Neisseria meningitidis has recently emerged as the leading cause of meningitis in children and young adults in the United States (Centers for Disease Control and Prevention [CDC], 2000). The average annual rate of invasive disease such as meningitis, meningococcemia, and arthritis is approximately 1.1 cases per 100,000 population, or 2600 cases per year (Estabrook, 2000). Approximately 20% of patients with meningococcemia die, and approximately 5% of patients with meningococcemia with meningococcal meningitis die (Edwards & Baker, 1999). Because of widespread use of an effective vaccine, invasive disease resulting from Haemophilus influenzae B is now exceedingly rare. Vaccines for Streptococcus pneumoniae also are available with the hope that the incidence of disease caused by susceptible strains will show a similar sharp decline. Thus, the relative frequency of disease caused by N meningitidis is likely to increase.

Highly publicized outbreaks of diseases related to N meningitidis in communities and on college campuses have resulted in much public confusion about how best to prevent and treat disease related to this organism. The purpose of this article is to discuss the epidemiology, primary and secondary prevention, diagnosis, and acute management of menin-
ginitis and meningococcemia caused by
*N meningitidis*.

**EPIDEMIOLOGY**

The *N meningitidis* organism is transmitted by means of respiratory droplets from carriers. Humans are the only known natural reservoir. Carriage rates vary from 95% during group A epidemics to 50% among military recruits to about 10% among the randomly sampled population (Hughes & Lepow, 1999). The carrier rate is typically higher where crowding occurs, such as on military installations, in prisons, at sporting events, and in dormitories (Hughes & Lepow, 1999). Increased carriage rates are also associated with smoking, upper respiratory tract infections, influenza, and tonsillectomy (Hughes & Lepow, 1999).

In the United States, about 90% of meningococcal disease is caused by serogroups B and C. Group B disease is more often sporadic, whereas group A and C disease is more likely to be epidemic (Hughes & Lepow, 1999). The highest attack rates occur in the winter or early spring (Estabrook, 2000). Although rare but well-publicized outbreaks of meningococcal disease occur on college campuses, about 46% of cases occur in children younger than 2 years, with another 25% of cases occurring in patients older than 30 years (Estabrook, 2000; Hughes & Lepow, 1999). Fifty-eight percent of patients who have invasive meningococcal disease present with meningitis (Estabrook, 2000).

**Definition of a Case**

Periodically the media report that “a case of meningitis” has been found in a community. This announcement is rarely specific enough to determine either the offending agent or the degree of generalized health concern. Careful case definitions are important to identify others who are at risk for the condition and to allay public concern. The definition of a **confirmed** invasive meningococcal disease includes isolation of *N meningitidis* from blood, cerebral spinal fluid, or other typically sterile fluid. **Presumptive** cases are those in which gram-negative diplococci are identified in any typically sterile body fluid. **Probable** cases are identified in the setting of a clinical illness that is consistent with meningococcal disease with positive results of antigen tests but without a positive culture from body fluid normally found sterile (American Academy of Pediatrics [AAP], 1996). A patient with confirmed, presumptive or probable meningococcal disease on the basis of these definitions is considered an “index case.”

**Definition of Exposure**

The media attention surrounding a single case of meningococcal disease in a community often results in scores of telephone calls to health care providers by concerned patients and families who are questioning their risk of contracting the disease. Thus, identifying children who are at high risk for the disease and who require antimicrobial prophylaxis is imperative.

Patients at high risk for contracting meningococcal disease include household contacts (especially young children), persons in day care or nursery school who have been exposed to an index case within 7 days, persons with direct exposure to the secretions of an index case (eg, through kissing, sharing toothbrushes, or sharing eating utensils), or persons who have been frequently exposed to an index patient by eating or sleeping with the patient. Also included in the high-risk category are health care professionals who have been exposed through mouth-to-mouth resuscitation or unprotected contact during endotracheal intubation within 7 days before the onset of the illness (AAP, 1996). Nasopharyngeal cultures are of no use in determining who should receive prophylaxis (AAP, 2000).

The vast majority of exposures are considered low-risk exposures. Low-risk exposures include (a) casual contact with an index patient (without direct exposure to the index patient’s oral secretions), (b) exposure to a high-risk contact of the index patient without direct contact with the index patient himself or herself, and (c) exposure to the index patient by medical personnel who have not had direct exposure to the index patient’s oral secretions.

**PRESENTATION/ACUTE MANAGEMENT**

**Case Presentation**

A 15-year-old white girl who lives in a large suburban community near Houston, Texas, complained to her mother about a subjective fever. She took acetaminophen and went to sleep. The next morning her mother found her lying on the floor of her bedroom; she was unresponsive. She apparently had been vomiting and a purplish rash had developed on her upper extremities. Paramedics took her to a nearby hospital, where she was noted to have a temperature of 105°F and to be hypotensive. Normal saline solution boluses were administered, along with dopamine, norepinephrine, vancomycin, ceftriaxone, and penicillin. Further extension of her rash was noted. She was transported immediately via Life-Flight helicopter to Memorial Hermann Children’s Hospital and was admitted directly to the pediatric ICU. Upon admission she was noted to have purpura fulminans, hypotension, disseminated intravascular coagulopathy, and respiratory failure. The patient was intubated emergently, and antibiotics and pressors continued to be administered. The presumptive diagnosis of meningococcemia was made based on her presentation, but it was never proven by culture. Her hospital course was complicated by hypertension, gram-negative sepsis, fungemia, and acute renal tubular necrosis requiring dialysis. Necrotic tissue developed in her upper and lower extremities, and although grafting was attempted, she ultimately required bilateral below-the-knee amputations and bilateral upper extremity amputations. In addition, she required a diverting colostomy for wound healing and a gastrostomy tube for nutrition. The length of her initial hospitalization was 90 days. She continues to receive rehabilitation services as she recovers from the complications of her disease.
This case illustrates a complicated course of meningococcal disease. The sudden and severe presentation, coupled with the possible long-term sequelae, is frightening to patients, families, and providers and contributes to much misunderstanding in the diagnosis, treatment, and prevention of this disease.

Acute Diagnosis

Invasive meningococcal disease (meningococcemia, meningitis, or both) can present with the classic findings of abrupt onset of flulike symptoms including fever, chills, malaise, vomiting, prostration, drowsiness, disorientation, hallucinations, convulsions, and an urticarial, maculopapular, or petechial rash. Rapid progression over several hours leads to purpura, dissemination, hallucinations, convulsions, and an urticarial, maculopapular, or petechial rash. Acute onset of flulike symptoms including fever, chills, malaise, vomiting, prostration, drowsiness, disorientation, hallucinations, convulsions, and an urticarial, maculopapular, or petechial rash.

Initial Management

Aggressive management in an ICU optimizes outcomes for patients presenting with presumed meningococcemia. The airway must be main-

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ingococcemia may be one of several diagnoses entertained by the practitioner faced with a gravely ill patient with fever, mental status changes, and a petechial rash (Box). Therefore, empiric therapy for *N meningitidis* with ceftriaxone (for pneumococcus and *H influenzae*) and vancomycin (for resistant streptococcal strains) may be prudent while awaiting results of urine or CSF latex agglutination, CSF gram stain, and blood culture testing (AAP , 2000; Estabrook, 2000). Patients with *N meningitidis* who are allergic to penicillin may receive chloramphenicol. Tetracycline for patients older than 8 years may be considered if Rocky Mountain spotted fever is in the differential diagnosis based on travel history or region of residence (AAP, 2000).

**BOX** Partial differential diagnosis for meningococcemia

**Infectious**

- Viral meningitis
- Echovirus (types 6, 9, 16)
- Coxsackievirus (A2, A4, A9, and A16)
- Rubella
- Rubeola
- Atypical rubeola

**Nonviral infectious agents**

- Bacterial meningitis (pneumococcal, *H influenzae*)
- Mycoplasma
- Leptospirosis
- Syphilis
- Septicemia resulting from gram-negative organisms or overwhelming septicemia resulting from gram-positive organisms
- Bacterial endocarditis
- Epidemic typhus
- Rocky Mountain spotted fever
- Ehrlichiosis
- Scarlet fever

**Miscellaneous**

- Encephalopathies (variety of causes)
- Acute hemorrhagic encephalitis
- Serum sickness
- Henoch-Schonlein purpura
- Various poisons
- Erythema multiforme or erythema nodosum resulting from a variety of causes
- Immune thrombocytopenic purpura
- Kawasaki disease
- Systemic lupus erythematosus and other febrile mucocutaneous diseases

Data from AAP, 2000; Estabrook, 2000.

Patients known to have infection caused by *N meningitidis* are treated with a recommended dose of 250,000 IU of penicillin intravenously per dose given every 6 hours for 7 days.

**PROPHYLAXIS AND PREVENTION**

**Medications for Prophylaxis**

After an index case has been identified, prophylaxis of high-risk contacts is indicated. A variety of medications with variable efficacies are available (Table). The age of the patient and the route and ease of administration of the medication play a role in determining which medication is chosen. Because secondary cases of meningococcemia can occur weeks after the index case has been identified, meningococcal vaccine can be considered as part of the prophylaxis if the causative strain is in the vaccine.

The goal of antimicrobial prophylaxis is the eradication of any nasopharyngeal carriage of *N meningitidis* in contacts of the index case. The medications listed in the Table for chemoprophylaxis penetrate well into the secretions of the nasopharynx and thus eliminate colonization. By eliminating the organism in close contacts of the case, the spread of the disease is interrupted. The antibiotics commonly used to treat
meningococcal disease such as penicillin often fail to eliminate nasopharyngeal carriage; therefore, some experts suggest treating the index case with a medication that will eliminate the nasopharynx colonization (Table) (Salzman, 1996).

**Vaccine Controversy**

Highly publicized cases of meningitis caused by *N meningitidis* have focused attention on appropriate use of the meningococcal vaccine, especially on college campuses. Unfortunately, headlines such as “Campus meningitis preventable for $65” (Manning, 1999a) and “Freshmen face highest risk of deadly bacterial strain” (Manning, 1999b) do not fully explain the public health policy dilemma. A more complete understanding of the uses of the vaccine is indicated.

The meningococcal vaccine, approved for use in children 2 years of age and older, is a quadrivalent product effective against *N meningitidis* groups A, C, Y, and W-135; vaccine against group B disease is not available. According to the AAP *Red Book*, the various components of the vaccine are immunogenic at various ages (AAP, 2000). For instance, group A meningococcal vaccine is reported to be immunogenic in children 3 months of age and older, but adult levels of immunogenicity are not achieved until ages 4 or 5 years; when the vaccine is given in response to control epidemics of group A disease, response to the other meningococcal group polysaccharides is poor. Groups Y, W-135, and C induce antibody response after 2 years of age. To further complicate the issue, the need and timing of reimmunization are not fully known (AAP, 2000). Fortunately, adverse effects of the vaccine are unusual and mild, including erythema at the injection site for 1 to 2 days.

Routine administration of the meningococcal vaccine is not recommend-

### TABLE Chemoprophylaxis medications for high-risk contacts and index cases

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Duration</th>
<th>Efficacy</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin</td>
<td>≤1 mo old</td>
<td>5 mg/kg every 12 h, orally</td>
<td>2 d</td>
<td>72%-90%</td>
</tr>
<tr>
<td></td>
<td>&gt;1 mo old</td>
<td>10 mg/kg (max 600 mg) every 12 h, orally</td>
<td></td>
<td>Orange urine; staining of contact lenses possible; can interfere with oral contraceptives, seizure medications, and anticoagulants; avoid in pregnancy</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≤12 y old</td>
<td>125 mg, intramuscularly</td>
<td>One dose</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>&gt;12 y old</td>
<td>250 mg, intramuscularly</td>
<td></td>
<td>Mixed with 1% lidocaine to decrease injection pain</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>≥18 y</td>
<td>500 mg, orally</td>
<td>One dose</td>
<td>90%-95%</td>
</tr>
</tbody>
</table>


Adverse effects of the vaccine are unusual and mild, including erythema at the injection site for 1 to 2 days.

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The high-risk group are patients with functional or anatomic asplenia and patients with immune abnormalities such as alterations in their terminal complement component or properdin deficiencies. Travelers to endemic areas of the world should consider vaccination.

For college-aged children, the AAP recommends that health care providers “...should inform and educate students and parents about the risk of meningococcal disease and the existence of a safe and effective vaccine and immunize students at their request or if educational institutions require it for admission” (AAP, 2000, p. 401). The American College Health Association and the Advisory Committee on Immunization Practices have similar recommendations that advise college freshmen of an increased risk of meningococcal disease and the availability of an effective vaccine (CDC, 2000).

When an outbreak or cluster of invasive meningococcal cases in a defined population is recognized, such as in a particular school or community, vaccination may be recommended by local or state public health authorities if the strain causing the problem belongs to one of the vaccine-preventable serogroups; in general, a rate of more than 10 occurrences per 100,000 population occurring within a 3-month will trigger prophylactic vaccination. The state and local health authorities will delineate the exact population
subset selected to receive the vaccine. Chemoprophylaxis for close contacts may also be indicated as previously described; vaccination in these cases can serve as an adjunct to provide longer-lasting protection (AAP, 1996; CDC, 1997).

CLINICAL IMPLICATIONS

Primary care providers have a responsibility to be aware of the presenting signs and symptoms of disease caused by *N meningitidis* and to rapidly triage patients suspected of having one of these conditions to the nearest emergency department. Health care providers are uniquely situated to provide accurate information during school or community outbreaks of disease caused by *N meningitidis* and have the ability to help allay public anxiety that is invariably seen during such outbreaks. Practitioners should be familiar with case definitions of exposure to disease caused by *N meningitidis* so that appropriate postexposure prophylaxis can be administered. Finally, primary care providers will be a valuable resource to parents and patients as they weigh the pros and cons of routine vaccination for these bacteria.

SUMMARY

The rapid onset and potentially devastating consequences of disease caused by *N meningitidis* are frightening to patients, parents, and health care providers. Rapid identification of potential cases, knowledge of basic resuscitation measures, and rapid transfer to a facility with the capacity to adequately manage these patients are necessary to maximize the outcome.

REFERENCES


