Listeriosis

***Listeria monocytogenes* is a gram-positive bacillus that causes severe food-borne infections in vulnerable hosts.** Outbreaks of *L. monocytogenes* infection have been linked to contaminated dairy products, chicken, and hot dogs. Pregnant women, neonates, older adults, and immunosuppressed persons are particularly susceptible to severe *L. monocytogenes* infection. In pregnant women, *L. monocytogenes* causes an amnionitis that may result in abortion, stillbirth, or neonatal sepsis. In neonates and immunosuppressed adults, it can cause disseminated disease (granulomatosis infantiseptica of the newborn) and an exudative meningitis.

L. monocytogenes is a facultative intracellular pathogen, and therefore, T cells play a particularly important role in the host immune response. The bacteria bind to receptors on host epithelial cells and macrophages and are phagocytosed. The bacteria escape from the phagolysosome using a pore-forming protein, listeriolysin O, and two phospholipases. In the host cell cytoplasm, Act A, a bacterial surface protein, binds to host cell cytoskeletal proteins and induces actin polymerization. This in turn generates sufficient force to propel the bacteria into adjacent, uninfected host cells. Resting macrophages fail to kill the intracellular bacteria, whereas macrophages that are activated by IFN-γ can. Accordingly, an effective host response to *L. monocytogenes* depends on IFN-γ produced by NK cells early in the course of the infection and T cells in chronic infection. Patients with defects in cell-mediated immunity, such as those with reduced levels of CD4+ lymphocytes, are at increased risk for listeriosis.

MORPHOLOGY

In acute infections, *L. monocytogenes* evokes an exudative pattern of inflammation with numerous neutrophils. The meningitis it causes is macroscopically and microscopically indistinguishable from that resulting from infection with other pyogenic bacteria (Chapter 28). **The finding of gram-positive, mostly intracellular bacilli in the CSF is virtually diagnostic.** More varied lesions may be encountered in neonates and immunosuppressed adults. Focal abscesses alternating with grayish or yellow nodules representing necrotic amorphous tissue debris can occur in any organ, including the lung, liver, spleen, and lymph nodes. In infections of longer duration, macrophages appear in large numbers, but granulomas are rare. Infants born with *L. monocytogenes* sepsis often have a papular red rash over the extremities, and listerial abscesses can be seen in the placenta. A smear of the meconium will disclose the gram-positive bacilli.

Anthrax

Anthrax is characterized by necrotizing inflammatory lesions in the skin or gastrointestinal tract or systemically. It is caused by *Bacillus anthracis*, a large, spore-forming gram-positive rod-shaped bacterium found in environmental sources. Livestock become infected by spores in their environment or feed. Humans usually become infected by eating or handling meat or products (e.g., wool or hides) from infected animals. There are a small number of cases of anthrax each year, most of which occur in the developing world. Anthrax spores can be made into a fine powder, creating a potent biologic weapon that is a potential bioterrorism threat. In 1979, accidental release of *B. anthracis* spores at a military research institute in Russia killed 66 people. In 2001, 22 people in the United States were infected with *B. anthracis*, mostly through spores delivered in the mail.

There are three major forms of anthrax.

- *Cutaneous anthrax*, which makes up 95% of naturally occurring infections, begins as a painless, pruritic papule that develops into a vesicle within 2 days. As the vesicle enlarges, striking edema may occur around it, with development of regional lymphadenopathy. After the vesicle ruptures, the remaining ulcer becomes covered with a characteristic black eschar, which dries and falls off as the person recovers. Bacteremia is rare.
- *Inhalational anthrax* occurs when airborne spores are inhaled. The spores are carried by phagocytes to lymph nodes where they germinate, producing bacilli that release toxins that cause hemorrhagic mediastinitis. After a prodromal illness of 1 to 6 days characterized by fever, cough, and chest or abdominal pain, there is abrupt onset of increased fever, hypoxia, and sweating. Frequently, meningitis develops from bacteremia. Inhalational anthrax rapidly leads to shock and frequently death within 1 to 2 days.
- *Gastrointestinal anthrax* is usually contracted by eating undercooked meat contaminated with *B. anthracis*. Initially, the person has nausea, abdominal pain, and vomiting, followed by severe, bloody diarrhea and, sometimes, bacteremia. Mortality is approximately 40%.

Pathogenesis. *B. anthracis* produces potent toxins and an antiphagocytic polyglutamyl capsule. The mechanisms of action of anthrax toxins are well understood (Fig. 8-19). They have A and B subunits. The B subunit is also called the *protective antigen*, because antibodies against it protect against the toxins. Following infection the B subunit is released into the circulation and binds to a cell surface

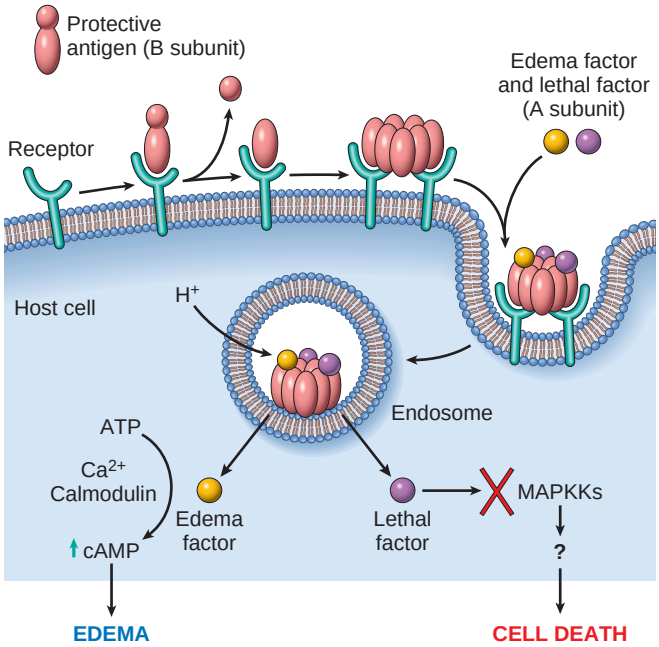

Figure 8-19 Mechanism of action of anthrax toxins. Note that each B subunit binds either EF or LF but not both (as shown for simplicity). (Adapted from Mourez M, Lacy DB, Cunningham K, et al: 2001: A year of major advances in anthrax toxin research. Trends Microbiol 2002;10:287.)