporins. The structural nucleus and mode of action of **cephalosporins** resemble those of penicillin. Cephalosporins, such as *cephalothin, cefamandole,* and *cefotaxime,* are often used as substitutes for penicillin.

Polypeptide Antibiotics

Bacitracin. **Bacitracin** is a polypeptide antibiotic effective primarily against gram-positive bacteria. It inhibits synthesis of cell walls and is used only topically.

Vancomycin. **Vancomycin** is a member of the small glycopeptide group that inhibits peptidoglycan synthesis. It is used against penicillinase-producing staphylococci that cause life-threatening infections. Vancomycin is used to treat MRSA and has led to the selection of **VRE (vancomycin-resistant enterococci).**

Antimycobacterial Antibiotics

Isoniazid (INH). **Isoniazid,** used in treating tuberculosis, is believed to inhibit synthesis of mycolic acids, which are part of the cell wall of mycobacteria.

Ethambutol. **Ethambutol** is effective only against mycobacteria and is used in chemotherapeutic treatment of tuberculosis. It inhibits the incorporation of mycolic acid into the cell wall.

Inhibitors of Protein Synthesis

Chloramphenicol. *Chloramphenicol* is a broad-spectrum antibiotic that affects protein synthesis. Structurally simple, it is often synthesized chemically. It may cause a blood disorder, aplastic anemia. It is the drug of choice for typhoid fever and certain types of meningitis, for which the risk is considered justified.

Aminoglycosides. **Aminoglycosides** are a group of antibiotics with amino sugars and an aminocyclitol ring. Examples are *streptomycin* (used for tuberculosis treatment), *neomycin* (used in topical ointment with bacitracin and polymyxin B), and *gentamicin* (effective against most gram-negatives, especially *Pseudomonas*). *Tobramycin* is administered by aerosol to treat cystic fibrosis patients infected with pseudomonads. Aminoglycosides sometimes are toxic to the auditory nerve or the kidneys.

Tetracyclines. **Tetracyclines** are broad-spectrum antibiotics that are also effective against chlamydias and rickettsias. They inhibit protein synthesis. They produce such side effects as tooth discoloration and liver damage. Commonly encountered are *tetracycline, oxytetracycline (Terramycin),* and *chlortetracycline (Aureomycin).* Some newer semisynthetic versions, such as *doxycycline* and *minocycline,* are retained in the body longer. New derivatives of minocycline are represented by *tigecycline (Tygacil);* they have a broad spectrum of activity.

Macrolides. **Macrolides** are named for their macrocyclic lactone ring and are especially effective against gram-positive bacteria. *Erythromycin* inhibits protein synthesis and is used in treating infections resistant to penicillins, as well as legionellosis and mycoplasmal pneumonia. Other macrolides are *azithromycin* and *clarithromycin;* compared to erythromycin they have a broader spectrum and penetrate tissues better. **Ketolides** are new semisynthetic macrolides developed to combat microbial resistance. An example is *telithromycin (Ketek).*

Streptogramins. The **streptogramins** are a unique group of antibiotics developed to combat resistance to vancomycin. Synercid is a combination of two cyclic peptides *quinupristin* and *dalfopristin,* which are distantly related to macrolides.

Oxazolidinones. The **oxazolidinones** are a new class of totally synthetic antibiotics. They have a unique target, binding to the 50S ribosomal subunit close to the point where it interfaces with the 30S subunit. *Linozolid (Zyvox),* a member of the group, is used mainly to combat MRSA.

Injury to the Plasma Membrane

Polymyxin B is effective against gram-negative bacteria, even *Pseudomonas.* It is available for topical use in the antiseptic ointment that also contains *bacitracin* and *neomycin.* Many of the antimicrobial peptides discussed later in the chapter target the synthesis of the plasma membrane. Some new antibiotics that target the synthesis of the plasma membranes are *platensimysin, linezolid,* and *daptomycin.*

Inhibitors of Nucleic Acid (DNA/RNA) Synthesis

Rifamycins. *Rifampin,* the best known of the **rifamycin** family, is used in tuberculosis therapy. These drugs inhibit the synthesis of mRNA.

Quinolones and Fluoroquinolones. The first of the **quinolone** group was *nalidixic acid,* which selectively inhibits the enzyme DNA gyrase needed for DNA replication. This led to the development of a prolific group of synthetic quinolones, the **fluoroquinolones.** *Norfloxacin* and *ciprofloxacin* (*Cipro*) are the most widely used. A third generation of fluoroquinolones that have a broader spectrum and can be taken orally include *moaxifloxacin* and *gatifloxacin.*

Competitive Inhibitors of the Synthesis of Essential Metabolites

Sulfonamides. The **sulfonamides (sulfa drugs)** act by competitive inhibition of folic acid, a precursor to nucleic acids. *Silver sulfadiazine* is used on burn patients. The most widely used sulfa-containing preparation is the combination of *trimethoprim* and *sulfamethoxazole.* These are structural analogs that inhibit synthesis of DNA at different stages.

Antifungal Drugs

Agents Affecting Fungal Sterols. In fungal membranes, the principal sterol is ergosterol; in animal membranes, it is cholesterol. This forms a basis for selective toxicity.

Polyenes. *Amphotericin B* is the most commonly used of the **polyene antibiotics.** Their activity is based on damage to fungal plasma membranes by combining with the membrane sterols. *Amphotericin B* is used for systemic fungal infections.

Azoles. **Imidazole** antifungals such as *miconazole* and *clotrimazole* are **azole antibiotics** used topically against cutaneous fungal infections. *Ketoconazole,* taken orally, is a substitute for amphotericin B for many systemic fungal infections. **Triazoles** such as *fluconazole* and *itraconazole* are used for systemic fungal infections. *Voriconazole* and *posaconazole* are new azoles.

Allylamines. The **allylamines** are a recently developed class of antifungals that inhibit ergosterol synthesis in a different manner and are often used when resistance to azoles appears. *Terbinafine* and *naftifine* are examples.

Agents Affecting Fungal Cell Walls. A primary target for selective toxicity is the β-glucans that are unique to fungal cell walls. A new class of antifungals, **echinocandins,** interferes with synthesis of glucans. An example is *caspofungin (Cancidas).*

Agents Inhibiting Nucleic Acids. *Flucytosine,* an analog of cytosine, interferes with synthesis of RNA, and therefore protein synthesis.

Other Antifungal Drugs. *Griseofulvin* is a fungistatic drug that interferes with mitosis. Although taken orally, this drug binds selectively to keratin in skin, hair, and nails, preventing fungal growth at these sites. *Tolnaftate* is a topical agent used as an alternative to miconazole for athlete's foot infections. *Undecylenic acid* is a fatty acid with antifungal activity. *Pentamidine isethionate* is used in treating *Pneumocystis* pneumonia.

Antiviral Drugs

The number of antiviral drugs, compared to that of antibacterial drugs, is very limited. A drug used to treat influenza, *amantadine,* was the first to be licensed, though its mode of action is unknown. Most new antivirals are directed at control of HIV.

Nucleoside and Nucleotide Analogs. Among the nucleoside analogs, *acyclovir* is widely used for many herpesvirus infections. Others are *famciclovir, ganciclovir, cidoflovir,* and *ribavirin.* The nucleoside analog *lamivudine* is used to treat hepatitis B and nucleotide analog, *adefovir dipivoxil (Hepsera)* has been recently introduced to counter resistance to lamivudine.

Interferons. Cells infected with a virus often produce interferon, which inhibits further spread of the infection. Interferons are cytokines; *alpha interferon* is used for viral hepatitis infections. A new drug, *imiquimod,* stimulates the production of interferons.

Antivirals for Treating HIV/AIDS

Antiretrovirals. RNA viruses depend upon the enzyme reverse transcriptase, which is an enzyme humans do not have. HIV is an RNA virus, and the antiretroviral group is largely directed at it; in fact, the term *antiretroviral* implies that it is used to treat HIV. Most antiretrovirals are nucleoside analogs such as *zidovudine (AZT),* which is an analog of thymidine. Another example is *cidofovir,* which is used to treat cytomegalovirus eye infections and is considered a possible treatment for smallpox. The only example of a nucleotide analog is *tenovir.* An antiretroviral that is a non-nucleoside agent is *nevirapine.*

Other Enzyme Inhibitors. The inhibitors of the enzyme neuraminidase, *zanamivir (Relenza)* and *oseltamivir phosphate (Tamiflu),* are used for treating influenza. Another approach to controlling HIV is to inhibit enzymes that control the last stage of viral reproduction, which requires protease enzymes. The **protease inhibitors** *atazanavir, indinavir,* and *saquinavir* are examples. Other enzymatic targets of HIV are the enzymes that integrate viral DNA into the host's DNA, forming a provirus—by **integrase inhibitors.** Entry into the cell by fusion can be blocked by **fusion inhibitors** such as *envuvirtide.*

Antiprotozoan and Antihelminthic Drugs

Antiprotozoan Drugs. *Quinine* still has limited use against malaria, but it has generally been replaced with synthetic derivatives, such as *chloroquine* and *mefloquine. Quinacrine,* used against giardiasis, functions similarly. *Diiodohydroxyquin (iodoquinol)* is an amoebicide. *Metronidazole* is used for treating many protozoan diseases and also is effective against certain anaerobic bacteria. It probably causes disruption of DNA under anaerobic conditions. Newer antiprotozoan drugs are *tinidazole (Fasigyn)* and *nitazoxanide.*

Antihelminthic Drugs. *Niclosamide* inhibits ATP production in tapeworms. *Praziquantel* also is effective against tapeworms and several fluke-caused diseases. *Mebendazole* and *albendazole* are used to treat ascariasis. *Ivermectin* is widely used in the livestock industry for helminth control. It also is useful in the treatment of some infestations by mites (scabies), ticks, and head lice.

TESTS TO GUIDE CHEMOTHERAPY

The Diffusion Methods

The **disk-diffusion method (Kirby-Bauer test)** uses a dish of agar medium seeded uniformly with a test organism. Filter paper disks impregnated with known concentrations of chemotherapeutic agents are placed on the agar surface. If the chemotherapeutic agent is effective, a zone of inhibition (no growth) is observed around the disk. The diameter of the zone can be used to calculate the susceptibility of the organisms to the agent.

A more advanced diffusion method, the **E test,** includes an estimate of the **minimum inhibitory concentration (MIC).**

Broth Dilution Tests

A series of dilutions of an antibiotic can be placed in tubes (shallow wells in a plastic plate usually are used in practice) and inoculated with test bacteria. After incubation they are examined for turbidity. The **minimum inhibitory concentration (MIC)** of the antimicrobial is defined as the lowest concentration that prevents growth. Subculturing from the tubes that show no growth will determine whether the bacteria have been killed or only inhibited. The lethal concentration that actually kills the bacteria is

called the **minimum bactericidal concentration (MBC).** Many of these tests are highly automated and use light scattering to determine bacterial growth. Hospital personnel responsible for infection control prepare periodic reports, called **antibiograms,** on the susceptibility to antibiotics encountered clinically.

RESISTANCE TO ANTIMICROBIAL DRUGS

Resistance to antimicrobial drugs, a threat to the usefulness of antibiotics, arises from random mutations. These can spread *horizontally* by conjugation or transduction, for example. The resistance is often carried by plasmids, such as resistance (R) factors, or transposons (small segments of DNA). Once acquired, the mutation is transmitted by normal reproduction.

There are only a few major mechanisms by which bacteria become resistant:

- *Enzymatic destruction or inactivation of the drug.* The best known example of this is the action of β-lactamase, which inactivates penicillins. The notorious pathogen MRSA is a well-known result of this mechanism. MRSA infections that are associated with hospitals are referred to as *health-care associated MRSA.* Outbreaks caused by *community-associated MRSA* occur in the general community, affecting otherwise healthy persons.
- *Prevention of penetration to the target site within the microbe.* This is most often seen in gram-negative bacteria.
- *Alteration of the drug's target site* and *rapid efflux (ejection) of the drug* tend to be common with the tetracycline-type antibiotics.

EFFECTS OF COMBINATIONS OF DRUGS

Two drugs given simultaneously may be more effective than either given alone; this is called **synergism.** Other combinations can show **antagonism,** in which the two drugs are less effective than either used alone.

THE FUTURE OF CHEMOTHERAPEUTIC AGENTS

The most pressing concern currently is the spread of resistance to antibiotics.

Antimicrobial Peptides

Higher organisms, including humans, often exhibit extraordinary resistance to microbial infections. This is often due to **antimicrobial peptides** (sometimes called *cationic peptides*). Examples are *magainin* from the skin of frogs and *nisin,* which is used as a food preservative. Antimicrobial peptides called **defensins** are found on humans. Their mode of action is primarily to form destructive channels in the microbe's cell membranes. A new class of antibiotics, the **cyclic lipopeptides** (*daptomycin* was the first approved), also attacks the cell membrane.

Insects lack a mammalian-type immune system, and some moths, for example, produce antimicrobial peptides such as *cecropin.*

Antisense Agents

Another approach to microbial control is short strands of synthetic agents, called **antisense agents.** The principle is to identify sites on DNA or RNA of the pathogen that are responsible for its pathogenic effects. Segments of DNA are then synthesized that will selectively bind to and neutralize this site. An antiviral based on this principle, *fomivirsen,* has been approved for treatment of cytomegalovirus retinitis.

A newly introduced method inhibits microbes from giving rise to proteins for which they are encoded, for example, when a virus attempts to take over a cell's metabolism in order to make viral proteins. This is **RNA interference (RNAi)** and is the basis of drugs called **small** (or **short**) **interfering RNAs (siRNAs).** These are similar in principle to antisense agents. This approach is promising, though commercial drugs are not available currently.

SELF-TESTS

In the matching section, there is only one answer to each question; however, the lettered options (a, b, c, etc.) may be used more than once or not at all.

I. Matching

___ 1. Plasmids that carry antibiotic resistance.

___ 2. Chemotherapeutic agents produced by microorganisms.

___ 3. Disk-diffusion test for antibiotic sensitivity.

___ 4. Diffusion test that also measures minimum inhibitory concentration of an antibiotic.

___ 5. Periodic reports on antibiotic sensitivity in hospitals.

a. Antibiotics
b. E test
c. Chemotherapy
d. Kirby-Bauer test
e. R factors
f. Antibiograms

II. Matching

___ 1. Activity based on damage to the sterols in plasma membrane of fungi.

___ 2. Inhibition of protein synthesis.

___ 3. Inhibition of RNA synthesis.

___ 4. Inhibition of synthesis of cell wall peptidoglycans.

___ 5. Inhibition of DNA synthesis.

___ 6. Inhibition of synthesis of cell wall mycolic acids.

a. Cephalosporins
b. Chloramphenicol
c. Amphotericin B
d. Isoniazid
e. Sulfonamides
f. Rifampin

III. Matching

___ 1. Similar structurally to penicillin.

___ 2. A synthetic drug used in tuberculosis chemotherapy.

___ 3. Antifungal, a polyene.

___ 4. Causes plasma membrane leakage; useful against *Pseudomonas*.

___ 5. An antiviral drug; a nucleoside analog.

___ 6. Antifungal; an allylamine.

___ 7. An antiviral drug; a nucleotide analog.

a. Cephalosporin
b. Polymyxin B
c. Ethambutol
d. Idoxuridine
e. Voriconazole
f. Terbinafine
g. Adefovir dipivoxil

IV. Matching

___ 1. Used in treating diseases caused by protozoa.

___ 2. An antifungal drug taken orally that concentrates in keratin.

___ 3. Useful against tapeworms.

___ 4. A drug that is useful against symptoms of genital herpes.

___ 5. An antifungal drug of the polyene type.

___ 6. A macrolide antibiotic.

___ 7. A streptogramin-type antibiotic.

a. Erythromycin
b. Griseofulvin
c. Amphotericin B
d. Niclosamide
e. Metronidazole
f. Acyclovir
g. Synercid

V. Matching

___ 1. Inhibits ATP production in tapeworms.

___ 2. Used in the treatment of malaria.

___ 3. Used in the treatment of *Pneumocystis* pneumonia.

___ 4. Stimulates production of interferons.

a. Chloroquine
b. Niclosamide
c. Pentamidine isethionate
d. Imiquimod

VI. Matching

___ 1. Used in treating HIV infections, a nucleoside analog.

___ 2. Acts by competitive inhibition of folic acid, usually in combination with sulfamethoxazole.

___ 3. A derivative of penicillin G designed to be retained for a longer time in the body.

___ 4. A penicillin designed to be resistant to penicillinase; no longer in use.

___ 5. A synthetic fluoroquinolone that acts against the gyrase enzyme.

___ 6. An amoebicide.

___ 7. Very broad spectrum; carbapenem group.

a. Zidovudine
b. Diiodohydroxyquin
c. Methicillin
d. Ampicillin
e. Procaine penicillin
f. Trimethoprim
g. Norfloxacin
h. Primaxin

VII. Matching

___ 1. Zidovudine, an analog of thymidine.

___ 2. Inhibits DNA synthesis of bacteria.

___ 3. An arsenic derivative used against syphilis before the development of modern antibiotics.

___ 4. A rifamycin-type drug used for therapy of tuberculosis; inhibits synthesis of mRNA.

___ 5. An antifungal drug; interferes with synthesis of RNA.

___ 6. A possibility for use against smallpox.

a. Nalidixic acid
b. Flucytosine
c. Salvarsan
d. Rifampin
e. AZT
f. Cidofovir

VIII. Matching

___ 1. Inhibitor of protein synthesis; inexpensive; may cause aplastic anemia.

___ 2. An aminoglycoside antibiotic used in tuberculosis treatment; may cause deafness or kidney damage.

___ 3. A cytokine.

___ 4. An antiviral protease inhibitor.

___ 5. Used mainly against life-threatening staphylococcal infections resistant to penicillin.

a. Chloramphenicol
b. Vancomycin
c. Streptomycin
d. Indinavir
e. Interferon

Fill in the Blanks

1. Cell walls of most bacteria contain _____, the target of activity by penicillins.

2. The treatment of disease with chemicals taken into the body by injection or ingestion is called _____.

3. Many bacteria develop resistance to penicillin by producing the enzyme _____.

4. The usual principle of antibiotic activity is _____, meaning it kills the harmful organism without damaging the host.

5. The term *penicillin* is applied to a group of antibiotics that all have a(n) _____ in their structure.

6. The aminocyclitol ring and amino sugars are found in the _____ group of antibiotics.
7. The lowest concentration of a chemotherapeutic agent that will prevent growth is the _____.
8. The lowest concentration of a chemotherapeutic agent that will kill the pathogen (as contrasted to inhibition) is called the _____.
9. Miconazole and ketoconazole are examples of the _____ group of antifungals.
10. Many antibiotics inhibit protein synthesis by reacting with the _____ of the bacterium, which differ greatly between prokaryotic and eukaryotic cells.
11. When antibiotics eliminate much of the natural microbiota, there may be an overgrowth of resistant pathogens; this is called _____.
12. Aztreonam is a variant of penicillin with a single-ring structure; this group of antibiotics is called _____.
13. Magainin, squalamine, and cecropin are examples of the new antimicrobial _____ agents isolated from animals.
14. A new antiviral drug, envuvirtide, is intended to block entry into the host cell; it is a _____ inhibitor.
15. The M in MRSA refers to _____.

Critical Thinking

1. List and briefly discuss four criteria used to evaluate antimicrobial drugs.

2. Using antibiotics as a supplement in animal feed has been linked to *Salmonella* infections in humans. Why did this practice begin? Why has it continued? What risks are associated with the continued use of antibiotics as an animal feed supplement?

3. What advantages and disadvantages are associated with the use of broad-spectrum antibiotics?

4. Define *synergism*. For what purposes should combinations of antimicrobial drugs be used?

ANSWERS

Matching

I. 1. e 2. a 3. d 4. b 5. f
II. 1. c 2. b 3. f 4. a 5. e 6. d
III. 1. a 2. c 3. e 4. b 5. d 6. f 7. g
IV. 1. e 2. b 3. d 4. f 5. c 6. a 7. g
V. 1. b 2. a 3. c 4. d
VI. 1. a 2. f 3. e 4. c 5. g 6. b 7. h
VII. 1. e 2. a 3. c 4. d 5. b 6. f
VIII. 1. a 2. c 3. e 4. d 5. b

Fill in the Blanks

1. peptidoglycan 2. chemotherapy 3. penicillinase 4. selective toxicity 5. β-lactam ring 6. aminoglycoside 7. minimum inhibitory concentration (MIC) 8. minimum bactericidal concentration (MBC) 9. azole 10. ribosomes 11. superinfection 12. monobactams 13. peptides 14. fusion 15. methicillin

Critical Thinking

1. a. Selective toxicity—The drug should be toxic to the pathogen but not to the host.
   b. The drug should not produce hypersensitivity in most hosts.
   c. The drug must be soluble in body fluids so that it can rapidly penetrate body tissues. It must also remain in the body long enough to be effective.
   d. Microorganisms shouldn't become readily resistant to the drug.
2. Antibiotics were first added to animal feed to lower the incidence of infection in closely penned animals. Another reason that antibiotics are still added to animal feed is that they accelerate the growth of the animal. The practice has been linked with *Salmonella* infections in humans from meat and milk. FDA testing has shown that most milk and meat have little or no detectable antibiotics, but many people still consider the practice undesirable. Continued use of antibiotics in animal feed will result in the development of antibiotic-resistant strains of bacteria.