by immunosuppressive disorders or drugs. They may emerge during or after antimicrobial drug therapy. Contributing factors include:

1. **Widespread use of antimicrobial drugs, especially broad-spectrum agents.** Antibiotics affect the bacteria for which they are prescribed, transient organisms, other pathogens, and normal flora. When the normal flora is suppressed, space and nutrients become available to support the growth of organisms resistant to the effects of that antibiotic. The resistant organisms soon become the predominant strain. Once established, resistant bacteria can cause superinfection in the original host, spread to other hosts, and even spread their resistance properties for that antibiotic to other species of bacteria. In addition to resistance to the effects of one antibiotic, cross-resistance to similar antibiotics also occurs because most antibiotics are variations of a few basic types.
2. **Interrupted or inadequate antimicrobial treatment of infections.** Clients often stop taking a prescribed antibiotic when symptoms subside or they feel better. In such circumstances, only the most susceptible bacteria are affected and resistant organisms can become established residents.
3. **Type of bacteria.** Both gram-positive and gram-negative bacteria are producing more antibiotic-resistant strains. Gram-positive organisms include staphylococci, streptococci, and enterococci. Gram-negative bacteria associated with high rates of antibiotic resistance include *Pseudomonas aeruginosa* and *Serratia, Enterobacter,* and *Acinetobacter* species. These organisms are inherently resistant to penetration of antibiotics and acquire resistance by multiple mechanisms. One mechanism is an outer membrane with openings (porins) that regulate passage of antibiotics. Some gram-negative bacteria (eg, *E. coli*) have more permeable porins than others (eg, *P. aeruginosa*). Thus, *P. aeruginosa* organisms are generally resistant to many antibiotics.
4. **Type of infection.** Infections often associated with high rates of resistance include lower respiratory tract infections and those associated with cystic fibrosis or osteomyelitis. These infections are often difficult to treat because they tend to recur; involve multiple, gram-negative, or resistant organisms; and involve anatomic locations that antibiotics do not penetrate well.
5. **Condition of the host.** Clients who are malnourished, severely ill, immunosuppressed, or receiving mechanical ventilation are at high risk for infections, including those caused by antibiotic-resistant organisms.
6. **Location or setting.** Resistant organisms are especially likely to emerge in critical care units and large teaching hospitals, where seriously ill clients often require extensive antibiotic therapy. The constant presence of antibiotics provides strong pressures for selection and replication of resistant organisms.

Resistant organisms and the antibiotics to which they develop resistance vary in geographic areas, communities, and hospitals according to the use of particular antibiotics. Nationally, resistant bacterial strains of major concern include penicillin-resistant *Streptococcus pneumoniae,* methicillin-resistant *Staphylococcus aureus* and *Staphylococcus epidermidis,* vancomycin-resistant enterococcus, and multidrug-resistant tuberculosis (MDR-TB). Actually, all of these organisms are resistant to multiple antibiotics. The first three are described in Box 33–2; MDR-TB is discussed in Chapter 38. Viruses and fungi also develop resistance to antimicrobial drugs, as discussed in Chapters 39 and 40.

Mechanisms of Resistance

Bacteria have developed numerous ways to acquire resistance to antimicrobial drugs, including:

- Production of enzymes that inactivate the drugs. For example, beta-lactamase enzymes change the chemical structure of penicillins and cephalosporins by opening the beta-lactam ring and preventing the antibiotic from binding with its target site (called penicillin-binding proteins) in the bacterial cell wall.
- Genetic mutations that change antibiotic target sites or change the genetic code to produce new targets. These changes decrease bacterial susceptibility to an antibiotic, largely by altering binding sites.
- Changing their metabolic pathways to bypass antibiotic activity.
- Changing their cell walls to produce porins that prevent penetration of the drug.
- Acquiring the ability to pump drug molecules out of the cell. Multiple, nonspecific efflux systems become activated to remove foreign chemicals.
- Transferring genetic material (DNA or plasmids) between microorganisms. Bacteria have efficient mechanisms for genetic exchange that allow them to spread antibiotic resistance from one bacterial strain to another, including different species or types of bacteria. Thus, when a new antibiotic is used, resistance may rapidly appear and be disseminated to multiple bacteria.

HOST DEFENSE MECHANISMS

Although the numbers and virulence of microorganisms help to determine whether a person acquires an infection, another major factor is the host's ability to defend itself against the would-be invaders.

Major defense mechanisms of the human body are intact skin and mucous membranes, various anti-infective secretions, mechanical movements, phagocytic cells, and the immune and inflammatory processes. The skin prevents penetration of foreign particles, and its secretions and normal bacterial flora inhibit growth of pathogenic microorganisms. Secretions of the GI, respiratory, and genitourinary tracts (eg, gastric acid, mucus) kill, trap, or inhibit growth of microorganisms. Coughing, swallowing, and peristalsis help to remove foreign particles and pathogens trapped in mucus, as does the movement of cilia. Phagocytic cells in various organs and tissues engulf and digest