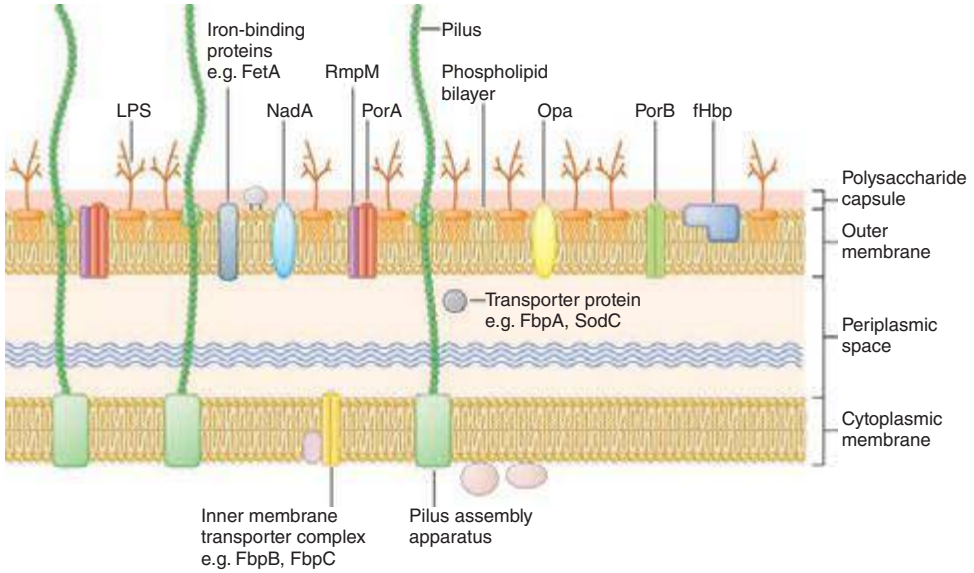

FIGURE 180-2 Cross-section through surface structures of *Neisseria meningitidis*. LPS, lipopolysaccharide. *(Reprinted with permission from M Sadarangani, AJ Pollard: Lancet Infect Dis 10:112, 2010.)*

and are responsible for the majority of cases of invasive meningococcal disease worldwide. The apparent genetic stability of these meningococcal clones over decades and during wide geographic spread indicates that they are well adapted to the nasopharyngeal environment of the host and to efficient transmission. While MLST has become established as the main method of genotyping meningococci in many reference laboratories over the past decade, whole-genome sequencing is set to replace this approach in the decade ahead, with almost 1000 genomes already available in the United Kingdom's national library (*www.meningitis.org/genome-library*).

The group B meningococcal genome is >2 megabases in length and contains 2158 coding regions. Many genes undergo phase variation that makes it possible to control their expression; this capacity is likely to be important in meningococcal adaptation to the host environment and evasion of the immune response. Meningococci can obtain DNA from their environment and can acquire new genes—including the capsular operon—such that *capsule switching* from one serogroup to another can occur.

EPIDEMIOLOGY

Patterns of Disease Up to 500,000 cases of meningococcal disease are thought to occur worldwide each year, and ~10% of the individuals affected die. There are several patterns of disease: epidemic, outbreak (small clusters of cases), hyperendemic, and sporadic or endemic.

Epidemics have continued since the original descriptions of meningococcal disease, especially affecting the sub-Saharan meningitis belt of Africa, where tens to hundreds of thousands of cases (caused mainly by serogroup A but also by serogroups W and X) may be reported over a season and rates may be as high as 1000 cases per 100,000 population. Serogroup A epidemics took place in Europe and North America after the First and Second World Wars, and serogroup A outbreaks have been documented over the past 30 years in New Zealand, China, Nepal, Mongolia, India, Pakistan, Poland, and Russia.

Clusters of cases occur where there is an opportunity for increased transmission—i.e., in (semi-)closed communities such as schools, colleges, universities, military training centers, and refugee camps. Recently, such clusters have been especially strongly linked with a particular clone (sequence type 11) that is mainly associated with the serogroup C or W capsule but was first described in association with serogroup B. Wider and more prolonged community outbreaks (hyperendemic disease) due to single clones of serogroup B meningococci account for ≥10 cases per 100,000. Regions affected in the past decade include the U.S. Pacific Northwest, New Zealand (both islands), and the province of Normandy in France.

Most countries now experience predominantly sporadic cases (0.3–5 cases per 100,000 population), with many different disease-causing clones involved and usually no clear epidemiologic link between one case and another. The disease rate and the distribution of meningococcal strains vary in different regions of the world and also in any one location over time. For example, in the United States, the rate of meningococcal disease fell from 1.2 cases per 100,000 population in 1997 to <0.15 case per 100,000 in 2012 **(Fig. 180-3)**. Meningococcal disease in the United States was previously dominated by serogroups B and C; however, serogroup Y emerged during the 1990s and became more common than serogroup C in 2007. In contrast, rates of disease in England and Wales rose to >5 cases per 100,000 during the 1990s because of an increase in cases caused by the ST11 serogroup C clone. As a result of a mass immunization program against serogroup C in 1999, almost all cases in the United Kingdom are now attributed to serogroup B **(Fig. 180-4)**. Over the last decade, most industrialized nations have seen a general decrease in meningococcal disease; this decrease is linked to immunization against serogroup C meningococci in Europe, Canada, and Australia and to adolescent immunization programs for A, C, Y and W in the United States. However, other factors, including changes in population immunity (probably the explanation for the cyclic nature of meningococcal disease rates) as well as a reduction in smoking and passive exposure to tobacco smoke (driven by bans on smoking in buildings and public spaces) across wealthy countries are likely to have contributed to the fall in cases.

Factors Associated with Disease Risk and Susceptibility The principal determinant of disease susceptibility is age, with the peak incidence in the first year of life **(Fig. 180-5)**. The susceptibility of the very young presumably results from an absence of specific adaptive immunity in combination with very close contact with colonized individuals, including parents. Compared with other age groups, infants appear to be particularly susceptible to serogroup B disease: >30% of serogroup B cases in the United States occur during the first year of life. In the early

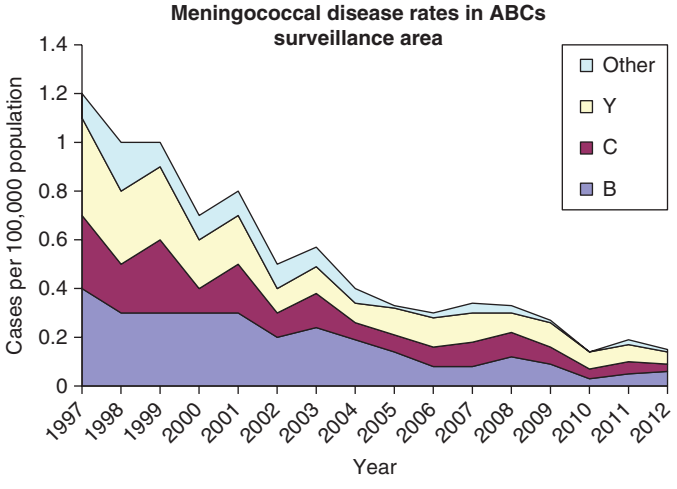

FIGURE 180-3 Meningococcal disease in the United States over time. ABCs, active bacterial cores. *(Adapted from ABC Surveillance data, Centers for Disease Control and Prevention; www.cdc.gov.)*