

on macrophages. In response, these cells release proinflammatory cytokines (IL-6 and TNF) and generate bactericidal reactive nitrogen intermediates, reducing but usually not eliminating the infection.

The inflammatory lesions are likely triggered by T cells and cytokines. *Borrelia*-specific antibodies, made 2 to 4 weeks after infection, direct complement-mediated phagocytosis and killing of the bacteria; however, *B. burgdorferi* escapes the antibody response through antigenic variation. Similar to *Borrelia hermsii*, a cause of endemic relapsing fever, *B. burgdorferi* has a plasmid with a single promoter sequence and multiple coding sequences for an antigenic surface protein, VlsE, each of which can shuttle into position next to the promoter and be expressed. Thus, as the antibody response to one VlsE protein is mounted, bacteria expressing an alternate VlsE protein can escape immune recognition. Chronic manifestations of Lyme disease, such as the late arthritis, are probably caused by the immune response against persistent bacteria.

### MORPHOLOGY

Skin lesions caused by *B. burgdorferi* are characterized by edema and a lymphocytic-plasma cell infiltrate. In early Lyme arthritis, the synovium resembles early rheumatoid arthritis, with villous hypertrophy, lining-cell hyperplasia, and abundant lymphocytes and plasma cells in the subsynovium. A distinctive feature of Lyme arthritis is an arteritis, which produces onionskin-like lesions resembling those seen in lupus (Chapter 6). In late Lyme disease there may be extensive erosion of the cartilage in large joints. In Lyme meningitis the CSF is hypercellular, due to a marked lymphoplasmacytic infiltrate, and contains antispinochete IgGs.

### Anaerobic Bacteria

Many anaerobic bacteria are normal flora in sites of the body that have low oxygen levels. The anaerobic flora cause disease (abscesses or peritonitis) when they are introduced into normally sterile sites or when the balance of organisms is upset and pathogenic anaerobes overgrow (e.g., *Clostridium difficile* colitis with antibiotic treatment). Environmental anaerobes also cause disease (tetanus, botulism, and gas gangrene).

#### Abscesses Caused by Anaerobes

**Commensal bacteria from adjacent sites (oropharynx, intestine, and female genital tract) are the usual cause of abscesses, so the species found in an abscess often reflect the normal flora in that site.** Abscesses are usually caused by mixed anaerobic and facultative aerobic bacterial infections. Because most anaerobes that cause abscesses are part of the normal flora, it is not surprising that these organisms do not produce significant toxins.

The bacteria found in head and neck abscesses reflect oral and pharyngeal flora. Common anaerobes at this site include the gram-negative bacilli *Prevotella* and *Porphyromonas* species, often mixed with the facultative *S. aureus* and *S. pyogenes*. *Fusobacterium necrophorum*, an oral commensal, causes Lemierre syndrome, characterized by infection of the lateral pharyngeal space and septic jugular vein thrombosis. Abdominal abscesses are caused by the anaerobes of the gastrointestinal tract, including gram-positive

*Peptostreptococcus* and *Clostridium* species, as well as gram-negative *Bacteroides fragilis* and *E. coli*. Genital tract infections in women (e.g., Bartholin cyst abscesses and tubo-ovarian abscesses) are caused by anaerobic gram-negative bacilli, such as *Prevotella* species, often mixed with *E. coli* or *Streptococcus agalactiae*.

### MORPHOLOGY

Abscesses caused by anaerobes contain discolored and foul-smelling pus that is often poorly walled off. Otherwise, these lesions pathologically resemble those of the common pyogenic infections. Gram stain reveals mixed infection with gram-positive and gram-negative rods and gram-positive cocci mixed with neutrophils.

#### Clostridial Infections

*Clostridium* species are gram-positive bacilli that grow under anaerobic conditions and produce spores that are present in the soil. Four types of disease are caused by *Clostridium*:

- *C. perfringens*, *C. septicum*, and other species cause cellulitis and myonecrosis of traumatic and surgical wounds (*gas gangrene*), uterine myonecrosis often associated with illegal abortions, mild food poisoning, and infection of the small bowel associated with ischemia or neutropenia that often leads to severe sepsis.
- *C. tetani*, the cause of *tetanus*, proliferates in puncture wounds and in the umbilical stump of newborn infants and releases a potent neurotoxin that causes increased muscle tone and generalized spasms of skeletal muscles (lockjaw). Tetanus toxoid (formalin-fixed tetanus toxin) is part of the DPT (diphtheria, pertussis, and tetanus) immunization, and this has greatly decreased the incidence of tetanus worldwide.
- *C. botulinum*, the cause of *botulism*, grows in inadequately cooked foods and releases a potent neurotoxin that blocks synaptic release of acetylcholine and causes flaccid paralysis of respiratory and skeletal muscles.
- *C. difficile* overgrows other intestinal flora in antibiotic-treated people, releases toxins, and causes *pseudomembranous colitis* (Chapter 17).

Clostridial infections can be diagnosed by culture (cellulitis, myonecrosis), toxin assays (pseudomembranous colitis), or both (botulism).

**Pathogenesis.** *Clostridium perfringens* does not grow in the presence of oxygen, so tissue death is essential for growth of the bacteria in the host. **These bacteria release collagenase and hyaluronidase that degrade extracellular matrix proteins and contribute to bacterial invasiveness, but their most powerful virulence factors are the many toxins they produce.** *C. perfringens* secretes 14 toxins, the most important of which is  $\alpha$ -toxin. This toxin has multiple actions. It is a phospholipase C that degrades lecithin, a major component of cell membranes, and so destroys red cells, platelets, and muscle cells, causing myonecrosis. It also has a sphingomyelinase activity that contributes to nerve sheath damage.

Ingestion of food contaminated with *C. perfringens* causes a brief diarrhea. Spores, usually in contaminated meat, survive cooking, and the organism proliferates in