THINK ABOUT 6-2

a. Explain why parasites do not usually kill their host.
b. Explain how routine laboratory tests might not show the presence of mycoplasma, rickettsia, or protozoans in the body.

Other Agents of Disease

Helminths

Helminths or worms are not microorganisms, but are often included with microbes because they are parasites and cause infections in humans throughout the world. They are multicellular, eukaryotic organisms that are divided into many subgroups, depending on their physical characteristics. They may be very small, barely visible, or up to 1 meter in length. Their life cycle consists of at least three stages, ovum (egg), larva, and adult. The ova or larvae may be ingested in contaminated food or water, or may enter through the skin or be transmitted by infected insects. They are often found in the intestine but can inhabit the lung or blood vessels during parts of their life cycle.

Helminths are usually diagnosed by observation of ova or eggs in stool specimens (Fig. 6-8*D*). Helminth infections are more commonly found in young children and in North America include pinworms (Fig. 6-9), hookworms, tapeworms (Fig. 6-10), and *Ascaris* or giant roundworms. When large numbers of worms are present in the body, systemic effects may develop, such as severe anemia.

Prions

Prions are protein-like agents that are transmitted by consumption of contaminated tissues such as muscle or the use of donor tissues contaminated with the protein. There is a great deal that is not known about prion disorders and some researchers question whether prions are actually the agent of diseases. The following information is from current publications of the Centers for Disease Control and Prevention (CDC).

A prion is an abnormal molecule that is transmissible in tissues or blood of animals or humans. It induces proteins within the brain of the recipient to undergo abnormal folding and change of shape. This renders the protein molecule non-functional and causes degenerative disease of the nervous system. Prion diseases in humans include Creutzfeldt-Jakob disease and variant Creutzfeldt-Jakob disease (see Chapter 14). These are rapidly progressive and fatal. It is thought that variant Creutzfeldt-Jakob disease is caused by consumption of meat that has been contaminated with nervous tissue from an infected animal such as beef cattle. In areas where bovine spongiform encephalopathy (BSE), the animal prion infection, is prevalent, consumption of ground meats, sausages, or offal should be avoided.

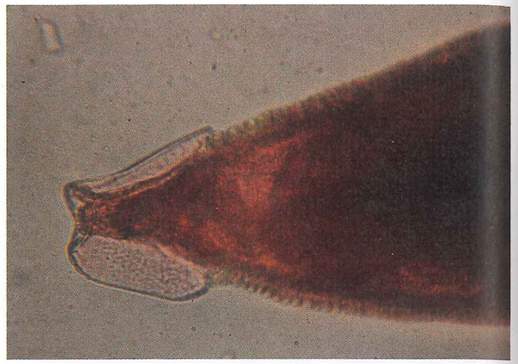

FIGURE 6-9 Pinworm. This micrograph shows the mouth structure of the pinworm *Enterobius vermicularis*, which causes the disease enterobiasis. *(From VanMeter K, Hubert R:* Microbiology for the Healthcare Professional, *St. Louis, 2010, Mosby.)*

FIGURE 6-10 Tapeworm. Two main features of the tapeworm are the scolex, which has muscular suckers surrounded by hooks for attachment, and the individual body segments called *proglottids. (From VanMeter K, Hubert R:* Microbiology for the Healthcare Professional, *St. Louis, 2010, Mosby.)*

Algae

Algae are eukaryotic microorganisms widespread in fresh and marine waters; they are a main component of plankton and are usually not a concern for human disease. Medical concerns involving algae include: human consumption of marine animals that have fed on algae and accumulated toxins produced by the algae and recent disorders attributed to the algae *Pfiesteria piscicida*.

Resident Flora (Indigenous Normal Flora, Resident Microbiota)

Many areas of the body, such as the skin, nasal cavity, and mouth, have a resident population of mixed microorganisms, primarily bacteria. Different sites host different species. For example, streptococci, *Haemophilus*, and staphylococci are a few of the microbes found in the upper respiratory tract; staphylococcus and *Candida*, among others, occur on the skin. Some areas of the body such as the lungs, bladder, and kidneys lack resident flora or are sterile under normal circumstances, and properly obtained specimens from these areas should not contain microorganisms (Table 6-3).

TABLE 6-3 Location of Resident Flora

Resident Flora Present	Sterile Area
Skin	Blood, cerebrospinal fluid
Nose, pharynx	Lungs
Mouth, colon, rectum	
Vagina	Uterus, fallopian tubes, ovary
Distal urethra and perineum	Bladder and kidney

Certain microbes in the intestinal tract are of great benefit to the host in the synthesis of vitamin K and in some digestive processes. These microbes are not pathogenic under normal circumstances but may cause disease if they are transferred to another location in the body, or if the balance among the species is not maintained (e.g., one variety becomes dominant), or if the body's defenses are impaired (e.g., in immunodeficiency states). Such infections are termed *opportunistic*.

Resident flora are usually helpful in preventing other organisms from establishing a colony. For example, some antibacterial drugs intended to treat infection elsewhere in the body, will destroy part of the normal flora in the intestine, thus allowing for an imbalance in growth there or invasion by other microbes, causing opportunistic infection and diarrhea.

Principles of Infection

An **infection** occurs when a microbe or parasite is able to reproduce in or on the body's tissues. Infectious diseases may occur sporadically in single individuals, localized groups, and epidemics or worldwide pandemics. Certain infections are **endemic** to an area, consistently occurring in that population. Others may occur outside their normal geographic range or in higher than expected numbers; these infections are referred to as **epidemics**. Knowledge of the modes of transmission of microorganisms and methods of control is essential for the prevention and control of infection within the community.

Transmission of Infectious Agents

A chain of events occurs during the transmission of infecting organisms from one person to another (Fig. 6-11). The *reservoir*, or source of infection, may be a person with an obvious active infection in an acute stage, or a person who is asymptomatic and shows no clinical signs or symptoms. The latter may be in the early incubation stage of infection, or the person may be a *carrier* of the organism and never develop infection. Hepatitis B is an example of an infection that is often transmitted by unknown carriers or persons who have a *subclinical* form of infection that is very mild, with few or no manifestations. The reservoir also may be an animal or contaminated water, soil, food, or equipment.

The mode of transmission from the reservoir to the new host may be:

- *Direct* contact with no intermediary, such as touching an infectious lesion or sexual intercourse. Microbes may be in the blood, body secretions, or a lesion. Not all microorganisms can cross the blood-brain barrier or placental barriers. However, some microbes that can cross the placenta have serious effects on fetal development and health. *Treponema pallidum*, the cause of syphilis, can lead to multiple defects or death in the fetus, and *Toxoplasma gondii*, the cause of toxoplasmosis, results in many neurologic deficits.
- *Indirect* contact involving an intermediary such as a contaminated hand or food, or a *fomite*, an inanimate object such as instruments or bed linen that carries organisms. In some cases, there are several stages in transmission. For example, shellfish can be contaminated by human feces in the water. The microorganisms in the shellfish are then ingested and cause infection in another human.
- *Droplet* transmission (oral or respiratory) occurring when respiratory or salivary secretions containing pathogens such as tuberculosis bacteria are expelled from the body. The organisms from these secretions may be inhaled directly by another person close by or fall on nearby objects to be transmitted indirectly.
- *Aerosol* transmission involving small particles from the respiratory tract that remain suspended in the air and travel on air currents, infecting any new host who inhales the particles.
- *Vector-borne*, when an insect or animal serves as an intermediary host in a disease such as malaria.

Hands are considered a major culprit in spreading infection from many sources, in health care facilities, the home, office, or school. Frequent, proper handwashing is essential in infection control and has been shown to be the most commonly ignored procedure in maintaining personal and public health.

Nosocomial infections are infections that occur in health care facilities, including hospitals, nursing homes, doctors' offices, and dental offices. The CDC estimates that 10% to 15% of patients acquire an infection in the hospital. Reasons for these infections include the presence of many microorganisms in these settings, patients with contagious diseases, overcrowding, use of contaminated instruments, immunocompromised and weakened patients, the chain of transmission through staff, diagnostic procedures, and equipment, therapeutic aids, and food trays. Also, many microbes in health

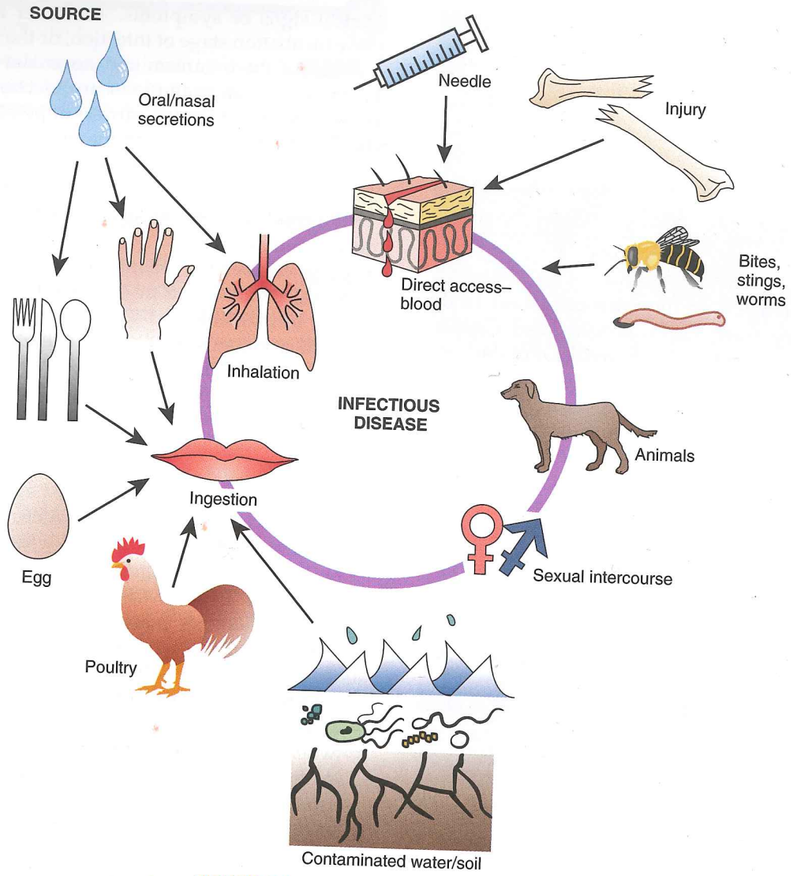

FIGURE 6-11 Transmission of infectious agents.

care settings are resistant to several drugs. Common nosocomial infections include urinary tract infections (the highest number), pneumonia, diarrhea, and surgical wound infection. Most infections in health care facilities are spread by direct contact between persons or contaminated objects. Recently there have been several outbreaks of infection in hospitals by a more dangerous strain of the bacterium, *Clostridium difficile* (c-diff), particularly in intensive care units where most individuals are taking antimicrobial drugs. The resulting disruption of normal flora allows *C. difficile* to multiply and cause severe diarrhea and many deaths. Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are also increasingly seen as a source of nosocomial infection that is very challenging to treat (this is in the community, not just the hospital). The importance of obtaining a complete and accurate health history with respect to hospitalization and prior infections cannot be overstated.

Host Resistance

The healthy individual is quite resistant to infection. With some infections, such as tuberculosis, host resistance is a primary factor in determining the risk of active infection following exposure (Box 6-1).

Interferons are proteins produced by human host cells in response to viral invasion of the cell. These interferons then influence the activity of nearby host cells, increasing their resistance to viral invasion and interfering with viral replication. Interferons also stimulate the immune system and are used in cancer treatment for this reason. Unfortunately, they have not proved to be as beneficial in the widespread treatment of cancer or other immune-based diseases as expected.

Factors that *decrease* host resistance include:

- Age (infants and the elderly)
- Genetic susceptibility
- Immunodeficiency of any type
- Malnutrition

BOX 6-1 Host Resistance and Microbial Virulence

Host Resistance	Increased Microbial Virulence
Intact skin and mucous membrane	Production of exotoxins and endotoxins
Body secretions—stomach acid, tears	Production of destructive enzymes
Nonspecific phagocytosis	Spore formation
Effective inflammatory response	Entry of large number of organisms into body
Absence of disease	Presence of bacterial capsule and pili
Effective immune system	
Interferon production (virus)	

- Chronic disease, including cardiovascular disease, cancer, and diabetes
- Severe physical or emotional stress
- Inflammation or trauma affecting the integrity of the skin or mucosa, including burns, lack of protective secretions, bladder catheters, or other invasive procedures. Sometimes infection occurs easily because of a very small break in the skin or mucous membrane, or in an area of inflammation. As discussed in Chapter 5, the loss of skin and other defenses in a burn patient often results in secondary infection at the site.
- Impaired inflammatory response, for example, due to long-term glucocorticoid medication
- Severe or multiple infections are very common in homeless individuals, in whom multiple factors decrease host resistance. For example, poor nutrition, open lesions, inadequate hygiene, fatigue, lack of access to health care, and possible drug or alcohol abuse combine to create a high risk of infections such as tuberculosis.

Prophylactic antimicrobial medication may be required by any individuals with low resistance before exposure to possible infecting microbes, for example, before an invasive procedure.

Virulence and Pathogenicity of Microorganisms

Pathogenicity refers to the capacity of microbes to cause disease. Nonpathogens can become pathogens. When a member of the resident flora is introduced into another area of the body, it may become an opportunistic pathogen. For example, if *Escherichia coli* from the colon enter the urinary tract, they will cause infection. (This microbe is the most common cause of cystitis.)

Virulence is the degree of pathogenicity of a specific microbe, based on:

- Invasive qualities, allowing it to directly damage host cells and tissues and spread
- Toxic qualities, including production of enzymes, exotoxins, and endotoxins that damage host cells or interfere with a host function such as nerve conduction
- Adherence to tissue by pili, fimbriae, capsules, or specific membrane receptor sites. Certain organisms tend to establish infection in particular areas of the body, considered hospitable to that microbe; for example, streptococci are common in respiratory and ear infections.
- Ability to avoid host defenses (e.g., the presence of a capsule or mutation with altered antigenicity). Microorganisms undergo frequent **mutation**. Slight changes in the organism may occur spontaneously or in response to environmental conditions, including the presence of drugs. When bacteria or viruses mutate, antibodies that matched the earlier form are no longer effective, so the individual is no longer protected. Vaccines or drugs are unlikely to be effective against the new form. This is why a new influenza vaccine must be developed and administered each year.

Virulence is often expressed in the *case fatality rate*, the percentage of deaths occurring in the number of persons who develop the disease. In parasitic infections host resistance and the ability of a microbe to cause disease often coexist in a delicate balance.

New Issues Affecting Infections and Transmission

There has been increasing concern and fear about new emerging diseases and "superbugs," microbes that have caused very serious illness in otherwise healthy individuals or do not respond to any drugs. Emerging infectious diseases are identified by a new or unique set of signs or symptoms, or by increased spread. Careful monitoring and collection of data are essential to identify new threats so that preventive measures may be put in place. The severe acute respiratory syndrome (SARS) epidemic in the Toronto area was well established before information about cases occurring in travelers from Southeast Asia was received. In some cases the incubation period is so short that it is difficult to prevent an epidemic even if health statistics are collected, for example, in cholera infections. In such situations the focus must be on preventing the spread of infection to the wider community. Increased global travel, changing environments and global weather patterns, and changes in food and water supplies are some of the factors leading to altered disease patterns. Epidemiologists at the CDC, World Health Organization (WHO), as well as a greater number of local agencies collect and analyze reports on new diseases and other trends. They also update the list of notifiable diseases, approximately 60 diseases that must be reported to public health agencies. The CDC reports are published in *Morbidity and Mortality Weekly Report*. The United Nations (UN) has also assumed a role in a number of global issues related to infectious diseases such as AIDS, tuberculosis, and malaria.

Following the SARS threat (see Chapter 13) in 2003, these agencies cooperated to quickly identify a

previously unknown microbe, a coronavirus, and work on controlling the spread of the infection. As more deaths occurred and a second wave of infection developed, they were able to identify factors in the transmission of the virus.

The CDC and WHO have published guidelines for health care facilities to manage the screening procedures, rapid containment, and treatment of serious infectious diseases that may lead to a pandemic. These measures have proved effective in several recent outbreaks, such as the influenza A H1N1 outbreak in Mexico in 2009. Precautions were instituted in several countries, and at the time of writing these precautions appear to have been successful in preventing a full-blown pandemic. Health care workers in all settings were required to screen clients and put respiratory precautions in place for those who were symptomatic.

In some cases, organisms such as the Ebola virus are spreading and have become highly virulent and have the power to cause serious infection, even in a healthy host. At this time, there are no drugs available to control this and related viral infections. Certain strains of a common microorganism, such as *E. coli*, a normal part of resident intestinal flora, have suddenly developed new strains that have caused life-threatening infections. The so-called flesh-eating bacteria are specific strains of a beta-hemolytic streptococcus that are highly invasive, secreting proteases, enzymes that break down tissue, resulting in the life-threatening disease necrotizing fasciitis. These bacteria also produce a toxin-causing shock.

The effectiveness of immunizations over long time periods is difficult to assess. It appears that some vaccines are losing their protective qualities over time. The increasing incidence of pertussis (whooping cough), mumps, and measles appears related to decreasing immunity from vaccines given in childhood. This indicates a need for booster immunization and the importance of continued monitoring of all infectious diseases, including those in which routine immunizations are in place. Many jurisdictions now offer re-immunization with MMR vaccine in the teen years. The recommended immunization schedules for children 0 to 6 and 7 to 18 as well as a catch-up schedule are updated regularly and approved by the American Academy of Pediatrics, the Advisory Committee on Immunization Practices of the CDC, and the American Academy of Family Physicians.

The other issue to be addressed is the increasing number of microbes that are resistant to several drug groups, thus making infection control much more difficult. The multi-drug resistant microbes include strains of *Mycobacterium tuberculosis*, *Plasmodium falciparum*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and *Neisseria gonorrhoeae*. Currently there is much more emphasis on reduced use of antibacterial drugs to treat minor infections or as prophylactics to lessen the problem. It is important for health care workers to remain up to date on current recommendations about infection control measures in their scope of practice.

Control of Transmission and Infection

Isolation of infected persons is rarely carried out on a large scale, and there are fewer diseases that must be reported to government bodies. It is not feasible to test every client or patient for the presence of infection before initiating care. Therefore infection control, understanding the transmission, and breaking the chain of infection (Fig. 6-12) become much more important, particularly to health professionals, who must protect themselves, their families, and the community as well as their patients.

Universal precautions provide the basic guidelines by which all blood, body fluids, and wastes are considered "infected" in *any* client regardless of the client's apparent condition. There are two levels, one general for all individuals, and one specific to known infections at specific sites in the body, for example, the intestines. Gloves and appropriate protective apparel are then used to reduce the transmission of organisms in either direction, that is, from patient to caregiver and from caregiver to patient. Guidelines have been established for the disposal of such potentially dangerous items as needles, tissue, and waste materials. The CDC can be consulted for appropriate and up-to-date information.

To break the cycle and minimize the risk of infection:

- The reservoir or sources of infection must be located and removed. *Sources and contacts* must be identified in some situations, especially when asymptomatic carriers may be involved, or when travelers may be infected:
  - *Contaminated food or water or carrier food handlers* should be identified to prevent continued transmission or epidemics of infectious disease. As a precaution, some institutions test stool specimens from food handlers so as to identify carriers. Some intestinal pathogens can survive in feces outside the body for long periods of time and increase the risk of contaminating food or water.
  - In some cases, infection can be transmitted before clinical signs are evident in the infected person, and this permits widespread contamination if the incubation period is prolonged. For example, there is a prolonged "window" of time before hepatitis or human immunodeficiency virus (HIV) infection can be identified in persons. In institutions, infection such as Hepatitis A can spread very rapidly, particularly when the patient's health status is already compromised.
  - Infected travelers should refrain from travel to prevent spreading infectious diseases into new areas, and travelers who become ill should seek prompt health care and share their specific travel history with health care workers.

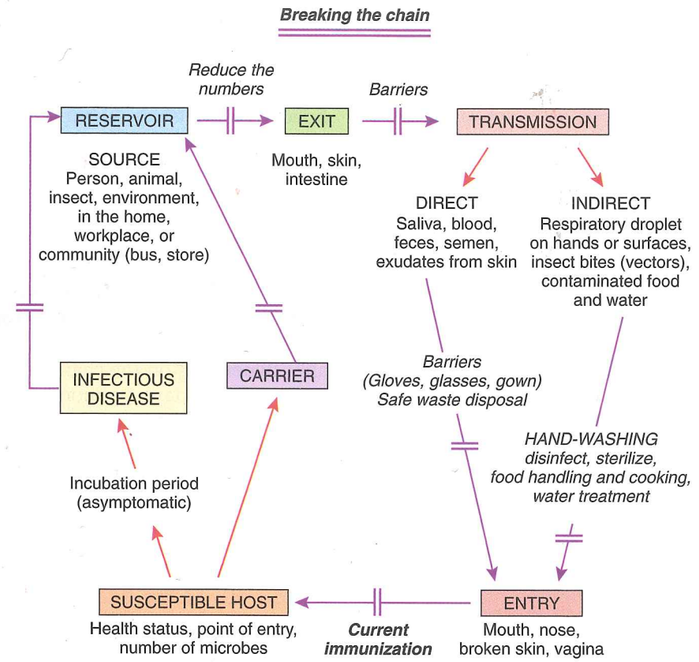

FIGURE 6-12 Infection cycle and breaking the chain.

- The portal of exit (secretions, e.g., blood, saliva, urine) of microbes from the reservoir should be blocked. This includes minimizing the effects of coughing and sneezing when the infected person is in close contact with other people. However, it is now evident that contaminated oral and nasal secretions are more dangerous when they are on the hands or on tissues than when they are airborne, so proper disposal of contaminated items is essential. It is advisable for anyone with or without an infection to use general universal precautions to prevent transmission by body fluids.
- Knowledge of the mode (droplet, fecal-oral) or modes of transmission of specific infections is essential to block transmission. Precautions must be undertaken in a prescribed manner; for example, the use of appropriate condoms following recommended guidelines is essential to prevent the spread of sexually transmitted disease during intimate sexual activity. Using disposable equipment, proper sterilization and cleaning, good ventilation, and frequent handwashing are some ways to reduce transmission:
  - Portals of entry and exit should be blocked by covering the nose and mouth with a mask and placing barriers over breaks in the skin or mucous membranes.
  - Reduce host susceptibility (increase host resistance) by maintaining immunizations and boosters according to guidelines. Proper nutrition to maintain skin and mucous membranes is also essential in reducing host susceptibility.

Additional techniques to reduce transmission include:

1. Adequate cleaning of surroundings and clothing.
2. **Sterilization** of fomites by exposure to heat using several methods, such as **autoclaving**. Time, packaging, and temperature are critical to success. Moist heat is preferable, because it penetrates more efficiently and can destroy microbes at lower temperatures. Incineration (burning) and autoclaving are also effective methods of destroying microbes in waste.
3. **Disinfectants** are chemical solutions that are known to destroy microorganisms or their toxins on inanimate objects. The literature on these solutions must be carefully checked to determine the limitations of the specific chemicals as well as the instructions for use. For example, few chemicals destroy spores. Adequate exposure time and concentration of the chemical are required to kill some viruses, such as hepatitis B. Other potential problems include inactivation of some chemicals by soap or protein (mucus, blood) or damage to metals or latex materials on instruments by the disinfectant. One of the more effective

disinfectants at present is *glutaraldehyde.* Flushing certain equipment and tubing (e.g., in a dental office), with disinfectant and water is a recommended daily activity.

4. **Antiseptics** are chemicals applied to the body that do not usually cause tissue damage, such as isopropyl alcohol-70%, which is the active ingredient in hand sanitizers. The chemical affects only surface organisms and does not penetrate crevices. Antiseptics reduce the number of organisms in an area but do not destroy all of them. Also, they may be diluted or removed quickly by body secretions. Some antiseptics, such as iodine compounds, may cause allergic reactions in some individuals.

THINK ABOUT 6-3

a. Explain why, when using an antiseptic, killing all the bacteria may not be the desired result.
b. Given that every client cannot be fully screened for infections, what precautions are essential to limit the transmission of microbes that are agents of disease? Relate your answer to your specific scope of practice.

Physiology of Infection

Onset and Development

Infectious agents can be present in the body for some time before any clinical signs are apparent. The microorganisms must gain entry to the body, choose a hospitable site, establish a colony, and begin reproducing (Fig. 6-13). Only if the host defenses are insufficient to destroy all the pathogens during this process will infection be established.

The *incubation period* refers to the time between entry of the organism into the body and appearance of clinical signs of the disease. Incubation periods vary considerably, depending on the characteristics of the organism, and may last days or months. During this time the organisms reproduce until there are sufficient numbers to cause adverse effects in the body.

The *prodromal period,* which is more evident in some infections than others, follows. This is the time when the infected person may feel fatigued, lose appetite, or have a headache, and usually senses that "I am coming down with something."

Next comes the *acute period,* when the infectious disease develops fully, and the clinical manifestations

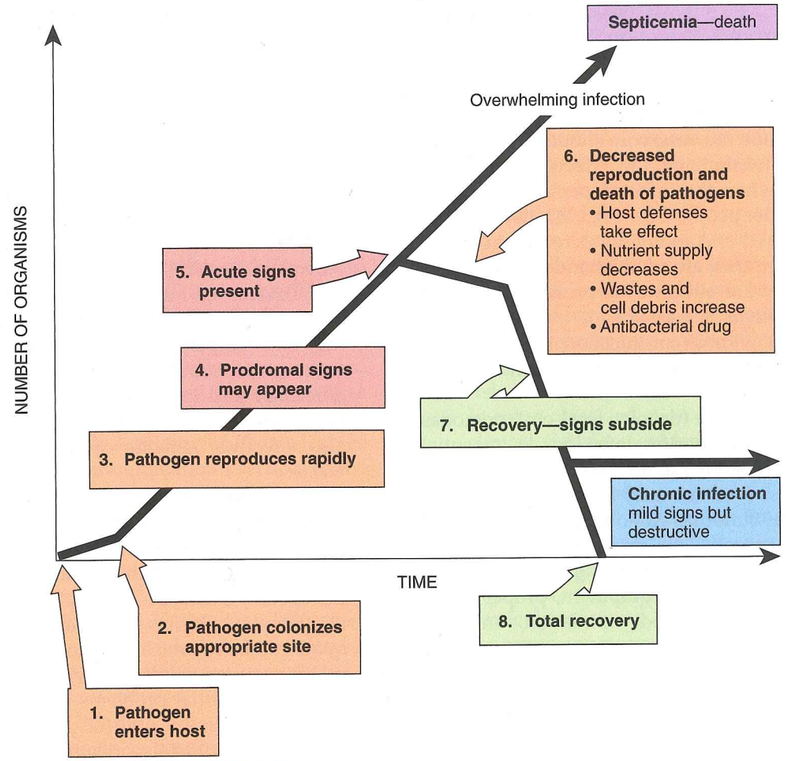

FIGURE 6-13 Onset and possible courses of infection.

reach a peak. The *onset* of a specific infection may be insidious with a prolonged prodromal period, or sudden or acute with the clinical signs appearing quickly with severe manifestations.

The length of the acute period depends on the virulence of the particular pathogen and host resistance. In many cases the acute period ends when host resistance, perhaps the immune system, becomes effective at destroying the pathogen. It may end when sufficient nutrients for the numbers of microbes decline, or when they are affected by wastes from dead organisms and necrotic tissue, thus decreasing their reproductive rate. The acute phase is followed by the recovery or convalescent period, when signs subside and body processes return to normal.

Patterns of Infection

Infections have varied patterns as defined by their characteristics and/or location.

- Local infections—organism enters the body and remains confined to a specific location
- Focal infections—pathogen spreads from a local infection to other tissues
- Systemic infections—infection spreads to several sites and tissue fluids, typically through the circulatory system
  - **Septicemia**—caused by multiplication of pathogens in the blood. This condition is the cause of sepsis, a toxic inflammatory condition arising from the spread of microbes
  - Bacteremia—presence of bacteria in the blood
  - Toxemia—presence of toxins in the blood
  - Viremia—presence of viruses in the blood
- Mixed Infections—several infectious agents concurrently establish themselves at the same site
- Acute infections—appear rapidly with severe symptoms but are short lived
- Chronic infections—less severe symptoms than acute but persist for a long period
- Primary infections—initial infection followed by complications caused by another microbe
- Secondary infections—follows a primary infection and is caused by a microbe other than that causing the primary infection. Opportunistic pathogens are often the cause of a secondary infection.
- Subclinical infections—does not cause and apparent signs or symptoms, although it may persist over long periods of time.

THINK ABOUT 6-4

a. Compare the prodromal period with the acute period of infection, using your own experience as an example (perhaps the last time you had a cold).
b. Compare subclinical infection and chronic infection.
c. Explain three reasons why infection may not occur after microbes enter the body.

Signs and Symptoms of Infection

Local Signs

The local signs of infection are usually those of inflammation: pain or tenderness, swelling, redness, and warmth (Fig. 6-14). If the infection is caused by bacteria, a purulent exudate, or pus, is usually present, whereas a viral infection results in serous, clear exudates. The color and other characteristics of the exudates and tissue may help to identify the microorganism. Figure 5-13 illustrates infection of a burn wound by two different microorganisms. Tissue necrosis at the site is likely as well. Lymphadenopathy occurs and is manifest by swollen and tender lymph nodes (Table 6-4).

Other local signs depend on the site of infection. For instance, in the respiratory tract, local signs probably include coughing or sneezing and difficulty in breathing. In the digestive tract, local signs might include vomiting or diarrhea.

Systemic Signs

Systemic signs include signs and symptoms common to significant infections in any area of the body. Fever, fatigue and weakness, headache, and nausea are all commonly associated with infection. The characteristics of *fever (pyrexia)* may vary with the causative organism. The body temperature may be very high or spiking and

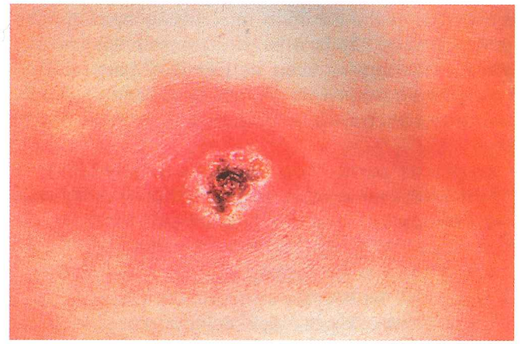

FIGURE 6-14 Staphylococcus abscess. *(From Braverman IM:* Skin Signs of Systemic Disease, *ed 3, Philadelphia, 1998, Saunders.)*

TABLE 6-4 Local and Systemic Signs of Bacterial Infection

Local Signs	Systemic Signs
Swelling	Fever
Erythema (redness)	Leukocytosis
Pain and tenderness	Elevated ESR
Lymphadenopathy	Fatigue, weakness, anorexia
Exudate, purulent	Headache, arthralgia

ESR, erythrocyte sedimentation rate.

may be accompanied by chills (see Chapter 5), or it may be elevated only slightly. In some viral infections the temperature is subnormal. With severe infection the nervous system may be affected, resulting in confusion or disorientation, seizures (convulsions), or loss of consciousness.

THINK ABOUT 6-5

List three local signs of infection and three systemic signs and explain what is causing these signs.

Methods of Diagnosis

Organisms can be identified by *culture and staining* techniques, using specific specimens such as sputum in patients in whom tuberculosis is suspected. It is important that specimens be procured carefully and examined quickly to achieve an accurate result. Many organisms can be grown easily on specific culture media in the laboratory, whereas other organisms such as viruses require a living host. Blood cultures may be examined to check the distribution or possible spread of the infecting agent. Frequently drug sensitivity tests, such as the Kirby Bauer method (Disc Diffusion Method) and the Minimum Inhibitory Concentration (MIC) method (Fig. 6-15), are also instituted. Drug therapy is often ordered immediately based on preliminary data and knowledge of the common infections occurring at the particular site, but it is helpful to establish the most effective therapy as soon as possible, particularly if there may be serious consequences to continued infection. Any test that calls for a culture requires several days.

- *Blood tests*, particularly variations in the numbers of leukocytes, are another general indicator of infection. With bacterial infections, **leukocytosis**, or an increase in white blood cells, is common, whereas viral infections often cause **leukopenia**, a reduction in the number of leukocytes in the blood. Changes in the distribution of types of leukocytes occur as well (differential count), depending on the organism, for example, **monocytosis** or **neutropenia**. Neutrophils tend to increase with acute infections, but lymphocytes and monocytes increase with chronic infection. C-reactive protein and erythrocyte sedimentation rate are usually elevated and are a general indicator of inflammation (see Chapter 5).

Blood tests also are useful in detecting antibodies and confirming a diagnosis, particularly in the case of viral infection. None of these factors by themselves provides a diagnosis, but they contribute to a final diagnosis. In hepatitis B infections, such tests can also be used to monitor the course of the infection because different antibodies form at various points in the course of this infection.

How to Read

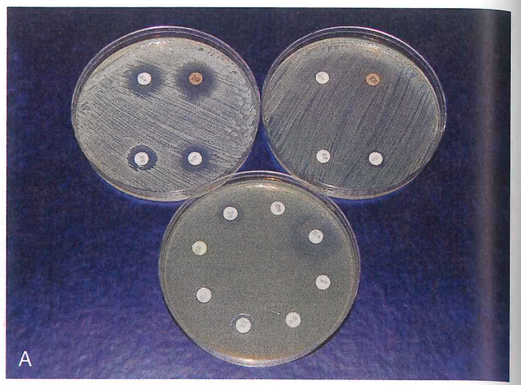

FIGURE 6-15 **A**, Disk diffusion (Kirby-Bauer method). The clear areas surrounding the antibiotic disks are called the *zones of inhibition*. The size of these zones can be used to determine the effectiveness of the antibiotic against the selected bacterium. **B**, Minimal inhibitory concentration. The minimal inhibitory concentration (MIC) for a specific agent is indicated by the absence of growth in the tube containing the lowest drug concentration. *(From VanMeter K, Hubert R:* Microbiology for the Healthcare Professional, *St. Louis, 2010, Mosby.)*

- In addition, *radiologic* examination may be used to identify the site of the infection and may assist in the identification of the agent. For example, lung congestion localized in one lobe (consolidation) usually indicates pneumococcal pneumonia.

Treatment and Antimicrobial Drugs

Guidelines for Use

It is not always necessary to use drugs to treat an infection because the body's normal defenses are often adequate to limit the infection. Also the usual growth pattern of the microbes is self-limiting as the colony uses up nutrients and produces more wastes. Current guidelines attempt to limit the use of antimicrobial drug so that the development of drug resistance can be reduced.

Increased use of antimicrobials has resulted in resistance of many organisms to certain drugs. Through mutations, *drug resistance* has developed in several ways as some bacteria have had changes in their metabolism allowing them to block drug action.

Improper use of an antibiotic can allow resistant organisms to dominate an infection that may have had very few resistant organisms at the onset. Improper use may result in an inadequate concentration of the drug being in contact for too short a time to be effective on all the organisms. In this case the weaker organisms will be killed, whereas stronger organisms with resistance mutations will survive, thrive and eventually dominate the infection.

Antimicrobial drugs may be administered prophylactically, before any invasive procedure, in high-risk clients (e.g., immunosuppressed patients). In treating an acute infection, frequently a *loading* or larger dose is administered initially to achieve effective blood levels quickly; this is often paired with a shorter duration of treatment.

Guidelines for effective drug therapy include: know very

1. The drug should be taken at regular, evenly spaced intervals over 24 hours to maintain blood levels that are adequate to control and destroy the organisms.
2. Antimicrobial drugs should be taken until the prescribed medication is completely used (usually 5 to 10 days), even if the symptoms have subsided, to ensure that the infection is completely eradicated and prevent the development of resistant organisms.
3. It is important to follow directions for administration with respect to food or fluid intake because drugs may be inactivated or drug absorption impaired if consumed with certain foods.
4. It is best to identify the specific organism and choose the most effective antibiotic that has the least effect on resident flora and human tissue.
5. Because many individuals have drug allergies, obtaining a complete drug history is essential, keeping in mind that an allergy usually includes all members of the chemically related drug group.
6. In viral infections, antiviral agents do not destroy the virus but merely inhibit its reproduction, providing an opportunity for host defenses to remove the virus. Antibacterial agents (antibiotics) are *not* effective against viruses. Antibacterials block synthesis of a bacterial cell wall or interfere with bacterial metabolism, but because viruses lack these components, antibacterials have no effect on them. Antibacterial drugs may be given in viral infection to reduce the risk of secondary bacterial infection in particularly vulnerable clients, but this is not a common practice. Use of an antimicrobial drug for a viral illness such as the common cold usually makes the person feel worse without any benefit.

Classification

Antimicrobials may be grouped in many ways in addition to their chemical classification. This section provides an overview of their classification, but a pharmacology reference should be consulted for details.

- *Antibiotic* is an older term and can be misleading. *Antibiotics* are drugs derived from organisms, such as penicillin from mold. Now many drugs are synthetic.
- *Antimicrobials* may be classified by the type of microbe against which the drug is active, such as antibacterials, antivirals, and antifungals. These drugs are unique to the type of organism and are not interchangeable.
- *Bactericidal* refers to drugs that destroy organisms, whereas *bacteriostatic* applies to drugs that decrease the microbe's rate of reproduction and rely on the host's defenses to destroy the organisms.
- *Broad spectrum* refers to antibacterials that are effective against both gram-negative and gram-positive organisms; *narrow spectrum* agents act against either gram-negative or gram-positive organisms, but not both. Narrow spectrum drugs are often preferred because they are less likely to upset the balance of resident flora in the body, which may result in an overgrowth of one organism and secondary or *superinfection*. For example, after a prolonged course of tetracycline, clients may develop a fungal (*Candida*) infection in the mouth, and women may develop vaginal candidiasis.
- The terms *first-generation* and *second-generation* drug now appear in texts, first generation referring to the original drug class, second generation referring to a later, improved version of the same drug group.

Mode of Action

Most antibacterial drugs may act in one of four ways:

1. Interference with bacterial cell wall synthesis is a bactericidal mechanism and is seen in drugs such as penicillin (see Fig. 6-3). Large doses of such drugs are usually safe in humans because human cells lack cell walls and are not directly affected by the drug.
2. A second mechanism is to increase the permeability of the bacterial cell membrane, allowing leakage of bacterial cell contents; this mechanism is exemplified by polymyxin.
3. Some drugs, such as tetracycline, interfere with protein synthesis and cell reproduction. These have significant effects on the developing fetus and young child.
4. Another group, including the sulfonamides, interferes with the synthesis of essential metabolites.

The common problems with antibacterial drugs are *allergic* reactions, both mild and severe, and digestive tract discomfort. Penicillin and its related compounds may cause anaphylaxis. Digestive tract discomfort may result from irritation of the stomach or the change in the

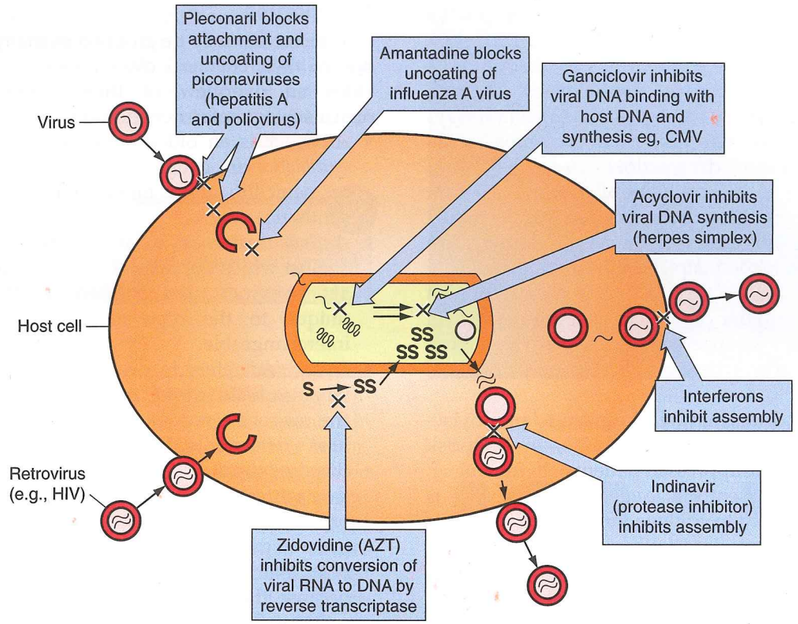

FIGURE 6-16 Examples of antiviral agents.

intestinal resident flora caused by the antibacterial action, often leading to diarrhea. Secondary infections, particularly fungal, may develop as the balance of resident flora is disturbed.

THINK ABOUT 6-6

a. Describe two mechanisms by which antibacterial drugs act on microorganisms.
b. Why do most antibacterial drugs not destroy human cells?
c. Explain the benefit of narrow spectrum over broad spectrum drugs.
d. Explain why a drug may have to be changed if an infection persists.

One drug, cefotaxime, is a third-generation cephalosporin and is related to the penicillin family. It has been developed to be more active against gram negative microbes and multi-drug resistant organisms. This drug can pass through the blood-brain barrier, thus it is more effective in treating some forms of meningitis as well.

Antiviral agents decrease the reproduction of viruses inside the host cell but cannot destroy the virus. They control but do not cure infection. In some cases the drugs are effective only against actively replicating viruses, not against those in the latent stage. These drugs may interfere with attachment of the virus to the host cell, with the shedding of the protein coat, with the action of enzymes such as reverse transcriptase required for synthesis of DNA and RNA or with protein synthesis (Fig. 6-16). The drugs may be virus specific; for example, acyclovir is effective against herpes simplex viruses. Antiviral drugs tend to have significant adverse effects on the host because they alter viral interaction within the host cell.

Genomics is the basis for several new types of antiviral drugs as the search continues for drugs targeting Hepatitis B and/or C, enteroviruses, HIV, and other viral pathogens. One type of drug is based on blocking segments of viral DNA or RNA with *antisense molecules*, rendering the nucleic acid incapable of expression or replication. Ribozymes are enzymes that split DNA or RNA into segments and inhibit replication of viral genes in the cell. These new agents appear to be active against several types of viruses; a few drugs are in clinical trials.

Antifungal agents may interfere with mitosis in fungi (e.g., griseofulvin), or they may increase fungal membrane permeability; amphotericin B may be administered intravenously for systemic infections. Because fungi are eukaryotic cells with many similarities to animal/human cells, systemic antifungal agents are often toxic to the animal/human cells and treatment with these agents usually requires strict medical supervision. Most antifungal agents are administered topically to skin or mucous membranes.

Antiprotozoal agents have a similar characteristic to the antifungal agents in that the targets are eukaryotic cells and can be toxic to human cells. Many pathogenic protozoa also have several stages in their life cycles that require treatment with different agents at different stages. With exception of quinine, most antiprotozoal agents are synthetic, such as metronidazole and pyrimethamine.

Antihelminthic agents have a variety of modes of action. These agents share the same drawback as the antifungal and antiprotozoal agents as they are attacking eukaryotic organisms. Some are designed to suppress a metabolic process that is more important to the helminth than the host while others inhibit the movement of the worm and/or prevent it from remaining in the specific organ. Some examples of these agents are piperazine (paralyzes muscles in the worm's body wall), niclosamide (prevents ATP formation) and ivermectin (blocks nerve transmission).

Example of Infection: Influenza (Flu)

Influenza is a viral infection that may affect both the upper and the lower respiratory tracts. Annually on average 10% to 20% of the population is affected in North America. Although the influenza infection itself may be mild, it is frequently complicated by secondary bacterial infections such as pneumonia. The mortality rate from complications can be high, particularly in those older than 65 years and those with chronic cardiovascular or respiratory disease. Influenza may occur sporadically, in epidemics or pandemics, usually during colder weather. Serious pandemics occurred in 1918 to 1919 (Spanish flu) with a very high mortality rate, again in 1957 (Asian flu), and in 1968 (Hong Kong flu). In 1997 there was an outbreak in Hong Kong of an avian flu transmitted from chickens to humans, and this potential crossover to a new species host is being closely monitored. Epidemiologists predict that serious pandemics will occur in the future.

The influenza viruses are classified as RNA viruses of the myxovirus group. There are three subgroups of the influenza virus—type A, the most prevalent pathogen, type B, and type C. Types A and B cause epidemics and pandemics that tend to occur in cycles. The influenza virus, particularly type A, is difficult to control because it undergoes frequent mutations leading to antigenic shifts or variations. This limits the ability of individuals to develop long-term immunity to the virus and requires the preparation of new vaccines annually to match the predicted new strains of the virus for the coming year. Unfortunately, new strains may emerge during the winter months, creating a slightly different infection. Some years the epidemic has occurred at an earlier time and individuals have not yet received their immunization. Technology to produce a new type of vaccine using viruses grown in a cell culture rather than in eggs is being developed. This process would permit more rapid production to meet an increased demand for vaccines.

In the spring of 2009 a new variant of type A influenza was identified in Mexico. This form of influenza was subsequently named 2009 type A H1N1 influenza. It was highly contagious and caused significant morbidity and mortality in children less than 18 and pregnant women. It is thought that those older than 65 may have some immunity to the virus from earlier outbreaks of similar viruses. The H1N1 influenza virus is genetically and antigenically similar to the virus that caused the Spanish flu pandemic in 1918. It contains genetic material from avian, pig, and human influenza types and is expected to mutate rapidly. The designation H1N1 refers to the specific type of antigens on the viral capsule (Fig. 6-17).

Some children developed severe acute respiratory syndrome and died quickly from the infection in 2009. At the time of writing it is unclear how the H1N1 virus causes this response in young children and teens particularly because most had no other health problems at the time of infection. Possible explanations being researched include formation of pulmonary emboli or altered capillary exchange in the alveoli of the lung. H1N1 flu reemerged in North America and Europe in late September of 2009. Immunization programs specific for H1N1 were begun but vaccine shortages and public resistance to vaccines may lead to high rates of morbidity and mortality in at risk populations.

The constituents of each multivalent vaccine, currently three in number, are specifically designated each year. WHO monitors the incidence and movement of the infection worldwide. Most new strains evolve in Southeast Asia. World Health Organization scientists collect and analyze specimens worldwide, then check the incidence of each strain so as to determine the most effective vaccine components. For example, one antigen might be called A/New Caledonia/20/99, which indicates the type (A), the geographic origin (New Caledonia), the strain number (20), and the year of isolation (1999) for a particular viral strain.

The vaccine may be administered as an intranasal spray (live vaccine) or intramuscular injection (inactivated or killed). It is now recommended that all individuals be immunized annually between November and February. For many health care providers immunization is a condition of employment. The vaccine that remains effective from 2 to 4 months reduces the severity of the infection in cases in which it does not provide total prevention.

The influenza virus was first isolated and identified in 1933. It is transmitted directly by respiratory droplet or indirectly by contact with a contaminated object. The virus can survive at room temperature as long as 2 weeks. It is destroyed by heat and some disinfectants such as ethanol and detergents.

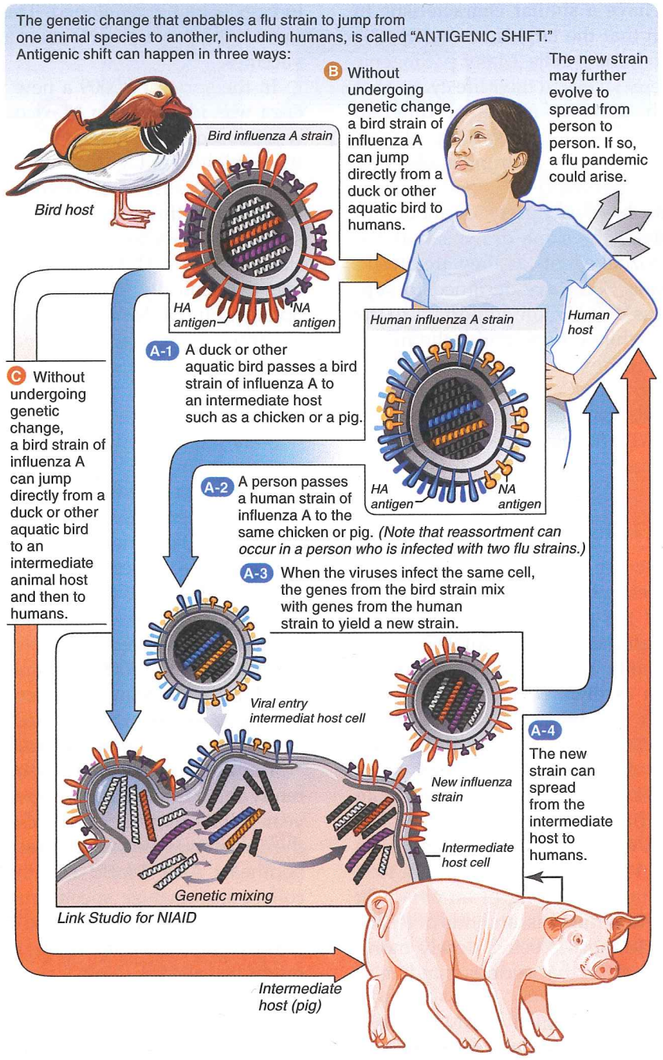

FIGURE 6-17 History of the 2009 Type A H1N1 influenza virus showing antigenic shift. *(From National Institute of Allergy and Infectious Disease [NIAID].)*

The virus enters the cells in the respiratory mucosa, replicates, and causes inflammation and necrosis of the tissue as well as shedding of the virus into the secretions and adjacent cells. The inflammation may also involve the sinuses, pharynx, and auditory tube, causing congestion and obstruction. The widespread necrosis of the respiratory mucosa typical of influenza leaves the area vulnerable to secondary infection by bacteria, which are often resident flora of the upper respiratory tract. The virus may extend into the lungs and cause viral pneumonia.

Influenza usually has a sudden, acute onset with fever and chills, marked malaise, headache, general muscle aching, sore throat, unproductive or dry cough, and nasal congestion. The infection is often self-limiting, although fatigue may persist for several weeks afterward. Continued fever or other signs usually indicate complications, such as the development of bacterial pneumonia.

Treatment is symptomatic and supportive unless bacterial infection or respiratory complications occur. Certain antiviral drugs such as oseltamivir (Tamiflu) if given promptly, may reduce the symptoms in some cases. The CDC recommended the use of oseltamivir (Tamiflu) or zanamivir (Relenza) for the 2008 to 2009 flu season. Other antiviral treatment has been tried, but adverse effects have occurred.

THINK ABOUT 6-7

a. Explain why influenza continues to be a common infection in North America.
b. State three ways the incidence might be reduced.
c. Explain why secondary bacterial infection is common in persons with influenza.

CASE STUDY A

Viral Gastroenteritis

G.B., 15 months old, had severe vomiting and diarrhea for 12 hours and no intake of fluid or food. She began vomiting blood and was quite dehydrated and lethargic. She was taken to the hospital, admitted, and treated with intravenous fluid, electrolytes, and glucose. A fecal specimen was submitted to the laboratory for diagnosis.

The report indicated an infection with rotavirus, an RNA virus and member of the reovirus class. This virus causes gastroenteritis. The incubation period is 1 to 2 days, and the virus is transmitted by the fecal-oral route, probably at G.B.'s nursery school, where several children have been ill. The virus replicates in the epithelial cells at the tip of villi in the small intestine. This cell damage results in lack of absorption of fluid and nutrients.

1. Explain, using the pathophysiology, how the virus could cause bleeding.
2. Using your knowledge of normal physiology, explain how the vomiting and diarrhea as well as the lack of intake could affect the child physiologically.
3. Describe several factors probably contributing to transmission in this case. How long before the vomiting began was the child probably exposed to the virus?
4. What does the classification "RNA virus" mean?
5. Why is it necessary to determine the specific cause of the vomiting and diarrhea? Is any other treatment for rotavirus infection indicated?

CASE STUDY B

Upper Respiratory Infection

K.W., age 9, suddenly developed a fever with very sore throat, headache, and malaise. When examined, her pharynx was red and her tonsils enlarged with pus on the surface and in the crypts. Her cervical lymph nodes were also enlarged. The physician suspected a bacterial infection, and therefore took a throat swab for examination and prescribed a course of penicillin so as to prevent complications.

Laboratory examination confirmed streptococcal infection, and continued treatment with penicillin. This microbe is gram-positive and it adheres to epithelial cells in the pharynx. It produces several exotoxins and resists phagocytosis. It is spread by oral droplet.

1. Suggest several precautions to prevent further transmission in this case.
2. What factor indicated this was a bacterial infection rather than viral?
3. Describe the typical appearance of *Streptococcus* under a microscope.
4. Explain the meaning of gram-positive and how this classification is helpful.
5. K.W. wanted to stop her medication several days later when the headache and fever disappeared. State two reasons why this is not advisable.

CHAPTER SUMMARY

- Infections are caused by pathogenic microorganisms. They may be classified and identified by their characteristics, such as size, shape, component parts, and requirements for growth and reproduction.
- Bacteria are single-cell organisms enclosed within a cell wall and sometimes an outer capsule. They reproduce by binary fission. They may secrete exotoxins, endotoxins, or enzymes that damage the human host cells.
- A virus is an intracellular parasite requiring a living host cell for reproduction. Each viral particle contains either DNA or RNA. They cause disease by destroying human cells during replication or by altering human cell DNA.
- Only a few fungi are pathogenic; *Candida* is an example of an opportunistic member of resident flora in the human body.
- Helminths are parasitic worms that can infect the gut, liver, bloodstream, or lungs.
- Prions are protein-like molecules that cause deformation of proteins within the central nervous system. Their mode of action is not well understood. Prions are transmitted by ingestion of undercooked meat contaminated with prions or by organ donation from an infected donor.
- Resident or normal flora refers to the large variety of nonpathogenic microbes normally present in diverse sites in the body, such as skin, mouth, nose and pharynx, intestines, and vagina.
- The degree of virulence of a specific pathogen determines the severity of the resulting infection.
- Transmission of pathogens may occur by direct or indirect contact, including oral or respiratory droplet, sexual contact, fomite, or vector.
- The infection cycle may be broken by reducing the reservoir of microbes, blocking transmission, or increasing host resistance.

- Universal precautions, as outlined by the CDC, assume that blood and body fluids from any person may be a source of infection; therefore appropriate preventive measures must be taken with all individuals.
- Signs of infection are not apparent until sufficient numbers of microorganisms are established and reproducing in the body. Local signs of infection include inflammation and necrosis of tissue. Systemic signs include fever, headache, fatigue, anorexia, and malaise.
- Infection may be eradicated without drug treatment when the microbial colony becomes limited in growth, perhaps because of insufficient nutrients, or when host defenses destroy the invader.
- Antibacterial drugs are classified by their activity (bactericidal or bacteriostatic, narrow or broad spectrum) and mechanism (e.g., interference with protein or cell wall synthesis).
- Adverse effects of antibacterial agents are allergic reactions, secondary infections, and increasing numbers of drug-resistant microbes.
- Antiviral drugs limit viral replication, thus reducing the active stage, but do not kill the virus or cure the infection.
- Influenza is a respiratory infection caused by a virus that frequently mutates, preventing long-term immunity by vaccination or experiencing the infection. Epidemics are common. Secondary bacterial infections such as pneumonia are common, particularly in the elderly.

STUDY QUESTIONS

1. Explain how each of the following contributes to the virulence of bacteria:
   a. production of endotoxin
   b. spore formation
   c. presence of a capsule
2. Predict how each of the following could reduce host resistance to infection:
   a. bone marrow damage
   b. circulatory impairment
   c. puncture wound
3. Explain two benefits of resident flora.
4. Differentiate infection from inflammation.
5. Describe three ways of reducing transmission of a respiratory infection.
6. Explain each of the following:
   a. why the clinical signs of infection are not present immediately after the microorganism enters the body
   b. why infection can often be cured without drug treatment
   c. why antibacterial agents might be prescribed for an infection
7. Explain why it is important to take the complete course of antimicrobial medication prescribed.
8. Explain why viral infections are difficult to treat.
9. State two local and two systemic signs of influenza.
10. Explain why a new influenza vaccine is prepared each year and consists of several components.

ADDITIONAL RESOURCES

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http://www.cdc.gov/mmwr Morbidity and Mortality Weekly Report.
http://www.asm.org American Society for Microbiology.
http://www.nlm.nih.gov National Library of Medicine.
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