cooling food. *C. perfringens* enterotoxin forms pores in the epithelial cell membranes, lysing the cells and disrupting tight junctions between epithelial cells.

The neurotoxins produced by *C. botulinum* and *C. tetani* both inhibit release of neurotransmitters, resulting in paralysis. Botulism toxin, eaten in contaminated foods or absorbed from wounds infected with *C. botulinum*, binds gangliosides on motor neurons and is transported into the cell. In the cytoplasm, the A fragment of botulism toxin cleaves a protein, called synaptobrevin, that mediates fusion of neurotransmitter-containing vesicles with the neuron membrane. By blocking vesicle fusion, botulism toxin prevents the release of acetylcholine at the neuromuscular junction, resulting in flaccid paralysis. If the respiratory muscles are affected, botulism can lead to death. The widespread use of botulism toxin (Botox) in cosmetic surgery is based on its ability to cause paralysis of strategically chosen muscles on the face. Tetanus toxin causes a violent spastic paralysis by blocking release of γ-aminobutyric acid, a neurotransmitter that inhibits motor neurons.

C. difficile produces toxin A, an enterotoxin that stimulates chemokine production and thus attracts leukocytes, and toxin B, a cytotoxin, which causes distinctive cytopathic effects in cultured cells. Both toxins are glucosyl transferases and are part of a pathogenicity island that is absent from the chromosomes of nonpathogenic strains of *C. difficile*.

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The most significant lesions are caused by *C. perfringens*; these are described next. **Clostridial cellulitis**, which originates in wounds, can be differentiated from infection caused by pyogenic cocci by its foul odor, its thin, discolored exudate, and the relatively quick and wide tissue destruction. On microscopic examination, the amount of tissue necrosis is disproportionate to the number of neutrophils and gram-positive bacteria present (Fig. 8-38). Clostridial cellulitis, which often has granulation tissue at its borders, is treatable by debridement and antibiotics.

In contrast, **clostridial gas gangrene** is life-threatening and is characterized by marked edema and enzymatic necrosis of involved muscle cells 1 to 3 days after injury. An extensive fluid exudate, which is lacking in inflammatory cells, causes swelling of the affected region and the overlying skin, which develops large bullous vesicles that rupture. Gas bubbles caused by bacterial fermentation appear within the gangrenous tissues. As the infection progresses, the inflamed muscles become soft, blue-black, friable, and semifluid as a result of the massive proteolytic action of the released bacterial enzymes. On microscopic examination there is severe **myonecrosis**, extensive hemolysis, and marked vascular injury, with thrombosis. *C. perfringens* is also associated with dusk-colored, wedge-shaped infarcts in the small bowel, particularly in neutropenic people. Regardless of the site of entry, when *C. perfringens* disseminates hematogenously there is widespread formation of gas bubbles.

Despite the severe neurologic damage caused by botulinum and tetanus toxins, the neuropathologic changes are subtle and nonspecific.

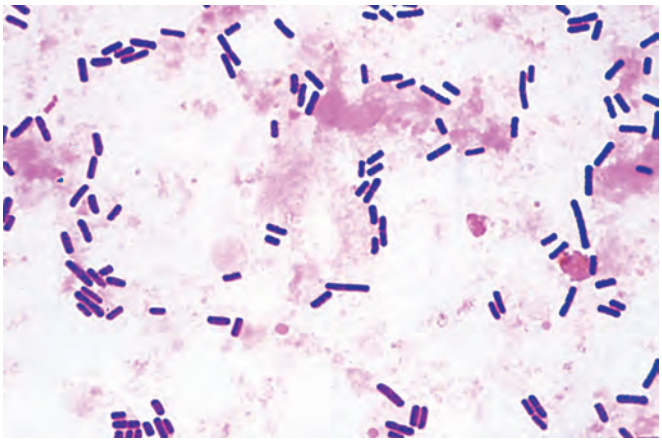

Figure 8-38 Boxcar-shaped gram-positive *Clostridium perfringens* intermingled with necrotic debris in gangrenous tissue.

Obligate Intracellular Bacteria

Obligate intracellular bacteria proliferate only within host cells, although some may survive outside of cells. These organisms are well adapted to the intracellular environment, with membrane pumps to capture amino acids and ATP for energy. Some are unable to synthesize ATP at all (e.g., *Chlamydia*), while others synthesize at least some of their own ATP (e.g., the rickettsiae).

Chlamydial Infections

C. trachomatis is a small gram-negative bacterium that is an obligate intracellular parasite. *C. trachomatis* exists in two forms during its unique life cycle. The infectious form, called the *elementary body,* is a metabolically inactive, spore-like structure. Host cells take up the elementary body by receptor-mediated endocytosis. The bacteria prevent fusion of the endosome and lysosome by an unknown mechanism. Inside the endosome the elementary body differentiates into a metabolically active form, called the *reticulate body*. The reticulate body uses ATP and amino acids from the host cell to replicate and forms new infectious elementary bodies.

The various diseases caused by *C. trachomatis* infection are associated with different serotypes of the bacteria: urogenital infections and inclusion conjunctivitis (serotypes D through K), lymphogranuloma venereum (serotypes L1, L2, and L3), and an ocular infection of children, trachoma (serotypes A, B, and C). The venereal infections caused by *C. trachomatis* are discussed here.

Genital infection by *C. trachomatis* is the most common sexually transmitted bacterial disease in the world. In 2010, approximately 1.3 million cases of genital chlamydia were reported to the CDC. Before the identification of *C. trachomatis*, people infected with this organism were diagnosed with nongonococcal urethritis.

Genital *C. trachomatis* infections (other than lymphogranuloma venereum, discussed later) are associated with clinical features that are similar to those caused by *N. gonorrhoeae.* Patients may develop epididymitis, prostatitis, pelvic inflammatory disease, pharyngitis, conjunctivitis, perihepatic inflammation, and proctitis. Unlike *N. gonorrhoeae* urethritis, *C. trachomatis* urethritis in men may be