Chapter 1

Introduction and epidemiology of meningococcal disease

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_Neisseria meningitidis_

_Neisseria meningitidis_, the meningococcus, is a Gram-negative diplococcal bacterium that is only found naturally in humans. The meningococcus is part of the normal microbiota of the human nasopharynx and is commonly carried in healthy individuals (Chapter 2). In rare cases systemic invasion occurs, which can lead to meningitis and/or septicemia. Other clinical manifestations of meningococcal infection include pneumonia, urethritis, conjunctivitis, septic arthritis, and pericarditis (Chapter 5).

The meningococcus was first described as a cause of meningitis in 1887 by Weichselbaum [1], a Viennese doctor, although a striking clinical account of an outbreak of cerebrospinal fever in Geneva was provided by Vieusseux in 1805 [2]. Today, the meningococcus is an important cause of serious bacterial infections in most regions of the world.

There are twelve meningococcal capsular groups, defined on the basis of unique capsular polysaccharides, which vary in their biochemical composition [3]. Six of these groups (A, B, C, W, X, and Y) are responsible for nearly all disease. The capsule serves as a major virulence factor and capsular polysaccharides have been utilized as vaccine antigens (Chapter 7). The meningococcus can be characterized in a variety of other ways and molecular techniques are increasingly used in place of...
traditional serological methods. Subtypes are defined by variation in the two variable regions (VR1 and VR2) of the class 1 outer membrane protein (PorA) [4]. Another immunogenic outer membrane protein used as a molecular marker (though historically not characterized using serological methods) is the iron-regulated FetA protein.

Multilocus sequence typing (MLST) is used to characterize seven ‘housekeeping’ genes and determine the sequence type (ST), which can be grouped into clonal complexes. Housekeeping genes are used because they are generally not under selective pressure for rapid change and therefore can be used to assess the genetic lineage of meningococci. The European recommendation for molecular typing of meningococci takes the form [5]:
1. capsular group;
2. PorA type;
3. FetA type; and
4. sequence type (clonal complex), for example B: 1.19,15: F5-1: ST33 (cc32).

Antigens employed in the new generation of vaccines designed to prevent group B disease will also become important targets for typing, including factor H binding protein (fHbp) (Chapter 7). Recently, whole genome sequencing has become increasingly used for molecular characterization of *N. meningitidis*, including antigen gene typing, determination of ST, and phylogenetic analyses.

**Disease surveillance**

The ideal surveillance for meningococcal disease is an active, population-based system in which clinical cases are followed up for comprehensive laboratory testing and strain characterization. Few countries reach this standard and may use passive rather than active surveillance, syndromic surveillance rather than laboratory confirmation, sentinel rather than whole population coverage, or some combination of the above. As such, caution is required in interpreting data from different jurisdictions and the true global incidence of meningococcal disease is unknown [6]. The European Union case definition is shown in Box 1.1 [7].