AMERICAN ACADEMY OF PEDIATRICS

Committee on Infectious Diseases

Meningococcal Disease Prevention and Control Strategies for Practice-Based Physicians (Addendum: Recommendations for College Students)

ABSTRACT. The numbers of reported cases of meningococcal disease in 15- to 24-year-olds and outbreaks of meningococcal serogroup C disease, including outbreaks in schools and other institutions, have increased during the past decade. In response to outbreaks on college campuses, the American College Health Association has taken an increasingly proactive role in alerting college students and their parents to the risk of this disease and informing them about the availability of an effective vaccine. Recent epidemiologic studies have demonstrated an increased risk of disease in college students living in dormitories, particularly among freshmen, compared with similarly aged persons in the general population. At least 60% of these cases are potentially preventable by vaccination with the quadrivalent meningococcal A, C, Y, and W-135 polysaccharide vaccine. These findings support immunization of college students, particularly freshmen living in dormitories. Hence, college students and their parents should be informed by health care professionals at routine prematriculation visits and during college matriculation of the risk of meningococcal disease and potential benefits of immunization. Vaccine should be made available to those requesting immunization. College and university health services also should facilitate implementation of educational programs concerning meningococcal disease and availability of immunization services.

ABBREVIATIONS. CDC, Centers for Disease Control and Prevention; ACHA, American College Health Association; AAP, American Academy of Pediatrics.

EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE IN THE UNITED STATES

An estimated 2400 to 3000 cases of invasive meningococcal disease occur each year in the United States.[1] Although the annual incidence of 0.8 to 1.3/100 000 persons is relatively low, fatality rates and significant sequelae are appreciable. Death occurs in approximately 10% of cases, ranging from 6% to 21% depending on the meningococcal serogroup in a 1992–1996 survey.[2] For serogroup C meningococcal disease in this population-based active surveillance, the fatality rate was 14%. Of survivors of meningococcal disease in Quebec during 1990 and 1991, 11% to 19% had significant sequelae, including limb loss, neurologic disabilities, and hearing loss.[3]

The incidence of meningococcal disease varies with age and is highest during the first year of life.[1] The age-specific incidence decreases thereafter but increases again in 15- to 24-year-olds (Fig 1). The number of cases in 15- to 24-year-olds also has increased in recent years.[4] In 1991, 310 cases were reported to the National Notifiable Diseases Surveillance System of the Centers for Disease Control and Prevention (CDC), whereas the annual number reported from 1995–1997 ranged from 602 to 621.

Serogroup prevalence varies with age, geographic area, and time. In a 1992–1996 CDC study of 7 surveillance areas, serogroup C accounted for 35% of cases, serogroup B was responsible for 32% of cases, and serogroup Y caused 26% of cases.[2] A higher proportion of serogroup B disease occurred in children younger than 2 years, whereas serogroup C disease was relatively more common in older children, adolescents, and adults.

Another factor in the epidemiology of meningococcal disease has been the increasing number of serogroup C meningococcal outbreaks reported in the United States during the past decade. Of 21 outbreaks between 1980 and 1993, 8 occurred between January 1992 and June 1993.[5] Eleven outbreaks were associated with schools or other types of institutions. From July 1994 to July 1997, 42 meningococcal outbreaks were identified through a survey of state health departments, and 26 of these were caused by serogroup C.[6] Four occurred in colleges, and 62% were institution based.

RECENT RECOMMENDATIONS FOR IMMUNIZATION OF COLLEGE STUDENTS

These outbreaks of meningococcal disease as well as sporadic cases on college campuses have prompted concern by college health officials. In 1997 on the basis of the tragic outcomes of some of these cases, the resulting impact on college communities, the institutional toll from public anxiety, and the availability of an effective and safe polysaccharide vaccine against the A, C, Y, and W-135 meningococcal serogroups, the American College Health Association (ACHA) urged that students should be informed about the risks of meningococcal disease and availability of a vaccine.[7] The ACHA recommended that college and university health services take a proactive role in alerting students and their parents about the risks and consequences of meningococcal disease, that college students consider meningococcal vaccination, and that college and university health services ensure that students have access to this vaccine. Many colleges subsequently have rec-

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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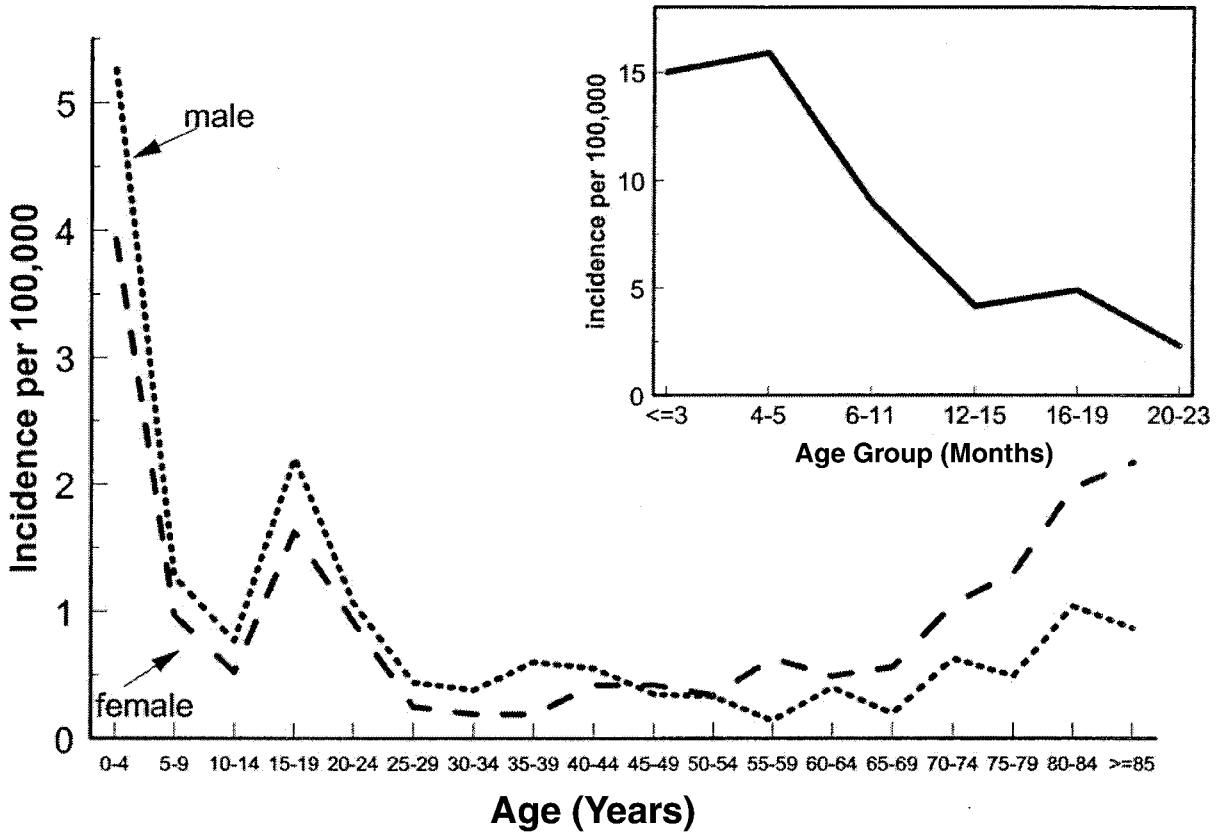

Fig 1. Race-adjusted rates of meningococcal disease by age group and sex, based on active surveillance in 7 geographic areas (California, Georgia, Maryland, Tennessee, Connecticut, Minnesota, and Oregon) in collaboration with the CDC, 1992–1996. Reprinted with permission from Rosenstein et al.[2]

ommended routine vaccination of entering freshmen. Because of insufficient epidemiologic data, these ACHA recommendations were not endorsed at that time by the American Academy of Pediatrics (AAP) Committee on Infectious Diseases or the CDC Advisory Committee on Immunization Practices. However, the CDC, in collaboration with the ACHA and the Council of State and Territorial Epidemiologists, initiated active surveillance for meningococcal disease in college students. To obtain additional data for consideration of appropriate recommendations concerning meningococcal immunization of college students, a case-control study also was undertaken. In July 1998, the Academy notified its membership in *AAP News* of the ACHA recommendations and the need for pediatricians to be "cognizant of these recommendations" and to be "prepared to provide vaccine to those students who wish to be vaccinated according to recommendations of their educational institutions."[8]

RISK OF MENINGOCOCCAL DISEASE IN COLLEGE STUDENTS

The risk of meningococcal disease in college students in nonoutbreak settings has been assessed in 5 studies.[1,9–12] The first was a survey in which a questionnaire was sent to 1900 universities requesting information on culture-confirmed cases of meningococcal disease during the academic years 1990–1991 and 1991–1992. The data demonstrated a 23- and a ninefold increased risk, respectively, in these 2 consecutive school years in students living in dormitories, compared with those living in other accommodations.[9] However, only 38% of the universities responded; results were based on a limited number of cases; and the role of other risk factors, such as age, living conditions, number of years in the school, and cigarette smoking, were not evaluated.

In a retrospective cohort study, Harrison et al[10] compared the incidence of invasive meningococcal disease from 1992–1997 in Maryland students enrolled in 4-year colleges with that in the general population of similar age. Although the incidences of disease were similar in the college and general 18- to 22-year-old populations (1.74 and 1.44/100 000, respectively), the disease rate was significantly higher in students living on campus than in those living off campus. The incidences, respectively, were 3.24 and 0.96/100 000 persons; the relative risk for college dormitory residents, compared with off-campus residents, was 3.4 (95% confidence interval, 1.0–11.6; $P = 0.05$). These findings were based on 67 cases of meningococcal disease in 16- to 30-year olds, of which 14 attended a Maryland college. In statewide surveillance of cases of all ages, a substantial peak in incidence was noted in children younger than 4 years and in 15- to 24-year-olds. The latter peak was primarily attributable to a relatively high incidence in 16- to 19-year olds. Of the 12 cases in college students

from whom isolates were available, 10 (83%) were caused by meningococcal serogroups C, Y, and W-135, for which polysaccharides are included in the currently available quadrivalent meningococcal vaccine. Investigators concluded that vaccinating college students, especially those living on campus, is reasonable.

In a study in the United Kingdom, university students also were found to be at increased risk of invasive meningococcal disease, compared with nonstudents of similar age.[12] The major risk factor in this 1994–1997 study was "catered hall accommodations," which are similar to dormitory residences in the United States. The rate of meningococcal disease of 2/100 000 in the general population in the United Kingdom is approximately twofold higher than that in the United States.[13]

A prospective surveillance of meningococcal disease in college students in the United States by the CDC during the 1998–1999 academic year demonstrated that the risk was greatest in freshmen living in dormitories, for whom the disease rate was 4.6/100 000 persons.[1] This rate was nearly fivefold higher than that of 1.0/100 000 in the general population and higher than that in other age-specific groups, with the exception of children younger than 2 years. In this study and the Maryland study, 54% and 72% of college cases, respectively, occurred among upperclasspersons.

The 90 cases in college students in this surveillance represented only approximately 3% of all cases occurring yearly in this country.[1] However, 71% of the cases in college students were caused by serogroups C, Y, and W-135, which are included in the currently available polysaccharide vaccine. With a vaccine efficacy of 85% or more,[14–16] 60% or more of cases in college students could be prevented by immunization.

In the CDC case-control study of 50 cases identified in the prospective surveillance of college students, dormitory residents who were freshmen were at higher risk, compared with other college students (odds ratio, 5.2; $P = 0.08$).[1,11] Among dormitory residents, freshmen were at increased risk (odds ratio, 2.4; $P = 0.095$). Several other factors also were independent risk factors, such as white race, heat from a radiator, and recent upper respiratory tract infection, but multivariate analysis indicated that freshmen who live in dormitories are at increased risk for invasive meningococcal disease irrespective of these other factors. Prior studies of risk factors in college students have implicated alcohol consumption, campus bar patronage, and cigarette smoking.[17,18]

Findings from these studies indicate that college students, particularly freshmen living in dormitories, are at increased risk of contracting meningococcal disease. The serogroup distribution of cases indicates that 60% or more of the cases are vaccine preventable. The potential benefit of immunization is further enhanced by the higher fatality rate and incidence of sequelae from serogroup C disease, the predominant serogroup in this age group, compared with serogroup B disease.[2,3]

MENINGOCOCCAL DISEASE AND IMMUNIZATION IN THE MILITARY

The increased incidence in college freshmen living in dormitories is analogous to that in US military recruits before routine meningococcal immunization was initiated in 1971. As is the case for many college freshmen, military recruit camps involve close contact of young adults from different areas of the country, facilitating rapid spread of virulent meningococcal strains among susceptible persons.

Between 1964 and 1970, the annual rate of hospitalization in the military for meningococcal disease was 25.2/100 000 persons, approximately 25-fold higher than the current incidence in the civilian population of similar age in the United States.[1] In field trials of serogroup C polysaccharide vaccine, the rate of serogroup C meningococcal disease was reduced by 89.5% in vaccinated recruits, compared with those not vaccinated.[14,15] Since the introduction of routine vaccination of military recruits, large outbreaks of meningococcal disease have not occurred, and the rates of disease in military personnel have remained low.[1] Military recruits currently are vaccinated routinely with the quadrivalent polysaccharide vaccine.

HIGH SCHOOLS AND OTHER CLOSED CIVILIAN POPULATIONS

The increasing number of meningococcal serogroup C outbreaks, a substantial number of which have occurred in elementary and secondary schools, and the demonstrated risk for college freshmen living in dormitories suggest that other groups of students also might be at heightened risk. However, no data are available to determine if other closed populations with characteristics similar to dormitory residents, such as boarding school students, adolescents attending summer camps, and those in detention centers, are at increased risk and whether immunization in these circumstances is indicated.

VACCINE REACTIONS

Adverse reactions associated with meningococcal vaccine are usually mild, consisting primarily of pain and redness at the injection site for 1 or 2 days or transient fever.[1] Severe adverse events, including allergic ones and neurologic events (eg, seizures, anesthesias, and paresthesias) are rare, occurring in less than 0.1/100 000 vaccine doses.[1]

OTHER AAP RECOMMENDATIONS FOR MENINGOCOCCAL IMMUNIZATION AND THE CONTROL OF DISEASE

Selective immunization with the currently licensed quadrivalent serogroup A, C, Y, and W-135 polysaccharide vaccine based on risk factors for meningococcal disease, rather than universal immunization of children and adolescents, is recommended by the Academy.[1,19] Routine childhood immunization is not recommended because of the low incidence of disease in the general population, the ineffectiveness of the current polysaccharide vaccine in preventing serogroup C meningococcal disease in children younger than 2 years (among whom the risk of en-

demic disease is highest), lack of a vaccine against serogroup B meningococcal disease, and the limited duration of protection.[20,21] Immunization is indicated for the control of outbreaks (as defined by the CDC[1]) and for other persons at increased risk of disease, including those with asplenia, a terminal complement component or properdin deficiency, and travelers to geographic areas where disease is hyperendemic or epidemic.

Because serum antibody concentrations decline rapidly in children during the first 3 years after immunization, reimmunization after 3 to 5 years of persons at increased risk or during outbreaks should be considered.[1,19,21] However, the immunologic response appears to be less than that after primary vaccination, suggesting hyporesponsiveness and raising concerns about immunologic tolerance.[22–26] In addition, the efficacy of reimmunization is not known. Hence, routine reimmunization in the absence of demonstrable increased risk of disease is not indicated.

Other recommendations for the control of meningococcal disease, including antimicrobial chemoprophylaxis (eg, rifampin) for close contacts of persons with invasive disease, are given in the *2000 Red Book*.[19] These recommendations, as well as those for the diagnosis and management of meningococcal disease in the *2000 Red Book*, also are discussed in detail in a 1996 joint AAP and Canadian Paediatric Society statement.[21] Chemoprophylaxis for close contacts is indicated regardless of their vaccination status because only 60% or more of cases are vaccine preventable.

Meningococcal polysaccharide-protein conjugate vaccines have been developed and are in clinical trials but remain investigational in the United States. One or more of these products is expected to be licensed in the next several years, at which time routine immunization of children may be considered. In the United Kingdom, where the rate of meningococcal disease, especially that for serogroup C disease, is substantially higher than that in the United States and serogroup C meningococcal conjugate vaccines are now available, a comprehensive public health program to vaccinate all children between 2 months and 17 years old and all students entering college recently has been initiated.[13]

ECONOMIC CONSIDERATIONS

The potential benefit and cost-effectiveness of immunizing college students with the licensed quadrivalent polysaccharide vaccine recently has been analyzed by the CDC.[1] Immunization of all freshmen living in dormitories would result in administration of 300 000 to 500 000 doses each year and is estimated to prevent 15 to 30 cases of meningococcal disease and 1 to 3 deaths each year. The cost per case prevented would be between $671 000 and $1.8 million and that for deaths prevented would be between $7 million and $20 million. This cost analysis suggests that, from a societal perspective, immunization of college students is not likely to be cost-effective. However, it does not take into account the personal tragedy of families experiencing the loss of children; consequences of severe sequelae, such as loss of a limb, neurologic disabilities, and hearing loss; public anxiety; and disruption of campus life after the occurrence of 1 or more cases of severe meningococcal disease.

IMMUNIZATION RECOMMENDATIONS FOR COLLEGE STUDENTS

College students, particularly freshmen living in dormitories, are at moderately increased risk of meningococcal disease, compared with other persons of similar age. The disease, however, can be life-threatening, and 60% or more of cases can be prevented with the currently available quadrivalent polysaccharide vaccine against serogroups A, C, Y, and W-135. In addition, adverse reactions generally are mild, and serious reactions are rare. On the basis of these considerations, the Academy recommends the following:

1. Students entering college, especially those who will be living in dormitories, and their parents should be informed during routine prematriculation medical visits about the increased risk of meningococcal disease and potential benefits of immunization as well as limitations of the vaccine, primarily the lack of protection against serotype B meningococcal disease. **(Evidence Grade II-2)**
2. Students should consider immunization in view of the risk of disease and potential benefits of immunization. Although the risk is greatest for college freshmen who will be living in dormitories, college upperclasspersons and graduate students living in dormitories also may choose to be immunized. **(Evidence Grade II-2)**
3. Physicians and other health care professionals providing care to college students, including those who will be matriculating within the following year and who may live in dormitories, should vaccinate students who wish to be immunized or refer them to an easily accessible source where the vaccine is available. **(Evidence Grade II-2)**
4. College and university health services should inform students of the risks of meningococcal disease and potential benefits of immunization, particularly before and after matriculation, and should facilitate the implementation of related educational programs and immunization services, including on-site availability of meningococcal vaccine. **(Evidence Grade II-2)**
5. Immunization is not recommended for students who will not be living in dormitories because their risk of meningococcal disease is not increased relative to that of persons of similar age in the general population. However, immunization is not contraindicated for these students and vaccine may be given if requested. **(Evidence Grade III)**
6. Routine reimmunization of college students who were immunized as freshmen is not indicated. However, for those who were immunized 3 to 5 years previously and are or will be in high-risk circumstances, such as travel to geographic areas with hyperendemic or epidemic meningococcal disease, reimmunization should be considered.[1]

Similarly, vaccine should be considered for matriculating freshmen who were immunized 3 or more years previously and will be living in dormitories. **(Evidence Grade III)**

EVIDENCE GRADING

I. Evidence obtained from at least 1 properly randomized, controlled trial.

II-1. Evidence obtained from well-designed, controlled trials without randomization.

II-2. Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than 1 center or research group.

II-3. Evidence obtained from multiple time series with or without intervention. Dramatic results in uncontrolled experiments, such as the results of the introduction of penicillin treatment in the 1940s, could be regarded as this type of evidence.

III. Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

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