Prolonged University Outbreak of Meningococcal Disease Associated With a Serogroup B Strain Rarely Seen in the United States

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**Background.** College students living in residential halls are at increased risk of meningococcal disease. Unlike that for serogroups prevented by quadrivalent meningococcal vaccines, public health response to outbreaks of serogroup B meningococcal disease is limited by lack of a US licensed vaccine.

**Methods.** In March 2010, we investigated a prolonged outbreak of serogroup B disease associated with a university. In addition to case ascertainment, molecular typing of isolates was performed to characterize the outbreak. We conducted a matched case-control study to examine risk factors for serogroup B disease. Five controls per case, matched by college year, were randomly selected. Participants completed a risk factor questionnaire. Data were analyzed using conditional logistic regression.

**Results.** Between January 2008 and November 2010, we identified 13 meningococcal disease cases (7 confirmed, 4 probable, and 2 suspected) involving 10 university students and 3 university-linked persons. One student died. Ten cases were determined to be serogroup B. Isolates from 6 confirmed cases had an indistinguishable pulsed-field gel electrophoresis pattern and belonged to sequence type 269, clonal complex 269. Factors significantly associated with disease were Greek society membership (matched odds ratio [mOR], 15.0; \( P = .03 \)), >1 kissing partner (mOR, 13.66; \( P = .03 \)), and attending bars (mOR, 8.06; \( P = .04 \)).

**Conclusions.** The outbreak was associated with a novel serogroup B strain (CC269) and risk factors were indicative of increased social mixing. Control measures were appropriate but limited by lack of vaccine. Understanding serogroup B transmission in college and other settings will help inform use of serogroup B vaccines currently under consideration for licensure.

**Keywords.** meningococcal disease; serogroup B; outbreak; university; risk factors.
and controlled by meningococcal polysaccharide vaccine. Since 2005, MenACWY has been recommended for groups at increased risk, including adolescents and college freshmen living in residential halls [4]. One-third of all meningococcal disease cases and one-quarter of outbreaks are caused by serogroup B, including among young adults aged 18–24 years [1, 5]. As MenACWY vaccination coverage increases on college campuses, the proportion of disease caused by serogroup B may increase in this population. Serogroup B outbreaks remain challenging as no licensed vaccine against serogroup B exists. Risk factors for serogroup B disease among university students have not been evaluated and may be different from those for serogroup C disease. Therefore, understanding serogroup B outbreak dynamics and modifiable risk factors are important for disease control and prevention.

We report an outbreak in Ohio associated with University A, a public university of approximately 21,000 students comprising 17,000 undergraduates. The main campus of University A is located in a town of approximately 22,000 people. Between January 2008 and November 2010, there were 13 reported cases of meningococcal disease among persons associated with the university, of which 10 were serogroup B. Despite appropriate control measures including health promotion and chemoprophylaxis with ciprofloxacin, a serogroup B outbreak at University A continued over 3 academic years, with a fatality in February 2010. An investigation was carried out in March 2010 to characterize the outbreak and conduct a case-control study to identify risk factors for serogroup B disease.

METHODS

Active Case Finding

We defined a university-associated case of meningococcal disease as a University A student or a nonstudent who reported socializing or interacting with University A students (University A–linked case), with onset of illness between January 2008 and November 2010. Following the Council of State and Territorial Epidemiologists definitions [6], cases were classified as follows: confirmed, isolation of Neisseria meningitidis from a normally sterile site; probable, detection in cerebrospinal fluid (CSF) or serum of N. meningitidis nucleic acid by polymerase chain reaction (PCR) or meningococcal antigen by latex agglutination; and suspected, gram-negative diplococci in CSF or serum without further identification. Cases were ascertained from the Ohio Department of Health (ODH) electronic disease reporting system.

Laboratory Investigation

Neisseria meningitidis isolates were identified and characterized using conventional microbiologic methods. Neisseria meningitidis serogroup was determined by slide agglutination at the ODH laboratory and by serogroup-specific real-time PCR in the Meningitis Laboratory at the Centers for Disease Control and Prevention (CDC) [7, 8]. All university-associated isolates were tested for antimicrobial susceptibility using Etest (AB Biodisk, Stockholm, Sweden) [9]. Isolates were characterized using pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) as previously described [10–12]. To better understand the molecular diversity of serogroup B strains circulating in Ohio, the PFGE and MLST data of these university-associated isolates and 11 additional serogroup B isolates collected in 2009–2010 from Ohio patients not associated with the University A outbreak were compared against meningococcal strains held in the CDC’s collection.

Matched Case-Control Study

Probable and confirmed serogroup B meningococcal disease cases were included if they occurred in a full-time student at University A and had an illness onset during the 2008–2009 or 2009–2010 academic years. Five controls per case, matched by academic year at the time of case illness onset, were selected using simple random sampling from the student roster. Case patients and control subjects were approached by email, telephone, text messaging, and in-person visits. A proxy was identified for the deceased case. At least 5 attempts were made at different times of day to contact each potential control subject. Informed consent was obtained prior to a 20-minute questionnaire. Participants were compensated for time. The questionnaire covered demographics, university profile, lifestyle (alcohol use, smoking, intimate contacts, exercise, studying, party and bar attendance), membership of organizations such as Greek society (fraternities and sororities), and medical history. The reference period for cases and controls was the 30 days prior to illness onset. The university provided room specifications and permanent home addresses.

All epidemiologic data were entered into Microsoft Access 2007 (Microsoft, Redmond, Washington). Annual official student population figures were used to calculate student attack rates. Because of the limited number of cases, exact methods were used to analyze matched case-control data. Univariate conditional logistic regression was used to calculate exact matched odds ratios (mORs) and 95% confidence intervals using SAS software, version 9.2 (SAS Institute, Cary, North Carolina). Multivariable analysis was not possible because of the small case numbers and high exposure prevalence among controls. Data were collected and analyzed as part of a public health response and were determined to be nonresearch, thus not requiring institutional review for protection of human subjects.

RESULTS

Active Case Finding

Between January 2008 and November 2010, we identified 13 meningococcal disease cases (7 confirmed, 4 probable, and 2
suspected) in either University A students (10) or University A–linked persons (3) (Figure 1). One confirmed case, a student at University A, died. All cases were residents of Ohio, all were 18–23 years old, and 62% (8/13) were male. Among University A students for whom information was available, 78% (7/9) were freshman and lived in residential halls (mandatory for freshmen and sophomores), and 3 were members of different Greek fraternities or sororities. The clinical presentation was available for 7 University A students: all had headache and fever; 4 also reported photophobia, neck stiffness, altered mental state, or rash; and 3 of 4 cases who were admitted to the intensive care unit were intubated. No cases of secondary transmission were identified, and no single location was associated with transmission. No further outbreak cases were identified after 31 October 2010. Ten of the 13 cases (8 University A students including the patient who died, and 2 University A–linked persons) had CSF specimens available for serogrouping and were determined to be serogroup B (Figure 1). The population-weighted annual average attack rate of serogroup B among University A students over 3 academic years (2008–2010) was 13 per 100 000. Elevated attack rates were observed among freshmen (50/100 000), men (20/100 000), and Greek society members (63/100 000).

**Laboratory Investigation**

Isolates from CSF were available on 6 confirmed cases (4 University A students and 2 University A–linked cases). All 6 isolates were fully susceptible to antibiotics, had an indistinguishable PFGE NheI pattern, and belonged to sequence type (ST) 269, clonal complex (CC) 269. The 11 Ohio serogroup B isolates not associated with the outbreak differed from the outbreak strain by PFGE and MLST. The outbreak strain PFGE NheI pattern did not match the existing 159 serogroup B profiles in the CDC’s database.

**Matched Case-Control Study**

Seven of the 13 cases met eligibility criteria (University A student, probable or confirmed serogroup B meningococcal disease, illness onset during 2008–2009 and 2009–2010 academic years) and were enrolled. Five (71%) were male, the median age was 19 years, 6 (86%) were freshmen, and all lived in residential halls. To enroll the required 35 student controls, 92 were contacted. Of the 57 potential controls who were not enrolled, 39 did not respond to contact attempts, 16 declined, 1 defaulted at interview, and 1 was ineligible.

On univariate matched analysis (Table 1), campus residence and demographics were similar between cases and controls. Factors significantly associated with disease were Greek society membership (mOR, 15.0; \( P = .03 \)), having >1 kissing partner (mOR, 13.66; \( P = .03 \)), and attending bars (mOR, 8.06; \( P = .04 \)). Although not statistically significant, partying, Greek rushing, tobacco smoke exposure, marijuana use, binge drinking, and having >1 sexual partner were reported more by cases than controls. Adequate exercise and being an honors student were reported more by controls than cases.
Our findings suggest that this prolonged outbreak was due to prevalent risk factors and a novel serogroup B strain (ST-269 of CC269). This is the first reported CC269 outbreak in the United States, comprising 3.8% of 520 serogroup B isolates obtained from Active Bacterial Core Surveillance sites (2001–2005) [13]. It has also been reported as an emerging clone in Quebec, Canada [14]. However, CC269 is more frequently found among serogroup B isolates in Europe, where it has been associated with community outbreaks [15, 16]. In this investigation, controlling for well-known risk factors (campus residence and class year) allowed us to evaluate other potential modifiable risk factors for serogroup B. Although the results should be interpreted with caution as statistical analyses were performed on a small number of cases and variables were highly correlated, we thought it important to investigate common behaviors among college students that are known risk factors for meningitis. The odds ratios allow us to identify those factors that might be the most important in informing public health interventions in the absence of a licensed vaccine.

Factors significantly associated with disease on univariate analysis (Greek society membership, >1 kissing partner, and attending bars) could be collectively considered as indicators of increased intensity of social mixing where the likelihood of sharing nasopharyngeal secretions or respiratory droplets is increased. Although no single event or location was associated with transmission, the findings are consistent with the literature and support the university’s targeted disease prevention messages and broader efforts to reduce harmful alcohol use.

Unlike most previously reported outbreaks of serogroup C, which are usually short in duration [5], this serogroup B outbreak was prolonged and indolent. A different serogroup B strain belonging to CC32 has caused similarly persistent epidemics in the general population of Oregon, with the highest rates in infants, and in northern France, with the highest rates among infants, toddlers, and teenagers [17, 18]. If serogroup B outbreaks have a relatively protracted “natural history” compared to serogroup C outbreaks, applying the same outbreak definitions for serogroup C as thresholds for public health interventions might not be appropriate. Serogroup B vaccines [19, 20] under development have potential to control serogroup B outbreaks on college campuses, but these vaccines will likely require a multidose schedule to be effective [21, 22]. Further understanding serogroup B transmission and risk factors in different populations and settings, such as through nasopharyngeal carriage studies, will inform strategies for serogroup B vaccine use.

Notes

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