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Global Epidemiology of Meningococcal Disease

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Meningococcal disease is a significant cause of mortality and morbidity throughout the world (40, 49). Although rates of endemic meningococcal disease range from 1 to 3/100,000 in the United States (26) to 10 to 25/100,000 in many parts of the developing world (47), this disease is noteworthy for causing major, periodic epidemics with attack rates exceeding 500/100,000 (10). The descriptive epidemiology and the patterns of illness of each of the major meningococcal serogroups have been characterized in several recent reviews (26, 40). Current epidemiologic efforts are focused on improving (i) the surveillance for meningococcal disease by using new techniques to identify clonal populations (7, 39) and (ii) the understanding of individual risk factors for illness and antecedents of epidemic disease by using both classical epidemiologic techniques and immunologic methods (24). In this report, we review recent developments in both areas of investigation, emphasizing the continued importance of surveillance (including serogrouping) and a multidisciplinary approach to the analysis of risk factors.

SURVEILLANCE: CHANGES IN THE PATTERNS OF DISEASE

Nine meningococcus serogroups can cause invasive disease, with most illness caused by serogroups A, B, and C. Attack rates are highest in infants from 3 months to 1 year old and then decrease with age. Currently available vaccines are effective in protecting against disease caused by serogroups A, C, Y, and W-135. Infants respond poorly to polysaccharide antigens, however, and vaccination has limited efficacy in preventing disease among those at highest risk. During the past decade, changes have occurred in the patterns of disease caused by each of these serogroups as new strains have emerged and spread.

Epidemic group A meningococcal disease has been documented in various parts of the developing world, with outbreaks beginning during the dry season and ending with the onset of the rainy season. Attack rates generally range from 100 to 500/100,000. Periodic outbreaks occur across sub-Saharan Africa at intervals of 8 to 12 years, with recent outbreaks occurring in Chad and Sudan (in 1988).

Outbreaks in developed countries have been infrequent since a pandemic swept Europe and North America following the Second World War. When group A disease occurs in a developed country, cases are concentrated in the poorest sectors of society (9, 45), reflecting other potential risk factors such as sanitation, crowding, and family size. The most recent such outbreak occurred in Auckland, New Zealand, during the winters of 1985 to 1987. Over 280 cases were reported, with attack rates almost 20-fold higher in the Maori and Pacific Islander communities than among the more affluent New Zealanders of European descent (D. Lennon, L. Voss, D. Hood, and B. Gellin, Pediatr. Res. **23**:374A, 1988). Isoenzyme typing, a technique that identifies strains on the basis of the electrophoretic mobility of a panel of enzymes, suggests that the strain responsible for the New Zealand outbreak was the same strain that caused an earlier outbreak in the northwestern United States among skid road inhabitants (B. Gellin, personal communication). Of 14 New Zealand group A isolates from patients with disease between 1980 and 1985, 13 were of the outbreak strain, indicating that this strain had been present in the population for several years prior to the outbreak. The factors that precipitated the 1985 outbreak are not known.

With increased international travel, global dissemination of an outbreak-associated strain may become more common. One example of this potential is provided by an epidemic of group A meningococcal disease occurring in association with the annual Moslem pilgrimage (Haj) to Mecca. Each year, over a million Moslems from throughout the world perform the Haj. In summer 1987, group A meningococcal disease brought into Saudi Arabia by arriving pilgrims spread throughout this gathering, resulting in several thousand cases of invasive disease (46). As the Hajis returned to their home countries, the virulent group A strain was carried throughout the world. Secondary outbreaks among Hajis, their contacts, and, eventually, individuals having no direct contact with Hajis occurred in Saudi Arabia, in other Gulf states (37), and in Pakistan. Although isolated secondary cases occurred in developed countries (11, 43), illness did not spread to the general community. Despite steps taken to prevent future outbreaks during the pilgrimage through vaccination of Hajis, transmission of pharyngeal carriage will not be affected. Other large-scale population movements (e.g., refugees) may present similar problems.

Group B meningococci are recognized to be the major cause of sporadic meningococcal disease in developed countries (26, 40). When outbreaks do occur, the attack rates usually range from 10 to 50/100,000, an order of magnitude less than attack rates during group A outbreaks. During the late 1970s, a group B clone (serotype 15, ET-5 complex) emerged in northwestern Europe and was responsible for outbreaks in Norway, Iceland, Denmark, the Netherlands, and Great Britain (42). Intercontinental spread of this clone had been documented, with outbreaks occurring in Cuba (in 1980), in Chile (in 1985), and currently in Rio de Janeiro and São Paulo, Brazil (7). Strains of this type have also been isolated from patients in the United States, although as of 1988, they have caused only a small fraction of sporadic meningococcal infections.

Group C meningococci have been implicated in large outbreaks (4), small disease clusters (30), and sporadic infections. Changes in the predominant strains and the disease pattern for this serogroup have also occurred. During the 1980s, the proportion of sporadic disease caused by group C organisms increased in several European countries; a single strain was responsible for much of the increase (29). In the United States, active surveillance for meningococcal infections conducted by the Centers for Disease Control in six regions of the United States during 1986 and 1987 found

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group C to be the major serogroup responsible for sporadic disease in two of the regions studied (Los Angeles County and the state of Tennessee). The absolute attack rate of disease in Los Angeles increased threefold as a result of increased rates of group C meningococcal disease. Isoenzyme typing of surveillance isolates from Los Angeles County identified a single clone as being responsible for this increase. Only 1 of 33 strains isolated from patients in 1980 to 1985 was this type. Isolates from Tennessee were divided between the Los Angeles type and a genetically related strain, differing at only one enzyme locus (B. Gellin, unpublished observations).

These changes in strain types and patterns of disease for each of the three major serogroups emphasize the need for continued surveillance and typing of strains isolated during outbreaks and sporadic disease episodes. Serotyping is especially important for group B strains, in which immunity may be type specific rather than group specific, and information about the strains predominating in a population will be important in developing an effective vaccine.

RISK FACTORS FOR MENINGOCOCCAL DISEASE

The second major focus of meningococcal disease epidemiology has been to determine risk factors for meningococcal disease. Although the descriptive epidemiology of endemic and epidemic meningococcal disease has been well documented, individual risk factors for illness are poorly understood. With the availability of preventive measures such as vaccination, predicting who will develop meningococcal disease and determining which risk factors lead to epidemic spread of illness become crucial for targeting intervention to populations at greatest risk.

Progress in characterizing risk factors for meningococcal disease has been slow, because it has been hampered by the infrequent occurrence of outbreaks in developed countries and the difficulty in conducting epidemiologic investigations in developing countries. Moreover, risk factors may vary between developed and developing countries, between endemic and epidemic disease, and among illnesses caused by various serogroups. When studies have been done, results often conflict. Methodologic problems have contributed to the confusion. Misclassification of cases can occur by including individuals without culture-documented meningococcal infection or by including patients with meningitis caused by meningococcal strains not of the epidemic type. Measurement of important variables such as crowding, socioeconomic status, and ventilation are not standardized and differ in various reports. Studies reporting a positive association may have reached a level of statistical significance by chance, whereas those finding no association may have had an insufficiently large sample size to detect a true risk factor.

An additional difficulty in determining risk factors for infection has been that potential risk factors are usually evaluated only as they relate to the occurrence of invasive disease. Before invasive disease develops, however, several steps must occur, beginning with exposure to a carrier, transmission of infection, and establishment of carriage or disease. Risk factors acting at the earlier stages may have only an indirect effect on disease occurrence or, depending on other associated factors, may have no effect at all.

By breaking down the development of meningococcal disease into its constituent steps and evaluating the contribution of potential risk factors at each step, a clearer picture of their impact emerges. We have developed a model

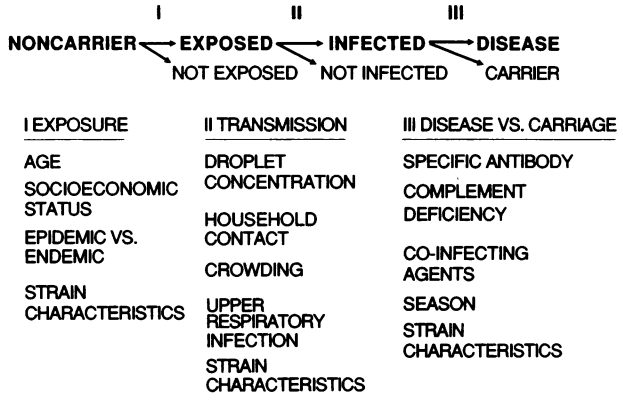

FIG. 1. Factors determining the occurrence of meningococcal disease.

for meningococcal infection that examines the sequence of events ending with invasive disease and have evaluated the role of potential risk factors at each step in the sequence. Although this model provides a framework for the evaluation of various potential risk factors, it also makes clear the gaps in our understanding of meningococcal disease epidemiology. The model includes three stages: first, exposure to a meningococcal carrier; second, acquisition of infection; and, third, development of carriage or invasive disease (Fig. 1).

Stage I: Exposure

Humans are the only natural host for meningococci. Therefore, infection can be acquired only after exposure to a carrier of the organism. The likelihood of contact with a carrier depends, in part, on the prevalence of carriage in the population. Reported carriage rates vary widely among studies, which have been conducted in both developed and developing countries during periods of both endemic and epidemic disease.

During periods of endemic disease in the United States, Greenfield et al. found an overall carriage rate of 5.7% (20), whereas Gold et al. found rates between 0.6 and 2.0% (17). In both studies, the most common groupable strains were serogroup B followed by serogroup Y. No group A strains were isolated in either study. Meningococcal carriage rates were highest in older children and young adults. In contrast, *N. lactamica* was most commonly found in children between 1 and 4 years old.

Three European studies evaluated carriage during outbreaks of serogroup B meningococcal disease. A survey conducted in two Belgium schools during a serotype B2 outbreak showed a carriage rate of 9.8% in a school with a student population that was of moderate to high socioeconomic class and a carriage rate of 32.6% in a school serving families of lower socioeconomic class. Most isolates from both schools were group B or W-135 (12). Serotyping of carriage strains and comparison with the outbreak strain were not done. During an outbreak of serotype B15 disease in England, a community survey showed 10.9% of individuals to be meningococcal carriers, with 1.4% carrying the outbreak strain. Among schoolchildren, rates were 12.6 and 1.5%, respectively (6). Similar rates were obtained by Caugant et al. during an outbreak in Norway (8). They found an overall carriage rate of 10.1%, with only 0.7 and 0.9% being carriers of the strains causing over 90% of the invasive disease.

In developing countries, carriage rates also vary with age, socioeconomic status, the presence of an ongoing epidemic, and the particular strains that are predominant in the area. During a nonepidemic period in northern Nigeria, 10% of those surveyed were carriers, with the highest rates occurring in young adults. Strains most frequently isolated were group B (58%) and group C (24%); only 11% were group A. No seasonal variation in carriage rate was noted (36). Blakebrough et al. examined carriage at a school and its surrounding village in northern Nigeria at times of both endemic and epidemic group A disease (2). Before the outbreak, 7% of schoolchildren were carriers, primarily of group C strains. During the outbreak, the overall carriage rate was not significantly different (9%), but a larger proportion of isolates were group A (72% versus 13% before the outbreak); 9% of children also carried *N. lactamica*. The village survey showed similar results, with a shift to serogroup A carriage during the outbreak period. Carriage studies during a previous group A outbreak in Nigeria gave similar results, identifying 7.4% of the population as meningococcal carriers, of whom 35% carried group A strains (27).

Strain characteristics also influence carriage rates. Clonal analyses of group B strains show different rates of carriage and disease for different strains. The duration of carriage varies with serogroup as well. Studies in developed and developing countries during periods of endemic disease show low rates of group A carriage relative to the other serogroups. However, since culture surveys measure the point prevalence of carriage, the rate is dependent on both the acquisition rate and the duration of carriage. Studies from Saudi Arabia and Nigeria document a mean duration of 1 month for group A carriage (2, 9). The Nigerian study showed a significantly longer duration for carriage of nongroup A *N. meningitidis*. Although the prevalence of group A carriage may be low, the incidence (the number who acquire this organism during a given period) tends to be relatively high. The high incidence of occult infection, as measured by antibody studies (2), increases the likelihood of exposure to someone carrying a strain from this serogroup. Reasons for the difference between serogroups in duration of carriage are not known.

Results of these carriage surveys suggest several conclusions: (i) carriage rates are highest in school-age children and young adults; (ii) carriage rates may be higher in persons of low socioeconomic status; (iii) carriage rates do not vary with the seasons; (iv) strains isolated during interepidemic and epidemic periods are heterogeneous, with a shift to group A carriage during group A outbreaks (this shift to carriage of the epidemic strain did not occur during group B outbreaks that have been studied); and (v) strain characteristics affect carriage rates, with carriage strains not necessarily corresponding to strains causing invasive disease.

Stage II: Acquisition of Infection

Not all individuals exposed to a meningococcal carrier will acquire infection. Meningococci are spread via respiratory droplets. Therefore, transmission of infection requires aspiration of infective particles by noncarriers. Factors that increase the likelihood of this include those that increase the number of aerosolized particles, prolong survival of the meningococci in the droplet, and increase the chance of contact of noncarriers with infective particles. The immunologic status of potential hosts may also be important, a factor that will be reviewed briefly. Organism-related factors, especially those affecting attachment to the pharyngeal mucosa, are also likely to be important.

Formation of respiratory droplets is enhanced by coughing and sneezing. If carriers express symptoms, either related to an intercurrent viral upper respiratory infection or produced by the carriage itself, the formation of respiratory droplets would be increased. Olcen et al. obtained pharyngeal cultures from 64 family members of patients with meningococcal disease, 25 (39%) of whom were carriers, with 22 carrying the same strain as the patient (38). Of 24 carriers interviewed, 20 (83%) reported upper respiratory infection symptoms, compared with 13 (35%) of 37 noncarriers. Similar results were noted by Moore et al., who found fever, sore throat, and cough to be more common in carriers of group A meningococci than in noncarriers (34).

Following the aerosolization of particles containing meningococci, factors that increase the survival of the organism in the environment may increase the likelihood of transmission of infection. A field study to evaluate the effect of season and ventilation on aerosolized bacteria was conducted in Mali and Burkina Faso in 1968 to 1969, in which air samples were obtained from various types of dwellings during both the dry and rainy seasons. Although no meningococci were isolated, greater concentrations of viable bacteria were present during the dry season (humidity, 18 to 68%) than during the rainy season (humidity, 56 to 92%) (16). The temperatures were similar in both seasons. No conclusions could be reached regarding the effect of ventilation on the indoor concentration of airborne bacteria. We know of no studies of the effect of temperature on the survival of meningococci in the environment, but expect that desiccation may occur more rapidly at higher temperatures.

Acquisition of infection depends not only on the concentration of infective particles in the environment but also on the chance that a noncarrier will inhale those particles. Household contact with a carrier was shown to increase the acquisition rate from 0.7% per month to 1.6% per month during an epidemic in northern Nigeria (2). A study conducted during a group C epidemic in Brazil showed a higher carriage rate in persons living with a patient who had meningococcal disease than among those who visited or worked in the household (35). Hassan-King et al. found not only a higher carriage rate in family members than in other household contacts, but also a higher carriage rate among persons who slept in the same room as a patient with meningococcal disease (27). Transmission also increases with increased crowding within a household. During the 1987 group A meningococcal disease outbreak in Saudi Arabia, 33% of persons in households having more than two persons per room were carriers, compared with only 20% of persons in households having less than two persons per room. Bedroom crowding was also associated with increased rates of carriage (B. Schwartz, unpublished observation).

The role of immunologic factors in establishing an infection is not clear. The presence of group-specific antibody elicited by vaccination does not affect the carriage rate (1, 3). Simultaneous carriage of more than one strain can also occur (3).

Stage III: Carriage versus Invasive Disease

Risk factors for invasive disease in persons with meningococcal infection are not completely understood. A combination of host factors, environmental factors, and organism characteristics may be important in affecting the balance between carriage and disease.

Invasive meningococcal disease occurs primarily in persons who are newly infected with the organism. In studying military personnel, Edwards et al. found that 31 (86%) of 36 patients had negative nasopharyngeal cultures during the 2 weeks before becoming ill and that 4 of these were culture negative the day before developing disease (14). The remaining 5 of 36 patients had positive cultures less than 4 days prior to the onset of illness. Moreover, meningococcal outbreaks occur not at times of high pharyngeal carriage but when the rate of acquisition of infection is increased (48).

The presence of serum bactericidal antibody (immunoglobulins G and M) is probably the most important host factor preventing invasive disease. In a seminal series of studies, Goldschneider et al. demonstrated a clear correlation between bactericidal antibody titers and host immunity (18). They found that in a large cohort of Army recruits, 94% of soldiers who subsequently developed meningococcal disease had group-specific bactericidal titers below 1:4, in contrast to healthy controls. Interestingly, meningococcal patients also had significantly lower group-specific bactericidal titers against heterologous serogroups, indicating that individual differences in generating an effective immune response may play an important role in disease susceptibility. The high rates of meningococcal disease in military recruits during the prevaccination era presumably resulted from bringing new recruits together, many of whom did not have previous exposure to the invasive serogroup or were not able to mount an effective humoral response. Disease rates in veteran soldiers, however, were much lower than in new recruits (5). The role of natural immunity in prevention of invasive disease also explains the high attack rates seen in younger age groups. Peak attack rates occur in infants of 6 to 9 months old, an age when maternally acquired antibodies are being lost. Carriage of *N. lactamica* and other nonpathogenic *Neisseria* species may provide immunity by stimulating protective antibodies that cross-react with pathogenic strains (17, 19).

Although specific antibody is generally protective, this immunity is not absolute. During an epidemic in the Gambia, Greenwood et al. documented illness in individuals with preexisting antibody titers considered protective (22). Overall, 4 of 25 patients had high bactericidal titers before becoming ill. Kayhty et al. measured group-specific antibody titers and the proportion of antibodies in the different immunoglobulin classes in acute-phase serum samples from Finnish patients with group A or C meningococcal disease at the time of hospital admission (31). They found that 16% had antibody levels deemed protective.

The occurrence of disease in persons with preexisting "protective" antibody levels has been addressed by Griffiss, who hypothesized that the activity of bactericidal antibodies might be blocked by immunoglobulin A antibodies induced either by other meningococcal strains or by cross-reacting enteric or respiratory bacteria (23). This mechanism postulates that since immunoglobulin A does not bind complement, it may block binding sites for other bactericidal antibody classes. Accordingly, outbreaks of disease might reflect transmission of cross-reacting organisms in previously immune populations.

Immune lysis by complement also plays an important role in protection from meningococcal disease. Therefore, persons with complement deficiency may develop disease despite protective antibody. Ellison et al. found primary or secondary deficiencies in 6 (30%) of 20 individuals with sporadic infection in the United States (15). Studies conducted during group A epidemics in Africa, however, indicated that this was not a significant factor in determining who developed disease (22).

The condition of the host pharyngeal mucosa and respiratory epithelium may also be important in protection from invasive disease. Concurrent viral upper respiratory infections may denude the mucosa (32) and increase invasion by the organism. Sporadic cases and outbreaks of meningococcal disease have clearly been associated with concurrent viral upper respiratory tract illness (33, 50). During an epidemic in Chad, patients with meningococcal disease were found to shed respiratory viruses and mycoplasma at a significantly higher rate than age- and sex-matched controls (P. Moore, unpublished observation). An investigation of a simultaneous outbreak of meningococcal disease and influenza showed that both meningococcal carriage and disease were significantly more common among patients with serologic evidence of influenza infection, despite similar levels of exposure between patients with and without the viral illness (50).

Other factors may also affect the integrity of the respiratory mucosa, degrading its effectiveness as a barrier to invasion. One explanation for the seasonality of epidemic group A disease is that during the dry season the mucosa is chronically irritated. This problem may be exacerbated by periodic dust storms. During the 1988 outbreak in Chad, the rate of disease had been declining until a dust storm occurred that was followed by a subsequent increase in cases (T. Lippeveld, personal communication), and Greenwood et al. found a significant association between the number of cases of meningococcal disease in Nigeria and the intensity of the harmattan, a dry, dusty wind from the Sahara (21). Exposure to cigarette smoke was also found to be related to developing disease (25).

Strain characteristics also affect the balance between carriage and disease (28). Different serogroups are clearly responsible for different patterns of meningococcal disease. Within serogroups, some strains are more closely associated with epidemic disease, whereas others are less likely to cause infection. Olyhoek et al. used isoenzyme electrophoresis and monoclonal typing to distinguish clonal populations in a large series of group A meningococcal isolates from 28 different epidemics (39). In all but one epidemic, a single clonal population was responsible for illness. Several clones were implicated in multiple epidemics, whereas others were unrelated to epidemic disease. Differences in the disease-to-carriage ratio have been shown for group B strains as well (8).

The effect of environmental factors on the risk of invasive disease is difficult to evaluate, since the same factors may affect the risk of exposure to a carrier and the likelihood that transmission will occur. For example, household contact with a carrier increases the transmission of infection (stage II) and also increases the occurrence of disease. Although carriage rates in household members of patients are increased approximately threefold (46), rates of disease in household members are increased several hundredfold (13). Household crowding may independently affect both the transmission of infection and the occurrence of disease (44). Transmission of potential cofactors, such as cross-reacting organisms or upper respiratory infection agents, could be increased in more crowded conditions. Since several different meningococcal strains are present in the population at any time, the occurrence of secondary cases in a household may be only a marker for the presence of a strain more likely to cause disease in that family. It is also possible that

increased household attack rates reflect a common genetic susceptibility to disease in family members.

OCCURRENCE OF MENINGOCOCCAL EPIDEMICS

Epidemics of meningococcal disease are composed of individual cases clustered in time and space. Therefore, factors that precipitate an epidemic must also be risk factors for individual cases. Since carriage rates do not correspond to the rate of invasive disease and may not increase significantly during an epidemic, risk factors for epidemic disease are likely to be those affecting the balance between carriage and invasive disease (stage III in the model).

A combination of factors must exist for an epidemic to occur. The descriptive epidemiology of meningococcal outbreaks provides a clue to what factors might be important. For example, periodic outbreaks of group A meningococcal disease occurred in both the United States and Africa before the 1950s. Although major epidemics in sub-Saharan Africa continue to follow this pattern, outbreaks in developed nations are infrequent and are generally restricted to the poorest sectors of society. Meningococcal outbreaks also tend to be seasonal, and the mean age for patients during an outbreak is above that for those with sporadic disease (41). These features suggest that socioeconomic status (or a correlate, such as sanitation or crowding), season, and immunity are important factors in the occurrence of epidemic disease. Strain characteristics are important as well. The introduction of a virulent strain into a previously unexposed population, as may have occurred during the Haj, may also precipitate a meningococcal outbreak. The clonal strain causing this outbreak, designated III-1 by Olyhoek et al. (39), was probably imported into Mecca by Asian pilgrims and subsequently caused a major epidemic in Chad and Sudan in 1988 (Moore, unpublished). However, the presence of a virulent strain alone is usually not sufficient to result in an epidemic.

Risk factors for epidemic disease can be divided into two groups: factors that are permissive (i.e., necessary but not sufficient for an outbreak to occur), and factors that act to initiate an outbreak. Immunologic susceptibility, appropriate climatic conditions, low socioeconomic status, and transmission of a virulent strain appear to be necessary for an outbreak to occur. If these conditions are present, an outbreak can then be precipitated by an initiating factor, such as exceptional climatic conditions (excessively dry season, dust storms) or the spread of an infectious cofactor. In the latter case, the spread of a respiratory pathogen, not meningococci, might be the primary initiating factor for a meningococal epidemic.

No longitudinal data exist to document changes in group- or type-specific specific immunity over time. Because of the importance of immune status in the development of invasive disease, however, waning herd immunity to a particular strain in a population seems necessary for an outbreak to occur. Although an outbreak of a coinfecting organism that induces cross-reacting antibodies might cause a meningococcal outbreak in an immune population, studies during outbreaks in The Gambia (22) and in Finland (31) indicate that only a small proportion of cases occur in persons with protective antibody titers.

The role of climatic factors in precipitating outbreaks is unclear. Although outbreaks occur during the dry season, many dry seasons can pass without epidemic disease. Some evidence suggests that the year preceding an epidemic may be drier than average. Evaluation of historical rainfall data from Burkina Faso and Mali since the 1940s found this pattern for four of six outbreaks (D. Le Comte, unpublished observations). Additional data must be evaluated to determine whether this pattern is consistent for other group A outbreaks.

Socioeconomic factors, being constant over time, are probably not directly related to the occurrence of outbreaks. An outbreak of meningococcal disease could be precipitated by an outbreak of a concurrent infection, however, which is more likely among those living in poorer, more crowded conditions. This hypothesis also needs further study.

CONCLUSIONS

The role of potential risk factors for meningococcal disease can best be evaluated when the steps preceding the onset of illness are examined separately. Different environmental, host-related, and strain-related factors are important during the different steps in the pathogenesis of invasive disease: exposure to a carrier, transmission of infection, and development of invasive disease. Determination of individual risk factors is also helpful in characterizing risk factors for epidemic disease, although assessment of the role of several key factors is hampered by insufficient longitudinal and population-based data.

Morbidity and mortality from meningococcal disease can be significantly reduced by using currently available vaccines in groups at high risk for disease, particularly during epidemics. Therefore, defining the risk factors for infection and continuing surveillance for disease remain important public health goals for the control of meningococcal disease. However, polysaccharide vaccines are ineffective in young children, and the duration of protection is limited in children vaccinated at 1 to 4 years of age (44). Therefore, development of polysaccharide-conjugate vaccines should be given high priority for the control of epidemic disease by routine immunization of young children. A protective serogroup A-conjugate vaccine might be effective in the Expanded Program of Immunization to interrupt the cyclic epidemics in the African meningitis belt.

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LITERATURE CITED

1. **Blakebrough, I. S., B. M. Greenwood, H. C. Whittle, and A. K. Bradley.** 1983. Failure of meningococcal vaccine to stop the transmission of meningococci in Nigerian schoolboys. Ann. Trop. Med. Parasitol. **77**:175–178.
2. **Blakebrough, I. S., B. M. Greenwood, H. C. Whittle, A. K. Bradley, and H. M. Gilles.** 1982. The epidemiology of infections due to *Neisseria meningitidis* and *Neisseria lactamica* in a northern Nigerian community. J. Infect. Dis. **146**:626–637.
3. **Broome, C. V.** 1986. The carrier state: *Neisseria meningitidis*. J. Antimicrob. Chemother. **18**(Suppl. A):25–34.
4. **Broome, C. V., M. A. Rugh, A. A. Yada, L. Giat, H. Giat, J. M. Zeltner, W. R. Sanborn, and D. W. Fraser.** 1983. Epidemic group C meningococcal meningitis in Upper Volta, 1979. Bull. W.H.O. **61**:325–330.
5. **Brundage, J. F., and W. D. Zollinger.** 1987. Evolution of meningococcal disease epidemiology in the U.S. Army, p. 5–45. *In* N. Vedros (ed.), The evolution of meningococcal meningitis,

vol. 1. CRC Press, Inc., Boca Raton, Fla.
6. **Cartwright, K. A. V., J. M. Stuart, D. M. Jones, and N. D. Noah.** 1987. The Stonehouse survey: nasopharyngeal carriage of meningococcal and *Neisseria lactamica*. Epidemiol. Infect. **99:** 591–601.
7. **Caugant, D. A., L. O. Froholm, K. Bøvre, E. Holten, C. E. Frasch, L. F. Mocca, W. D. Zollinger, and R. K. Selander.** 1987. Intercontinental spread of *Neisseria meningitidis* clones of the ET-5 complex. Antonie van Leeuwenhoek J. Microbiol. **53:** 389–394.
8. **Caugant, D. A., B. E. Kristiansen, L. O. Froholm, K. Bøvre, and R. K. Selander.** 1988. Clonal diversity of *Neisseria meningitidis* from a population of asymptomatic carriers. Infect. Immun. **56:**2060–2068.
9. **Counts, G. W., D. F. Gregory, J. G. Spearman, B. A. Lee, G. A. Filice, K. K. Holmes, J. M. Griffis, and the Pacific Northwest Meningococcal Study Group.** 1984. Group A meningococcal disease in the U.S. Pacific northwest: epidemiology, clinical features, and effect of a vaccination control program. Rev. Infect. Dis. **6:**640–648.
10. **Cvjetanovic, B.** 1978. Cerebrospinal meningitis, a disease with seasonal variations. Bull. W.H.O. **56:**81–102.
11. **Denamur, E., J. C. Pautard, J. P. Ducroix, K. Masmoudi, F. Eb, J. Y. Riou, and J. Orfila.** 1987. Meningococcal disease due to group A *Neisseria meningitidis* in contacts of Mecca pilgrims. Lancet **ii:**1211.
12. **De Wals, P., C. Gilquin, S. De Maeyer, A. Bouckaert, A. Noel, M. F. Lechat, and A. Lafontaine.** 1983. Longitudinal study of asymptomatic meningococcal carriage in two Belgian populations of schoolchildren. J. Infect. **6:**147–156.
13. **De Wals, P., L. Hertoghe, I. Borlee-Grimee, S. D. Maeyer-Cleempoel, G. Reginster-Haneuse, A. Dachy, A. Bouckaert, and M. F. Lechat.** 1981. Meningococcal disease in Belgium. Secondary attack rate among household, day-care nursery and preelementary school contacts. J. Infect. **3**(Suppl.):53–61.
14. **Edwards, E. A., L. F. Devine, C. H. Sengbusch, and H. W. Ward.** 1987. Immunological investigations of meningococcal disease. III. Brevity of group C acquisition prior to disease occurrence. Scand. J. Infect. Dis. **9:**105–110.
15. **Ellison, R. T., P. F. Kohler, J. G. Curd, F. N. Judson, and L. B. Reller.** 1983. Prevalence of congenital or acquired complement deficiency in patients with sporadic meningococcal disease. N. Engl. J. Med. **308:**913–916.
16. **Ghipponi, P., J. Darrigol, R. Skalova, and B. Cvjetanovic.** 1971. Study of bacterial air pollution in an arid region of Africa affected by cerebrospinal meningitis. Bull. W.H.O. **45:**95–101.
17. **Gold, R., I. Goldschneider, M. L. Lepow, T. R. Draper, and M. Randolph.** 1978. Carriage of *Neisseria meningitidis* and *Neisseria lactamica* in infants and children. J. Infect. Dis. **137:** 112–121.
18. **Goldschneider, I., E. C. Gotschlich, and M. S. Artenstein.** 1969. Human immunity to the meningococcus. I. The role of humoral antibodies. J. Exp. Med. **129:**1307–1326.
19. **Goldschneider, I., E. C. Gotschlich, and M. S. Artenstein.** 1969. Human immunity to the meningococcus. II. Development of natural immunity. J. Exp. Med. **129:**1327–1348.
20. **Greenfield, S., P. R. Sheehe, and H. A. Feldman.** 1971. Meningococcal carriage in a population of "normal" families. J. Infect. Dis. **123:**67–73.
21. **Greenwood, B. M., A. K. Bradley, and R. A. Wall.** 1985. Meningococcal disease and season in sub-Saharan Africa. Lancet **ii:**829–830.
22. **Greenwood, B. M., A. M. Greenwood, A. K. Bradley, K. Williams, M. Hassan-King, F. C. Shenton, R. A. Wall, and R. J. Hayes.** 1987. Factors influencing the susceptibility to meningococcal disease during an epidemic in The Gambia, West Africa. J. Infect. **14:**167–184.
23. **Griffiss, J. M.** 1982. Epidemic meningococcal disease: synthesis of a hypothetical immunoepidemiologic model. Rev. Infect. Dis. **4:**159–172.
24. **Griffiss, J. M., B. L. Brandt, and G. A. Jarvis.** 1987. Natural immunity to *Neisseria meningitidis*, p. 99–119. *In* N. Vedros (ed.), Evolution of meningococcal disease, vol. II. CRC Press, Inc., Boca Raton, Fla.
25. **Haneberg, B., T. Tonjum, K. Rodahl, and T. W. Gedde-Dahl.** 1983. Factors preceding the onset of meningococcal disease, with special emphasis on passive smoking, stressful events, physical fitness, and general symptoms of ill health. NIPH Ann. **6:**169–173.
26. **Harrison, L., and C. V. Broome.** 1987. The epidemiology of meningococcal meningitis in the United States civilian population, p. 27–45. *In* N. Vedros (ed.), The evolution of meningococcal meningitis, vol. I. CRC Press, Inc., Boca Raton, Fla.
27. **Hassan-King, M., B. M. Greenwood, H. C. Whittle, J. D. Abbott, and E. M. Sutcliffe.** 1979. An epidemic of meningococcal infection at Zaria, northern Nigeria. 3. Meningococcal carriage. Trans. R. Soc. Trop. Med. Hyg. **73:**567–573.
28. **Holbein, B. E.** 1981. Differences in virulence for mice between disease and carrier strains of *Neisseria meningitidis*. Can. J. Microbiol. **27:**738–741.
29. **Jones, D. M.** 1988. Epidemiology of meningococcal infection in England and Wales. J. Med. Microbiol. **26:**165–168.
30. **Kaiser, A. B., C. H. Hennekens, M. S. Saslaw, P. S. Hayes, and J. V. Bennett.** 1974. Seroepidemiology and chemoprophylaxis of disease due to sulphonamide-resistant *Neisseria meningitidis* in a civilian population. J. Infect. Dis. **130:**217.
31. **Kayhty, H., H. Jousimies-Somer, H. Peltola, and P. H. Makela.** 1981. Antibody response to capsular polysaccharides of groups A and C *Neisseria meningitidis* and *Haemophilus influenzae* type b during bacteremic disease. J. Infect. Dis. **143:**32–41.
32. **Knight, V., and J. A. Kasel.** 1973. Adenoviruses, p. 65–86. *In* V. Knight (ed.), Viral and mycoplasmal infections of the respiratory tract. Lea & Febiger, Philadelphia.
33. **Krasinski, K., J. D. Nelson, S. Butler, J. P. Luby, and H. Kusmiesz.** 1987. Possible association of *Mycoplasma* and viral respiratory infections with bacterial meningitis. Am. J. Epidemiol. **125:**499–508.
34. **Moore, P. S., L. H. Harrison, E. E. Telzak, G. W. Ajello, and C. V. Broome.** 1988. Group A meningococcal carriage in travelers returning from Saudi Arabia. J. Am. Med. Assoc. **260:** 2686–2689.
35. **Munford, R. S., A. Taunay, J. S. DeMorais, D. W. Frazer, and R. A. Feldman.** 1974. Spread of meningococcal infection within households. Lancet **ii:**1275–1278.
36. **Njoku-Obi, A. N., and J. A. C. Agbo.** 1976. Meningococcal carrier rates in parts of eastern Nigeria. Bull. W.H.O. **54:** 271–273.
37. **Novelli, V. M., R. G. Lewis, and S. T. Dawood.** 1987. Epidemic group A meningococcal disease in Haj pilgrims. Lancet **ii:**863.
38. **Olcen, P., J. Kjellander, D. Danielsson, and B. L. Lindquist.** 1981. Epidemiology of *Neisseria meningitidis*: prevalance and symptoms from the upper respiratory tract in family members to patients with meningococcal disease. Scand. J. Infect. Dis. **13:**105–109.
39. **Olyhoek, T., B. A. Crowe, and M. Achtman.** 1987. Clonal population structure of *Neisseria meningitidis* serogroup A isolated from epidemics and pandemics between 1915 and 1983. Rev. Infect. Dis. **9:**665–692.
40. **Peltola, H.** 1983. Meningococcal disease: still with us. Rev. Infect. Dis. **5:**71–90.
41. **Peltola, H., J. M. Kataja, and P. H. Makela.** 1982. Shift in the age distribution of meningococcal disease as a predictor of an epidemic? Lancet **ii:**595–597.
42. **Poolman, J. T., I. Lind, K. Jonsdottir, L. O. Froholm, D. M. Jones, and H. C. Zanen.** 1986. Meningococcal serotypes and serogroup B disease in Northwest Europe. Lancet **ii:**555–558.
43. **Public Health Laboratory Service (United Kingdom) Communicable Disease Surveillance Center.** 1987. Acute meningococcal infections: ex Mecca. Communicable Dis. Rep. **1987:**33.
44. **Reingold, A. L., A. W. Hightower, G. A. Bolan, E. E. Jones, H. Tiendrebeogo, C. V. Broome, G. W. Ajello, C. Adamsbaum, C. Phillips, and A. Yada.** 1985. Age-specific differences in duration of clinical protection after vaccination with meningococcal polysaccharide A vaccine. Lancet **ii:** 114–118.
45. **Salmi, I., O. Pettay, I. Simula, A. K. Kallio, and O. Waltimo.** 1976. An epidemic due to sulphonamide-resistant group A

meningococci in the Helsinki area (Finland). Scand. J. Infect. Dis. **8**:249–254.

46. **Schwartz, B., A. Al-Ruwais, and J. A. Ashi.** 1988. Comparative efficacy of ceftriaxone and rifampicin in eradicating pharyngeal carriage of group A *Neisseria meningitidis*. Lancet **ii**:1239–1242.
47. **Tikhomirov, E.** 1987. Meningococcal meningitis: global situation and control measures. World Health Stat. Q. **40**:98–108.
48. **Wenzel, R. P., J. A. Davies, J. R. Mitzel, and W. E. Beam.** 1973. Nonusefulness of meningococcal carriage rates. Lancet **ii**:205.
49. **World Health Organization.** 1973. Epidemiological surveillance and control of cerebrospinal meningitis in Africa. W.H.O. Chron. **27**:347–351.
50. **Young, L. S., F. M. LaForce, J. J. Head, J. C. Feeley, and J. V. Bennett.** 1972. A simultaneous outbreak of meningococcal and influenza infections. N. Engl. J. Med. **287**:5–9.