to damage in the liver and intestine. Similarly, *Schistosoma hematobium* travels to vessels in the urinary bladder and causes cystitis.

Release from the Body and Transmission of Microbes

Infectious microbes use a variety of "exit strategies" to ensure their transmission from one host to the next. Depending on the location of of infection, release may be accomplished by skin shedding, coughing, sneezing, voiding of urine or feces, during sexual contact, or through insect vectors. Some pathogens are released for only brief periods of time or periodically during disease flares, but others, such as the enteric pathogen *S. typhi*, may be shed for long periods by asymptomatic carrier hosts. Once released, pathogens also show wide variation in hardiness. Some survive for extended periods of time in dust, food, or water. Bacterial spores, protozoan cysts, and helminth eggs can remain viable in a cool and dry environment for months to years. By contrast, some fragile pathogens persist outside of the body for only short periods of time and must be passed quickly from person to person, often by direct contact.

Most pathogens are transmitted from person to person by respiratory, fecal-oral, or sexual routes. Viruses and bacteria spread by the respiratory route are infectious only when lesions are open to the airways. With coughing, the pathogens are aerosolized in droplets and released into the air. Some respiratory pathogens, including influenza viruses, are spread in large droplets that travel no more than 3 feet from the source, but others, including *M. tuberculosis* and varicella-zoster virus, spread in small droplets or within dust particles that can travel much longer distances.

Understandably, most enteric pathogens are spread by the fecal-oral route, that is, by ingestion of stool-contaminated water or food. Water-borne viruses involved in epidemic outbreaks that are spread in this fashion include hepatitis A and E viruses, poliovirus, and rotavirus. Other important pathogens spread by the fecal-oral route include *V. cholerae*, *Shigella*, *Campylobacter jejuni*, and *Salmonella*. Some parasitic helminthes (e.g., hookworms, schistosomes) shed eggs in stool that hatch as larvae that are capable of penetrating the skin of the next host. Sexual transmission often entails prolonged intimate or mucosal contact and is responsible for spread of a wide variety of pathogens, including viruses (e.g., *Herpes simplex*, HIV, human papilloma virus), bacteria (*T. pallidum*, *Gonococcus*), protozoa (*Candida*) and even arthropods (*Phthiris pubis*, or crab lice).

Besides these major routes of transmission, pathogens exist that exploit virtually every imaginable means for spreading to a new host. Saliva is responsible for transmitting viruses that replicate in the salivary gland or oropharynx, including Epstein-Barr virus and rabies virus, which may be spread by an amorous kiss or a frenzied bite, respectively. Protozoa and helminths have evolved particularly complex life cycles that often involve intermediate hosts bearing successive developmental stages of the pathogen. Some of the most important human pathogens are protozoa that are spread through blood meals taken by arthropod vectors (mosquitoes, ticks, mites). Finally, a few pathogens can be transmitted from animals to humans (termed *zoonotic infections*), either by direct contact, consumption of animal products, or via an invetebrate vector.

KEY CONCEPTS

Transmission and Dissemination of Microbes

- Transmission of infections can occur by contact (direct and indirect), respiratory route, fecal-oral route, sexual transmission, vertical transmission or insect/arthropod vectors.
- A pathogen can establish infection if it possesses virulence factors that overcome normal host defenses or if the host defenses are compromised.
- Host defenses against infection include:
  - Skin: tough keratinized barrier, low pH, fatty acids
  - Respiratory system: alveolar macrophages, mucociliary clearance by bronchial epithelium, IgA
  - GI system: acidic gastric pH, viscous mucus, pancreatic enzymes and bile, defensins, IgA, and normal flora
  - Urogenital tract: repeated flushing and acidic environment created by commensal flora
- Pathogens can proliferate locally, at the site of initial infection, or spread to other sites by direct extension (invasion) or by transport in the lymphatics, the blood, or nerves.

Host-Pathogen Interactions

Host Defenses against Infection

The outcome of infection is determined by the virulence of the microbe and the nature of the host immune response, which may either eliminate the infection or, in some cases, exacerbate or even be the principal cause of tissue damage. The host has a large and complex armamentarium of defenses against pathogens, including physical barriers and components of the innate and adaptive immune systems, which were discussed extensively in Chapter 6. The complexity of the immune system is a testimony to the remarkable selective pressures that infectious diseases place on humans and other animals; there is little doubt that the ability to survive in a world full of pathogenic microbes was (and remains) one of the most important forces shaping human evolution. Unfortunately, Darwinian forces also drive the continuing evolution of a remarkable array of highly diverse microbes, which are constantly threatening to get a step ahead of host defenses.

We will return to the issue of newly emerging infections later in this Chapter. In the next section, we discuss the various mechanisms by which pathogens evade the host and cause disease.

Immune Evasion by Microbes

Most pathogenic microbes have developed one or more strategies that allow them to evade host defenses (Fig. 8-2). The mechanisms of evasion are probably even more numerous than the mechanisms of effective host response, as any microbe that by chance acquires resistance to an effective host response is likely, over time, to rise in prevalence in the microbial population. Some salient examples of immune evasion by microbes are as follows: