Meningococcal Disease among United States Military Service Members in Relation to Routine Uses of Vaccines with Different Serogroup-Specific Components, 1964–1998

John F. Brundage, Margaret A. K. Ryan, Brian H. Feighner, and Frederick J. Erdtmann

Historically, military recruits have been at high risk of acquiring meningococcal disease. Beginning in the 1940s, the US military relied on mass treatment with sulfadiazine to control outbreaks in training camps. In the 1960s, a vaccine was developed in response to the emergence of sulfadiazine-resistant strains. Since 1971, all new recruits in the US military have been immunized against Neisseria meningitidis during their first days of service. Serogroups represented in vaccines given to service members have changed over time: the quadrivalent (A, C, Y, W135) vaccine has been given since 1982. In the US military, meningococcal disease rates decreased by ~94% from 1964 to 1998. After initiating routine immunization in 1971, crude rates decreased sharply and have remained low; in addition, there have been few cases of disease caused by serogroups represented in contemporaneously administered vaccines. In the US military, immunizations have been effective for the prevention of disease caused by vaccine-homologous serogroups of N. meningitidis.

Meningococcal disease is a frequent companion of armies, particularly in recruit camps and during large-scale mobilizations [1]. During the first year of mobilization of the United States in World War I, the crude rate of meningococcal disease was 150 cases per 100,000 troops per year, and the case-fatality rate was 39% [1–3]. During World War II, there were nearly 14,000 cases of meningococcal disease among soldiers in the US Army; however, as a result of earlier diagnosis and the availability of antibiotics, the case-fatality rate was only 4% [1, 4–7]. From the end of World War II to the early 1960s, mass treatment of recruits with sulfadiazine was used successfully to prevent outbreaks of meningococcal disease in training camps [8–11].

In 1963, there were recruit camp outbreaks of meningococcal disease caused by sulfadiazine-resistant strains of Neisseria meningitidis [11–15]. By the late 1960s, Gottschlicke, Artenstein, Goldschneider, and colleagues at the Walter Reed Army Institute of Research (Washington, D.C.) had characterized determinants of immunity to [16] and developed a polysaccharide vaccine against serogroup C strains of N. meningitidis. From 1969 through 1971, controlled field studies among military trainees documented the efficacy (89.5%) of the vaccine against serogroup C disease [17, 18]. By the fall of 1971, all new enlistees in the US Armed Forces were receiving serogroup C vaccine during their first days of military service. In 1978 and 1982, respectively, bivalent (serogroups A and C) and quad-
rivalent (serogroups A, C, Y, and W135) meningococcal vaccines were incorporated into routine recruit immunization schedules.

This report reviews the US military’s experience with meningococcal disease from 1964 through 1998. The review spans periods when there was no vaccination provided as well as periods of routine use of vaccines with different serogroup-specific components. The military’s experience over the entire period provides insights that may inform decisions regarding meningococcal vaccine uses in other populations and settings.

PATIENTS AND METHODS

The review period extended from 1964 through 1998. For analysis purposes, the overall period was divided into 3 phases (on the basis of sources and characteristics of available data). Phases 1, 2, and 3 extended from 1964–1979, 1980–1989, and 1990–1998, respectively.

**Phase 1.** For each year from 1964 to 1979, annual rates of meningococcal disease were calculated by dividing the number of soldiers on active duty who were hospitalized for meningococcal disease by the total person-years of active service of US Army soldiers. Meningococcal disease hospitalization data were obtained from an unpublished report by one of the study authors (F.J.E.) who was the Disease Control Consultant of the Preventive Medicine Consultant’s Division, Office of the Surgeon General, Department of the Army (Washington, D.C.). Data for the report were extracted from the Individual Patient Data System, an archive of automated records of hospitalizations in US Army hospitals worldwide (US Army Patient Administration Systems and Biostatistical Activity, Fort Sam Houston, Texas).

**Phases 2 and 3.** For each calendar year from 1980 through 1998, annual rates of meningococcal disease were calculated by dividing the number of enlisted active-duty service members who were hospitalized for meningococcal disease by the total person-years of active service of enlisted members of the US Air Force, Army, Marine Corps, and Navy. Cases were identified from among hospitalizations of enlisted active-duty members of all Services with discharge diagnoses indicative of meningococcal disease (codes 036.0–036.9, *International Classification of Diseases*, Ninth Revision, Clinical Modification). During phase 2 (1980–1989), hospitalization data were abstracted from an unpublished report prepared by 2 of the authors (M.A.K.R. and B.H.F.). For the report, the authors accessed standardized records of all hospitalizations in US military hospitals worldwide. During phase 3 (1990–1998), cases were ascertained from the Defense Medical Surveillance System, a longitudinal relational database system operated by the Army Medical Surveillance Activity, Directorate of Epidemiology and Disease Surveillance, US Army Center for Health Promotion and Preventive Medicine. On a regular basis, the Defense Medical Surveillance System receives standardized records of all hospitalizations of active-duty service members in US military hospitals worldwide.

Numbers of active-duty service members were ascertained from files maintained by the Directorate for Information Operations and Reports, Washington Headquarters Services, Department of Defense (for years before 1990), and by the Defense Manpower Data Center, Seaside, California (for years since 1990).

Finally, from 1964 through 1980, isolates from US Army cases were routinely sent to a central reference laboratory (Department of Bacteriology, Walter Reed Army Institute of Research, Washington, D.C.) for serogroup characterization. After 1980, there was no systematic collection or characterization of meningococcal case strains.

RESULTS

Hospitalization rates. During the 35-year review period, there were 3044 cases of meningococcal disease among active-duty service members for whom data were available (figure 1). The crude rate during the period was 6.5 cases per 100,000 person-years. During the period when no meningococcal vaccines were routinely used (1964–1971), the crude rate of meningococcal disease was 23.6 cases per 100,000 person-years. During the period when monovalent (serogroup C) vaccine was routinely used (1972–1978), the crude rate of meningococcal disease was 3.5 cases per 100,000 person-years (rate ratio for monovalent vaccine vs. no vaccine, 0.15). During the period when bivalent (serogroups A and C) vaccine was routinely used (1979–1982), the crude rate of meningococcal disease was 2.3 cases per 100,000 person-years (rate ratio for bivalent vs. monovalent vaccine, 0.65; rate ratio for bivalent vaccine vs. no vaccine, 0.10). Finally, during the period when quadrivalent vaccine (serogroups A, C, Y, and W135) was routinely used (1983–1998), the crude rate of meningococcal disease was 1.4 cases per 100,000 person-years (rate ratio for quadrivalent vaccine vs. bivalent vaccine, 0.60; rate ratio for quadrivalent vaccine vs. monovalent vaccine, 0.40; rate ratio for quadrivalent vaccine vs. no vaccine, 0.06). Thus, from the period of no vaccine to quadrivalent vaccine use, the crude rate of meningococcal disease decreased by 94.2%.

Serogroups of case isolates. From 1964 until 1966, >85% of case isolates were serogroup B. In 1967, without a specific intervention, serogroup B strains sharply decreased in frequency and proportion, while the frequency and proportion of serogroup C strains sharply increased. From 1968 through 1971, >85% of case isolates were serogroup C. Finally, from 1972
through 1980, the serogroups of case strains were rarely homologous to serogroups represented in contemporaneously administered vaccines (figure 2).

Case fatality. Case-fatality data were available for US Army personnel hospitalized from 1964 through 1981. The case-fatality rate for the entire period was 7.2%. During periods of no vaccine use, monovalent vaccine use, and bivalent vaccine use, case-fatality rates were 7.2%, 7.3%, and 6.9%, respectively (figure 3). Thus, in contrast to the incidence of meningococcal disease, case-fatality rates did not significantly change in relation to the use or antigenic components of vaccines.

DISCUSSION

The main findings of this review are that, among US military service members, rates of meningococcal disease decreased by >90% from 1964 to 1998. In addition, crude incidence rates decreased sharply after the initiation of routine immunization, and the rates remained low thereafter. Finally, there have been few documented cases of meningococcal disease caused by serogroups that were represented in contemporaneously administered vaccines.

Throughout the period of review, rates of meningococcal disease decreased after each addition of new antigens to the vaccine that was routinely used among military trainees. It is of particular note that, in 1978, the serogroup A component was added to the routinely used monovalent (serogroup C) vaccine because, historically, serogroup A strains had been responsible for the largest and most widespread outbreaks in the US military [1] and overseas civilian [19] populations. Even though there had been few cases involving serogroup A during the period of monovalent vaccine use (figure 2), the overall rates decreased after the introduction of the bivalent vaccine.

In this review, case-fatality rates from 1964 through 1981 were ~7% overall. In addition, case-fatality rates were remarkably stable from before to after the initiation of routine meningococcal immunization. Thus, despite advances in intensive care practices in recent years, case-fatality rates among US service members before 1981 were consistent with estimates of current fatality rates among similarly aged US civilians with meningococcal disease [20–22].

Several limitations of this study should be noted when interpreting the results presented here. The most important, per-
haps, is that different data sources were used for both case ascertainment and population description on the basis of differences in availability of data during the past half-century. To some degree, this concern may be mitigated by the relative uniformity with which the military has maintained disease data and population data over time. Also, the authors’ collective experience in identifying and interpreting different military data sources, including data from before the era of microcomputers, may have ensured that all relevant information was captured fairly completely.

Second, because of differences in the availability of data, the first phase of the review (1964–1980) included all service members of all ranks, whereas later phases included only enlisted service members (~85% of the total). Unlike officers, enlisted service members undergo “recruit training,” are more likely to live in dormitory-style barracks, and have much higher risks of meningococcal disease. Consequently, enlisted service members (but not officers) receive routine meningococcal immunization at the start of their military service. Because data for relatively low-risk officers were included for the prevaccine but not the post-quadrivalent vaccine period, the true effect of the vaccine may be underestimated in this review.

Third, because of the availability of data, the first phase of the analysis included the experience of the US Army only, and subsequent phases included the experiences of all of the armed services. Because the other armed services’ experiences were generally similar to that of the US Army, it is likely that overall conclusions based on the Army’s experience alone would be similar, if not identical, to those based on all available data. Thus, we do not consider this to be a significant source of bias.

Fourth, decreases in the rates of meningococcal disease over time may not have been entirely attributable to the effects of meningococcal vaccines. For example, in the US Army, rates of meningococcal disease due to serogroup B sharply decreased in the late 1960s in the absence of any meningococcal vaccine intervention; furthermore, in 1970–1971, rates of disease due to serogroup C decreased before the vaccine was being routinely used [1]. In general populations, meningococcal disease rates and distributions of serogroups among cases significantly fluctuate over time [23, 24]. Thus, we are unable to precisely estimate the independent effects of vaccination, given the natural variability of background rates and serogroup distributions.

Finally, around the time that meningococcal vaccines were
introduced into routine use, other countermeasures were being implemented by the US military to reduce morbidity associated with acute respiratory-transmitted illnesses in general. For example, such interventions as reduced crowding in barracks, head-to-toe sleeping arrangements, strict separation of individuals in different training units (“cohorting”), and early recognition, treatment, and aggressive antibiotic prophylaxis of contacts of cases may have all played roles in reducing the incidence of meningococcal disease. Unfortunately, it is impossible to estimate the effects of non–vaccine-related interventions on the incidence of meningococcal disease.

US national surveillance data suggest that overall rates of meningococcal disease have been relatively stable in recent years [24]. In the 1990s, however, concern increased about the risk of meningococcal disease among college students who live in close quarters [25–27]. Thus far, states and schools have addressed such concerns inconsistently, with implementation of different requirements and recommendations [28–30]. The long and successful experience of the military services with meningococcal vaccines may be useful in considering vaccine uses in other high-risk populations and settings.

References