adjuncts since they are effective in necrotizing infections due to other toxin-producing gram-positive organisms.

Other Clostridial Skin and Soft-Tissue Infections *Crepitant cellulitis* (also called *anaerobic cellulitis*) occurs principally in diabetic patients and characteristically involves subcutaneous tissues or retroperitoneal tissues, whereas the muscle and fascia are not involved. This infection can progress to fulminant systemic disease.

Cases of *C. histolyticum* infection with cellulitis, abscess formation, or endocarditis have also been documented in injection drug users. Endophthalmitis due to *C. sordellii* or *C. perfringens* has been described. *C. ramosum* is also isolated frequently from clinical specimens, including blood and both intraabdominal and soft tissues. This species may be resistant to clindamycin and multiple cephalosporins.

SECTION 6 DISEASES CAUSED BY GRAM-NEGATIVE BACTERIA

180 Meningococcal Infections

Andrew J. Pollard

DEFINITION

Infection with *Neisseria meningitidis* most commonly manifests as asymptomatic colonization in the nasopharynx of healthy adolescents and adults. Invasive disease occurs rarely, usually presenting as either bacterial meningitis or meningococcal septicemia. Patients may also present with occult bacteremia, pneumonia, septic arthritis, conjunctivitis, and chronic meningococcemia.

ETIOLOGY AND MICROBIOLOGY

N. meningitidis is a gram-negative aerobic diplococcus that colonizes humans only and that causes disease after transmission to a susceptible individual. Several related organisms have been recognized, including the pathogen *N. gonorrhoeae* and the commensals *N. lactamica*, *N. flavescens*, *N. mucosa*, *N. sicca*, and *N. subflava*. *N. meningitidis* is a catalase- and oxidase-positive organism that utilizes glucose and maltose to produce acid.

Meningococci associated with invasive disease are usually encapsulated with polysaccharide, and the antigenic nature of the capsule determines an organism's serogroup (Table 180-1). In total, 13 serogroups have been identified (A–D, X–Z, 29E, W, H–J, and L), but just 6 serogroups—A, B, C, X, Y, and W (formerly W135)—account for the majority of cases of invasive disease. Acapsular meningococci are commonly isolated from the nasopharynx in studies of carriage; the lack of capsule often is a result of phase variation of capsule expression, but as many as 16% of isolates lack the genes for capsule synthesis and assembly. These "capsule-null" meningococci and those that express capsules other than A, B, C, X, Y, and W are only rarely associated with invasive disease and are most commonly identified in the nasopharynx of asymptomatic carriers.

Beneath the capsule, meningococci are surrounded by an outer phospholipid membrane containing lipopolysaccharide (LPS, endotoxin) and multiple outer-membrane proteins (Figs. 180-1 and 180-2). Antigenic variability in porins expressed in the outer membrane defines the serotype (PorB) and serosubtype (PorA) of the organism, and structural differences in LPS determine the immunotype. Serologic methods for typing of meningococci are restricted by the limited availability of serologic reagents that can distinguish among the organisms' highly variable surface proteins. Where available, high-throughput antigen gene sequencing has superseded serology for meningococcal typing. A large database of antigen gene sequences for the outer-membrane proteins PorA, PorB, FetA, Opa, and factor H–binding protein is available online (*www.neisseria.org*). The number of specialized iron-regulated proteins found in the meningococcal outer membrane (e.g., FetA and transferrin-binding proteins) highlights the organisms' dependence on iron from human sources. A thin peptidoglycan cell wall separates the outer membrane from the cytoplasmic membrane.

The structure of meningococcal populations involved in local and global spread has been studied with multilocus enzyme electrophoresis (MLEE), which characterizes isolates according to differences in the electrophoretic mobility of cytoplasmic enzymes. However, this technique has mostly been replaced by multilocus sequence typing (MLST), in which meningococci are characterized by sequence types assigned on the basis of sequences of internal fragments of seven housekeeping genes. The online MLST database currently includes more than 27,000 meningococcal isolates and 10,500 unique sequence types *(pubmlst.org/neisseria/)*. A limited number of hyperinvasive lineages of *N. meningitidis* have been recognized

TABLE 180-1 STRUCTURE OF THE POLYSACCHARIDE CAPSULE OF COMMON DISEASE-CAUSING MENINGOCOCCI

Meningococcal Serogroup	Chemical Structure of Oligosaccharide	Current Disease Epidemiology
A	2-Acetamido-2-deoxy-D-mannopyranosyl phosphate	Epidemic disease mainly in sub-Saharan Africa; sporadic cases worldwide
B	α-2,8-*N*-acetylneuraminic acid	Sporadic cases worldwide; propensity to cause hyperendemic disease
C	α-2,9-*O*-acetylneuraminic acid	Small outbreaks and sporadic disease
Y	4-*O*-α-D-glucopyranosyl-*N*-acetylneuraminic acid	Sporadic disease and occasional small institutional outbreaks
W	4-*O*-α-D-galactopyranosyl-*N*-acetylneuraminic acid	Sporadic disease; outbreaks of disease associated with mass gatherings; epidemics in sub-Saharan Africa
X	(α1→4) N-acetyl-D-glucosamine-1-phosphate	Sporadic disease and large outbreaks in the meningitis belt of Africa

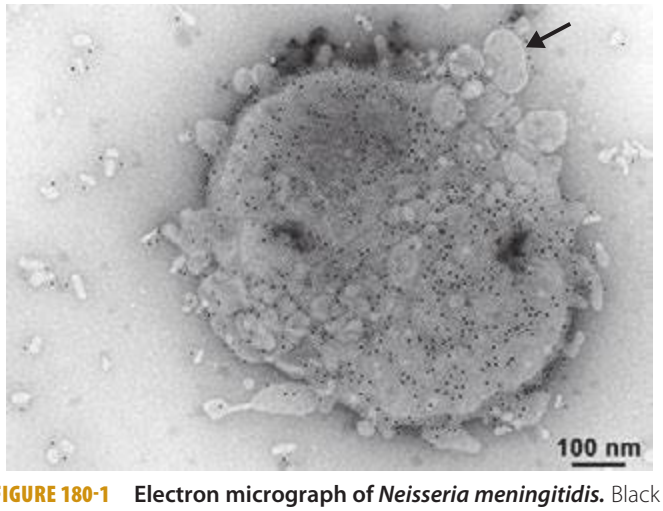

FIGURE 180-1 Electron micrograph of *Neisseria meningitidis*. Black dots are gold-labeled polyclonal antibodies binding surface opacity proteins. Blebs of outer membrane can be seen being released from the bacterial surface (*arrow*). *(Photo courtesy of D. Ferguson, Oxford University.)*