Chapter 8: Meningococcal Disease

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I. Disease Description

Meningococcal disease is a serious and potentially life-threatening infection caused by the bacterium *Neisseria meningitidis*. *N. meningitidis* can be classified into 12 serogroups based on its capsular polysaccharide; serogroups A, B, C, W, X, and Y are the primary causes of meningococcal disease worldwide.

Signs and symptoms of meningococcal disease include sudden onset of high fever, neck stiffness, confusion, nausea, vomiting, lethargy, and/or petechial or purpuric rash. Without prompt and appropriate treatment, the infection can progress rapidly and result in death.

II. Background

Epidemiology

The incidence of meningococcal disease has been steadily declining in the United States since the late 1990s. During 2015–2017, the incidence of meningococcal disease was 0.11–0.12 cases per 100,000 population in the United States, with 350 cases reported in 2017. Meningococcal disease incidence varies by age and is highest in infants less than 1 year of age, particularly during the first 6 months of life.[1,2]

Serogroup B currently accounts for about 40% of cases in the United States, with serogroups C, W and Y, as well as infections due to nongroupable (non-encapsulate) meningococci each causing a smaller proportion of cases overall.[1,3] The relative distribution of serogroups varies by age; serogroup B causes about 60% of cases in children and young adults <25 years of age, while serogroups C, W and Y cause about 65% of all cases of meningococcal disease among persons ≥25 years of age.[3] Although serogroup A was responsible for most large meningococcal disease outbreaks during the first half of the twentieth century, serogroup A disease is now exceedingly rare in the United States.[4–6] During 2013–2018, 10 outbreaks of serogroup B meningococcal disease occurred on college campuses, resulting in 39 cases and 2 deaths (range, 2–9 cases per outbreak.[7] In addition, outbreaks of serogroup C meningococcal disease have been reported among men who have sex with men (MSM) in major metropolitan areas.[8,9]

Meningococcal disease incidence historically had a cyclical pattern, with peaks in incidence occurring every 7–10 years. However, the declining incidence of meningococcal disease observed over the last 20 years does not reflect the previously observed cyclical periodicity of disease. Although it occurs year-round, meningococcal disease has a seasonal pattern with peak incidence in later winter and early spring.[1, 10]

Natural history

Humans are the only natural reservoir for *N. meningitidis*. Meningococci are gram-negative, aerobic diplococci that can attach to the surface of mucosal cells of the nasopharynx. In the nasopharynx, the bacteria multiply, bind to specific receptors, and are taken up by epithelial cells, which transport the meningococci across the mucosal epithelium. In a small number of persons, the bacteria penetrate the mucosa and gain access to the bloodstream, resulting in systemic disease.

Meningococcal bacteria can be transmitted from person-to-person, by asymptomatic carriers or persons with invasive disease, through direct contact with large droplet respiratory secretions or saliva.

Carriage

Asymptomatic nasopharyngeal carriage of *N. meningitidis* is common; 5%–10% of the population are asymptomatic nasopharyngeal carriers of *N. meningitidis* at any given time.[11] The frequency of carriage, like that of invasive disease, varies by age. In the Americas and western Europe adolescents and young adults have the highest rates of meningococcal carriage.[11] Although asymptomatic carriage of both pathogenic and nonpathogenic *N. meningitidis* is common, few carriers develop invasive disease. For the majority of people, carriage is an immunizing process that results in a systemic, serogroup-specific protective antibody response.[10]

Risk factors

Risk factors for meningococcal disease include organism, host, and environmental factors. Persons with anatomic or functional asplenia, persistent complement component deficiencies (e.g., C3, C5–C9, properdin, or factor D), human immunodeficiency virus (HIV), and those who are receiving complement inhibitors such as eculizumab (Soliris®, Alexion Pharmaceuticals or ravulizumab (Ultomiris, Alexion Pharmaceuticals) are at increased risk for meningococcal disease.[3,12]

Crowded living conditions can facilitate respiratory droplet transmission of meningococci. College freshmen residing in residence halls have been shown to be at greater risk of acquiring meningococcal disease than college students not living in residence halls (CDC unpublished data,[13]). Active or passive smoking and recent upper respiratory tract infections also increase risk of disease.[14] Historically, black individuals and persons of low socioeconomic status have been found to be at higher risk for meningococcal disease than white individuals and persons of high socioeconomic status; however, these differences have diminished in recent years.[1,15] Race and socioeconomic status are likely markers for differences in risk factors such as household crowding, or exposure to tobacco smoke.

Meningococcal disease is more commonly diagnosed among infants, adolescents, and young adults 16–23 years of age, and adults older than 65 years compared to other age groups. Infants less than 1 year of age have the highest incidence of meningococcal disease; the majority of cases in infants occur during the first 6 months of life.[1,2]

Those who have close contact with patients, such as household members, are at substantially increased risk for acquiring carriage and disease.[16] Rates of secondary disease are also elevated among daycare and preschool contacts of patients with meningococcal disease.[17]

Clinical characteristics

Diagnosing meningococcal disease is often challenging because its initial clinical manifestations are similar to more common but less serious illnesses. However, meningococcal disease can progress rapidly and so a rapid, accurate diagnosis is critical.

The common clinical presentations of meningococcal disease include meningitis, bacteremia, and bacteremic pneumonia. Meningitis is observed in approximately 50% of invasive cases and is characterized by abrupt onset of fever, headache, and stiff neck.[1] These clinical features may be accompanied by nausea, vomiting, photophobia, and altered mental status. In infants, symptoms may have a slower onset, signs may be nonspecific, and neck stiffness may not be present. Approximately 30% of meningococcal disease cases present as bacteremia without meningitis.[1] A portion of these cases will present as meningococcemia, the most severe manifestation of meningococcal bacteremia.[15] Signs of meningococcemia include sudden onset of fever and a characteristic petechial or purpuric rash, which may progress to purpura fulminans. The clinical course can include hypotension, acute adrenal hemorrhage, multiorgan failure, shock, and death. Patients with severe meningococcemia often respond poorly to treatment, and death can occur within hours of onset. Bacteremic pneumonia occurs in approximately 15% of cases and occurs most frequently in older persons.[1] Diagnosing meningococcal pneumonia is difficult because isolation of the organism from sputum does not distinguish persons who are carriers from those with pneumonia caused by the organism.[18]

Less common manifestations of meningococcal disease include myocarditis, endocarditis or pericarditis, arthritis, or non-invasive infections such as conjunctivitis or urethritis. Non-invasive meningococcal infections are not reportable; therefore, the incidence of these infections is not known. Descriptions of

the epidemiology and risk factors for meningococcal disease throughout this chapter refer exclusively to invasive, meningococcal disease cases.

The use of antibiotics has dramatically reduced mortality due to meningococcal disease, but even with prompt and appropriate antimicrobial treatment the case-fatality ratio remains 10%–15%, and may be as high as 40% among patients with meningococcemia.[10] Of those who survive invasive disease, 10%–20% experience sequelae, including limb loss from gangrene, extensive skin scarring, neurosensory hearing loss, mild to moderate cognitive defects, or seizure disorders.

Treatment

Because of the risks of severe morbidity and death, effective antibiotics should be administered promptly to patients suspected of having meningococcal disease. Multiple antimicrobial agents, including penicillins, are effective against *N. meningitidis*.Empirical therapy for suspected meningococcal disease should include an extended-spectrum cephalosporin, such as cefotaxime or ceftriaxone.Once the microbiologic diagnosis is established, definitive treatment with penicillin G, ampicillin, or an extended-spectrum cephalosporin (cefotaxime or ceftriaxone) is recommended.[19] Ceftriaxone clears nasopharyngeal carriage effectively after 1 dose; if antimicrobial agents other than ceftriaxone or cefotaxime are used for treatment of meningococcal disease, eradication of nasopharyngeal carriage with rifampin (4 doses over 2 days) or single doses of ciprofloxacin or ceftriaxone are recommended prior to discharge from the hospital.

Chemoprophylaxis

Close contacts of persons with meningococcal disease should receive antimicrobial chemoprophylaxis, regardless of immunization status, because they are at increased risk for infection.[19] Close contacts include: 1) household members, 2) childcare center contacts, and 3) anyone else directly exposed to an infected patient's oral secretions (e.g., via kissing, mouth-to-mouth resuscitation, endotracheal intubation or endotracheal tube management) in the 7 days before symptom onset. Health care personnel should receive chemoprophylaxis if they were managing an airway or exposed to respiratory secretions of a patent with meningococcal disease.

Chemoprophylaxis is not recommended for close contacts of patients with evidence of *N. meningitidis* only in non-sterile sites such as an oropharyngeal swab, endotracheal secretions, or conjunctival swab. Furthermore, there is no indication to treat persons who are asymptomatic nasopharyngeal carriers but who have no known close contact with a meningococcal disease patient.

Risk of secondary disease among close contacts is highest during the first few days after the onset of disease, which requires that chemoprophylaxis be administered as soon as possible. If given more than 14 days after the onset of disease, chemoprophylaxis is probably of limited or no benefit.[19] Oropharyngeal or nasopharyngeal cultures are not useful in determining the need for chemoprophylaxis and may unnecessarily delay the use of effective preventive measures.

Rifampin, ceftriaxone, and ciprofloxacin are 90%–95% effective in reducing nasopharyngeal carriage of *N. meningitidis* and are all acceptable antimicrobial agents for chemoprophylaxis (Table 1). Although azithromycin is not recommended for use as a first-line chemoprophylaxis agent, azithromycin has been recommended for chemoprophylaxis in the rare circumstance of sustained ciprofloxacin-resistance in a community. Use of azithromycin as a single oral dose has been shown to be effective for eradication of nasopharyngeal carriage and can be used on a limited basis where ciprofloxacin resistance has been detected.[20]

Table 1. Recommended chemoprophylaxis regimens for high-risk contacts of persons with invasive meningococcal disease

Drug	Age	Dose	Duration	Efficacy (%)	Cautions
Rifampin	<1 month	5 mg/kg, orally, every 12 hours	2 days		Discussion with an expert for infants <1 month
	≥1 month	10 mg/kg (maximum 600 mg), orally, every 12 hours	2 days	90–95	Can interfere with efficacy of oral contraceptives and some seizure prevention and anticoagulant medications; may stain soft contact lenses. Not recommended for pregnant women.
Ceftriaxone	<15 years	125 mg, intramuscularly	Single dose	90–95	To decrease pain at injection site, dilute with 1% lidocaine.
	≥15 years	250 mg, intramuscularly	Single dose	90–95	
Ciprofloxacin[a]	≥1 month	20mg/kg (maximum 500 mg), orally	Single dose	90–95	Not recommended for pregnant women.
Azithromycin		10 mg/kg (maximum 500 mg)	Single dose	90	Not recommended routinely. Equivalent to rifampin for eradication of *N.meningitidis* from nasopharynx in one study

Source: American Academy of Pediatrics. Meningococcal Infections. In: Kimberly DW, Brady MT, Jackson MA, Long SS, editors. Red Book: 2018–2021 Report of the Committee on Infectious Diseases, 31st ed.: American Academy of Pediatrics; 2018:550-61.

[a]*Use only if fluoroquinolone-resistant strains of* N meningitidis *have not been identified in the community.*

III. Importance of Rapid Case Identification

Immediate recognition and treatment of meningococcal disease is critical. Persons with suspected meningococcal disease should be treated promptly without waiting for laboratory confirmation. All suspected, probable, and confirmed meningococcal disease cases should be promptly reported to the appropriate health department to ensure that the proper prevention and control measures can be implemented.

IV. Importance of Surveillance

High-quality epidemiologic surveillance data along with collection of invasive meningococcal isolates from a broad and representative population are crucial to inform prevention and control strategies for meningococcal disease in the United States. These data are used to monitor disease trends, characterize risk factors for disease and severe outcomes of disease, make vaccine policy recommendations, monitor vaccine impact, and guide development of new vaccines.

V. Disease Reduction Goals

The *Healthy People 2020* goal is to reduce incidence of meningococcal disease to 0.3 cases/100,000 population.

VI. Case Definition

The following case definition has been approved by the Council of State and Territorial Epidemiologists (CSTE) and was published in 2014.[21]

Confirmed case:

- Detection of *N. meningitidis*-specific nucleic acid in a specimen obtained from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF]), using a validated polymerase chain reaction (PCR) assay; or
- Isolation of *N. meningitidis*
  - from a normally sterile body site (e.g., blood or CSF, or less commonly, synovial, pleural, or pericardial fluid); or
  - from purpuric lesions.

Probable case:

- Detection of *N. meningitidis* antigen
  - in formalin-fixed tissue by immunohistochemistry (IHC); or
  - in CSF by latex agglutination

Suspected case:

- Clinical purpura fulminans in the absence of a positive blood culture; or
- Gram-negative diplococci, not yet identified, isolated from a normally sterile body site (e.g., blood or CSF)

VII. Laboratory Testing

Rapid and reliable laboratory results are critical for prompt diagnosis and implementation of appropriate prevention and control measures. Refer to the CDC website (https://www.cdc.gov/meningococcal/laboratory.html) and Chapter 22 for specific information on specimen collection, identifying *N. meningitidis*, and determining *N. meningitidis* serogroups.

Specimen collection

Specimen collection and shipping are important steps in obtaining laboratory diagnosis or confirmation for vaccine preventable diseases. Guidelines have been published for specimen collection and handling for microbiologic agents.[22] Information is also available by using CDC laboratories as support for reference and disease surveillance;[23,24] this includes

- a central website (https://www.cdc.gov/laboratory/specimen-submission/index.html) for requesting lab testing, which includes the CDC Infectious Diseases Laboratories Test Directory, that not only contains a list of orderable tests for that institution but also detailed information on appropriate specimen types, collection methods, specimen volume, and points of contacts.
  - Meningococcal disease diagnostic testing: refer to test order CDC-10219 and use the 50.34 form Cdc-pdf [2 pages, 2.80 MB] required for submitting specimens to CDC or see Appendix 23, Form # CDC 50.34.
  - Surveillance only testing: refer to test order CDC-10220 for shipping instructions and requirements.
- Information on general requirements for shipment of etiologic agents (Appendix 24, https://www.cdc.gov/vaccines/pubs/surv-manual/appx/appendix24-etiologic-agent.pdf)—although written to guide specimen submission to CDC, this information may be applicable to submission of specimens to other laboratories; and
  - Note that meningococcal isolates/specimens are classified as a category B infectious substance.

VIII. Reporting and Case Notification

Case reporting within a jurisdiction

Each state and territory (jurisdiction) has regulations and laws governing the reporting of diseases and conditions of public health importance.[25] These regulations and laws list the diseases that are to be reported, and describe those persons or institutions responsible for reporting, such as health care providers, hospitals, laboratories, schools, daycare and childcare facilities, and other institutions. Detailed information on reportable conditions in each jurisdiction is available through CSTE.[26]

The Meningococcal Disease Surveillance Worksheet is included in Appendix 9 to serve as a guide for data collection during investigation of reported cases.

Case notification to CDC

Notification for suspect, probable, and confirmed cases of meningococcal disease should be sent to CDC using the event code 10150 in the National Notifiable Disease Surveillance System (NNDSS).[27] Case information should be reported through the NNDSS via the National Electronic Telecommunications System for Surveillance (NETSS), or the National Electronic Disease Surveillance System (NEDSS) within 14 days of the initial report to the jurisdiction or local health department. The jurisdiction in which the patient usually resides at the time of diagnosis should submit the case notification to CDC. The Meningococcal Disease Surveillance Worksheet is included in Appendix 9 to serve as a guide for data collection to be included in case investigations and case notification to CDC. Of note, for college students this typically means that the state in which the student attends school is responsible for reporting the case, not necessarily the state of the student's legal residence.[28] Case notifications should not be delayed because of incomplete information or lack of confirmation; data can be updated electronically as more information becomes available.

IX. Vaccination

For specific information about meningococcal vaccination, refer to The Pink Book [https://www.cdc.gov/vaccines/pubs/pinkbook/index.html], which provides general recommendations, including vaccine use and scheduling, immunization strategies for providers, vaccine content, adverse events and reactions, vaccine storage and handling, and contraindications and precautions.

X. Enhancing Surveillance

Active population-based and laboratory-based surveillance

CDC coordinates active, population- and laboratory-based surveillance for invasive meningococcal disease as part of the Active Bacterial Core surveillance (ABCs) system, through the Emerging Infections Program (EIP). ABCs operates in 10 sites that collect data from all patients from whom *N. meningitidis* was isolated or detected by PCR from a normally sterile body site. This surveillance program allows for collection of detailed information on meningococcal cases, including extensive information on underlying medical conditions. ABCs data have been used to track meningococcal disease trends over time; the ABCs web site is https://www.cdc.gov/abcs/index.html.

In addition, CDC has implemented enhanced surveillance for meningococcal disease through the Epidemiology and Laboratory Capacity (ELC) Vaccine Preventable Diseases (VPD) surveillance project. Through this initiative, data on key variables for monitoring meningococcal disease epidemiology and vaccine policy decisions, along with meningococcal isolates, are routinely collected from most state and territorial (jurisdiction) health departments. Reports on the enhanced meningococcal surveillance data are published online annually.

Streamlining reporting using electronic methods

Although many surveillance systems still rely on paper and pencil for data collection, use of data from sources such as electronic medical records, electronic case reporting,[29–35] and clinical laboratory information systems (LIMS) can significantly improve reporting speed, enhance data quality, and reduce workload.

XI. Case Investigation

All reports of suspected meningococcal disease should be investigated immediately. A critical component of case investigation is ensuring that all close contacts (see definitions) receive appropriate chemoprophylaxis as soon as possible to eradicate nasopharyngeal carriage of meningococci and prevent secondary disease (see Chemoprophylaxis, above). CDC is available to assist with epidemiologic and laboratory investigations during outbreaks.

XII. Outbreaks

Approximately 95% of meningococcal disease cases in the United States are sporadic; the other 5% are associated with outbreaks.[36] Guidance on the control of meningococcal disease outbreaks can be found on the CDC Meningococcal Outbreaks web page (https://www.cdc.gov/meningococcal/outbreaks/index.html).

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