Safety Data on Meningococcal Polysaccharide Vaccine from the Vaccine Adverse Event Reporting System

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Recent recommendations by the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices may lead to the increased use of the meningococcal polysaccharide vaccine. The Vaccine Adverse Event Reporting System (VAERS) is useful for the detection of previously unrecognized reactions and for the monitoring of known reactions. Limitations of VAERS include underreporting and the inability to establish a causal relationship between vaccination and adverse events in most cases. From July 1990 through 31 October 1999, 110 adverse events were reported after receipt of meningococcal vaccine alone. Thirteen (12%) were serious, including 6 injection site reactions, 3 allergic reactions, 1 case of Guillain-Barré syndrome, and 3 miscellaneous events. Fever (30%), headache (17%), dizziness (15%), injection site hypersensitivity (13%), urticaria (12%), and paresthesia (10%) were among the most common events reported. Fever and injection site and allergic reactions are most likely causally linked to the vaccine. That there were few reports of serious adverse events, with >6 million doses having been distributed, and no clear signal of a previously unrecognized serious reaction is reassuring with regard to the safety of meningococcal vaccine.

Meningococcal polysaccharide vaccines to protect against subgroups A, C, Y, and W135 of Neisseria meningitidis are licensed and distributed in the United States. The quadrivalent vaccine has been recommended by the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) for use in controlling outbreaks in persons aged ≥2 years but not for routine immunization except for certain high-risk groups [1]. These high-risk groups include persons who have terminal complement component deficiencies, those with functional or anatomic asplenia, those who are routinely exposed to N. meningitidis in solution that may be aerosolized (e.g., laboratory workers), and travelers to countries or those who reside in countries in which infection with N. meningitidis is hyperendemic or epidemic [1]. This vaccine has been used extensively for travelers, for outbreak control, for military recruits since 1982 [2], and in a statewide immunization campaign in 1998 that targeted people aged 2–22 years who lived in Rhode Island [3]. Recently, the ACIP recommended that those who provide medical care to college students give information to students and their parents about meningococcal disease and the benefits of vaccination. The ACIP also recommends that vaccination should be provided or made easily available to college freshmen who wish to reduce their risk of disease; other undergraduate students can also choose to be vaccinated [1, 4].
According to the package insert of the quadrivalent vaccine, “adverse reactions...are mild and infrequent, consisting of localized erythema lasting 1–2 days. Up to 2% of young children develop fever transiently after vaccination. As with the administration of any vaccine, one should expect possible hypersensitivity reactions” [5]. Subsequent studies have reported injection site reactions in >40% of subjects after receipt of the quadrivalent vaccine [6, 7]. However, only 2% reported transient arm immobility caused by the local reaction [6], and injection site reactions that last >72 h occurred in only 2%–3% of patients who received the group A and C vaccine [8]. Fever (temperature >38.0°C) has been reported in 5% and headache in 3% of 18-month- to 20-year-old subjects who received the group A and C vaccine [9]. Several studies have been conducted after mass vaccination campaigns of children and adolescents, in which 20,000 to ~1.2 million persons were vaccinated, primarily with the group A or A and C vaccines. In addition to fever, headache, and local reactions, rare occurrences of allergic reactions [10, 11], anaphylaxis [11, 12], seizures [11, 13], and unexplained weakness and paresthesias [11, 14] have been reported. A causal relationship between the vaccine and the adverse event could not be conclusively established in many cases. Millions of doses of meningococcal vaccine are administered in sub-Saharan Africa’s “meningitis belt” [15]. However, safety surveillance is suboptimal in such settings where infection is endemic.

We summarize the reports to the Vaccine Adverse Event Reporting System (VAERS) of adverse reactions after meningococcal polysaccharide vaccination in the United States population, given recent recommendations that favor the expansion of its use.

METHODS

VAERS is a passive surveillance system jointly administered by the US Food and Drug Administration (FDA) and CDC that receives reports of adverse events temporally related to immunization from health care providers, vaccine manufacturers, and the public [16]. VAERS is useful to detect previously unrecognized adverse events that may warrant further investigation, monitor increases in known reactions, identify factors or preexisting conditions that may increase the risk of adverse reactions, and possibly identify vaccine lots with high rates of reported adverse events or noteworthy reactions [17]. Important limitations of VAERS include the lack of consistent diagnostic criteria, the fact that data are acquired from a diverse group of voluntary reporters, underreporting, and difficulty in determining whether a vaccine caused the adverse event that was reported [16]. Reports are classified according to severity as “less serious,” “serious” (involving hospitalization, prolongation of hospitalization, life-threatening illness, or permanent disability), or “fatal.” All serious and fatal domestic reports are followed up by telephone or written inquiry by FDA staff or nurse-researchers on the staff of the VAERS contractor. We queried the VAERS database for all reports related to the meningococcal vaccine from the database’s inception on 1 July 1990 through 31 October 1999. Foreign reports were reviewed but not included in the summary tabulations.

We calculated adverse event reporting rates on the basis of the number of domestic reports per year divided by the net annual number of doses distributed in the United States as reported to the CDC (CDC Biologics Surveillance, 1996–1998, unpublished data) [18]. For the years 1991–1993, the CDC data do not include doses distributed to the military. For these years, we added data obtained from the military to the CDC data to obtain the total number of doses distributed. Lack of data on number of doses distributed by age and sex precludes calculation of age- and sex-specific reporting rates. The actual number of doses administered is not available. We tabulated frequencies of commonly reported adverse events, as coded in the Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART) system [19], stratified by the meningococcal vaccine alone or with other simultaneously administered vaccines. Serious events were further classified by medical condition after review of the descriptive information on each report and stratified by age (<18 years vs. ≥18 years) and use of the meningococcal vaccine alone or with other simultaneously administered vaccines. Analyzed separately were events reported from Rhode Island with a vaccination date in 1998 as part of a statewide immunization effort [3] and events reported from military sources. The number of doses distributed in Rhode Island in 1998 was obtained from the Rhode Island Department of Health to calculate the adverse event reporting rate for Rhode Island in 1998.

RESULTS

During the period from 1 July 1990 through 31 October 1999, a total of 298 reports of 283 adverse events that included the meningococcal vaccine as one of the vaccines administered were filed with VAERS. There were more reports than events because VAERS received >1 report for some events. Nineteen of the events were from foreign sources, leaving 264 events in the United States to summarize. Thirty-eight (14%) of the 264 reported events were classified as serious, and there were no reports of fatalities associated with the vaccine in the United States. Among the foreign reports, there was 1 death, 11 serious events, and 7 events classified as less serious.

Among the 264 domestic adverse events reported, the meningococcal polysaccharide vaccine administered was for the A and C groups in 9 events (3%) and for the A, C, Y, and W135 in 35 events (13%); for 220 events (83%), the specific groups...
in the vaccine were not specified. We do not further distinguish among the vaccines in this study because the small numbers of events in the vaccine subgroups do not allow for meaningful analysis.

From 1991 through 1998, 6,061,422 net doses were distributed among the US civilian and military populations, and 222 adverse events were reported, for an average reporting rate during this period of 3.7 adverse events reported per 100,000 doses distributed. Distribution data for 1990 and 1999 were not available. The number of reports by year and seriousness, along with reporting rates, are shown in table 1.

In 110 (42%) of the 264 events, the meningococcal vaccine was administered alone. These 110 events included 13 serious (12%) and 97 reports (88%) of less serious events. In the remaining 154 events (58%), the meningococcal vaccine was administered with 1–7 other vaccines. The other vaccines most commonly administered simultaneously with meningococcal vaccine were typhoid (53; 34%), hepatitis A (42; 27%), yellow fever (41; 27%), inactivated poliovirus (30; 19%), tetanus/diphtheria (27; 18%), and hepatitis B (24; 16%).

Median time to onset of the event was <1 day (range, 0–367 days; interquartile range, 0–2 days; 174 104 after meningococcal vaccination alone and 1 day (range, 0–267 days; interquartile range, 0–5 days; 174 148 after administration of meningococcal vaccine in combination with other vaccines. The distribution was similar whether meningococcal vaccine was administered alone or in combination with other vaccines, so the distribution of time to onset of adverse events by seriousness is shown in figure 1 for all domestic reports combined.

The distribution of the frequency of events by age and severity for the 249 events for which it was reported is given in figure 2. The quadrivalent meningococcal vaccine was approved and is recommended for people aged ≥2 years [5], although the ACIP states that children as young as 3 months of age may be vaccinated to elicit short-term protection against serogroup A meningococcal disease [1]. There was 1 report of a serious event and 4 reports of less serious adverse events in children aged <2 years. The serious event was in a 1-year-old child hospitalized for vomiting and diarrhea 96 days after receiving the meningococcal vaccine alone. There were also 2 reports of injection site reactions, 1 of prolonged screaming (8 h after vaccination), and 1 of somnolence.

For the 248 events (94%) for which the gender of the vaccine recipient was known, fewer reports involved males than females who received meningococcal vaccine alone. In addition, the proportion of serious events was lower among males than among females after receipt of meningococcal vaccine alone (8% vs. 18%) but was greater among males than among females after receipt of meningococcal vaccine in combination with other vaccines (23% vs. 7%).

**Commonly reported events.** The most commonly reported COSTART terms are shown in table 2. These 10 COSTART terms account for 90 events (82%) for the meningococcal vaccine alone and 111 events (72%) for the meningococcal vaccine in combination with other vaccines. Commonly reported adverse events reported after meningococcal vaccination alone included the previously recognized adverse events of fever and

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### Table 1. Adverse events reported to the Vaccine Adverse Event Reporting System from the United States that included the meningococcal polysaccharide vaccine.

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious</td>
<td>1</td>
<td>4</td>
<td>9</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>12</td>
<td>6</td>
<td></td>
<td></td>
<td>38</td>
</tr>
<tr>
<td>Less serious</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>20</td>
<td>23</td>
<td>17</td>
<td>15</td>
<td>29</td>
<td>80</td>
<td>34</td>
<td>226</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>4</td>
<td>7</td>
<td>29</td>
<td>23</td>
<td>19</td>
<td>15</td>
<td>33</td>
<td>92</td>
<td>40</td>
<td>264</td>
</tr>
<tr>
<td>No. of doses</td>
<td>—</td>
<td>465,292</td>
<td>885,835</td>
<td>986,123</td>
<td>624,714</td>
<td>859,183</td>
<td>532,677</td>
<td>710,168</td>
<td>997,430</td>
<td>—</td>
<td>6,061,422</td>
</tr>
<tr>
<td>Reporting ratec</td>
<td>—</td>
<td>0.9</td>
<td>0.8</td>
<td>2.9</td>
<td>3.7</td>
<td>2.2</td>
<td>2.8</td>
<td>4.7</td>
<td>9.2</td>
<td>—</td>
<td>3.7d</td>
</tr>
</tbody>
</table>

a 1 July through 31 December 1990.

b Reports through 31 October 1999; distribution data were not available for 1999.

c Per 10⁶ doses.

d Average.
injection site reactions (table 2: “injection site hypersensitivity,” “vasodilation,” and “pain”). Hypersensitivity reactions were also expected and were observed in VAERS reports (table 2: “injection site hypersensitivity,” “rash,” “urticaria”; table 3: “allergic reaction”).

Adverse reactions not included in the package insert of the quadrivalent vaccine were also noted. “Headache” was the second most common adverse event coding term reported after meningococcal vaccination alone. All but 1 report of “dizziness” after vaccination began the same day as vaccination, and 2 gave the actual time of onset of reactions as having occurred within 45 min. Eight of the 16 reports described other symptoms (i.e., nausea, flushing, paleness, light-headedness) that were suggestive of a vasovagal reaction that is sometimes reported after immunization [20]. Nine reports of “hypertension” reflect a transient change in blood pressure after receipt of the vaccine. One event reflected chronic hypertension in the context of newly diagnosed IgA nephropathy.

Four of 11 reports of “paresthesia” described persistence of paresthesia for 1 year, although only 1 report noted a specific neurological pathology (Guillain-Barré syndrome, discussed below). A 29-year-old woman experienced decreased sensation and “heaviness” of limbs beginning 4 days after vaccination and lasting at least 2 weeks before she was lost to follow-up. “Numbness,” insomnia, fatigue, sore joints, and other symptoms developed 4 months after receipt of meningococcal vaccine in a 36-year-old man who also received the anthrax vaccine 1 month before the onset of his symptoms; his symptoms were still present 8 months after the meningococcal vaccination. A 29-year-old woman developed “numbness and tingling” in all extremities at an unknown interval after vaccination, and “pain” persisted as the only symptom for 1 year after vaccination; no evidence of permanent neurological residual was reported after an extensive evaluation. In 6 of the cases of paresthesia, symptoms occurred in ≥2 extremities. In 2 other cases, the symptoms occurred in a single limb, but not the limb in which the vaccine was injected. In 1 case, Raynaud’s phenomenon was diagnosed after the patient’s hands and fingers turned white and became numb.

**Serious events after meningococcal vaccination alone.** The most common serious events are shown in table 3, grouped by medical condition. One case of Guillain-Barré syndrome in a 9-year-old boy was diagnosed 32 days after he received meningococcal vaccine alone, after 2 weeks of worsening paresthesias. He recovered after hospitalization for this illness. The 4 cases of Guillain-Barré syndrome after simultaneous administration of multiple vaccines occurred 7–16 days after vaccination; of note, 3 of the 4 patients also reported respiratory infections 1–2 weeks before the onset of Guillain-Barré syndrome. Two of these persons are reported to have recovered, and no information is available on the recovery status of the others.

Reports of serious injection site reactions after meningococcal vaccination alone include 4 girls aged 2–11 years, a 21-year-old woman, and a 48-year-old man. These events were
Table 3. Nonfatal serious adverse events after meningococcal vaccination reported to the Vaccine Adverse Event Reporting System.

<table>
<thead>
<tr>
<th>Condition</th>
<th>MV alone</th>
<th></th>
<th>MV in combination</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children and adolescents (&lt;18 y)</td>
<td>Adults (≥18 y)</td>
<td>Total</td>
<td>Children and adolescents (&lt;18 y)</td>
</tr>
<tr>
<td>Nervous system</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GBS</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>4</td>
</tr>
<tr>
<td>Convulsion</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Optic neuritis</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Diplopia</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>2</td>
<td>—</td>
<td>3a</td>
<td>—</td>
</tr>
<tr>
<td>Arthralgia and fatigue</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Nausea/vomiting or diarrhea</td>
<td>1</td>
<td>—</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Other</td>
<td>—</td>
<td>2</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>4</td>
<td>13a</td>
<td>3</td>
</tr>
</tbody>
</table>

NOTE. GBS, Guillain-Barré syndrome; MV, meningococcal vaccine.

* Age not reported for 1 event.

classified as serious because the patients were hospitalized in 4 cases and because of pain and limitation in arm use that continued to be present at the time of the report 4 and 6 weeks after vaccination in 2 cases. Two of the 6 patients received antibiotics, although no definitive evidence of infection was presented. All of the serious injection site reactions occurred within 24 h of vaccination.

The reports of allergic reactions included a 10-year-old boy and 3-year-old girl who developed urticaria and difficulty in breathing that required hospitalization within 1 day of vaccination. There was a third report of rash that developed on the arms, fingers, neck, and face within 1 h of vaccination associated with upset stomach that also resulted in hospitalization. The patient’s age was not reported.

Vomiting and diarrhea were reported in a 1-year-old child who was hospitalized 96 days after having received the vaccine. The serious adverse events in the “other” category after receipt of meningococcal vaccine alone included an 18-year-old woman who developed hematuria and proteinuria 3 days after vaccination and who had IgA nephropathy diagnosed and an 18-year-old woman recovering from mononucleosis who experienced chronic fatigue and weakness.

Serious events after receipt of meningococcal vaccine in combination with other vaccines. Serious neurological adverse events that occurred after administration of meningococcal vaccine in combination with other vaccines included 2 reports of convulsions. One case was in a 3-year-old girl who developed fever (temperature, ≥40.5°C) followed by a seizure 18 h after administration of meningococcal, cholera, and typhoid vaccines as well as γ-globulin. She was hospitalized, and the findings of her evaluation, including lumbar puncture, were reported to be normal. No information on her long-term status is available. The other report of convulsion was in an 18-year-old man who developed “involuntary muscle contraction lasting 10 seconds” 1 day after receipt of meningococcal and influenza vaccines. Results of CT and MRI, lumbar puncture, and electroencephalography were all reported to be normal.

Two cases of paresthesia, distinct from those previously discussed, were reported. One report was of a 28-year-old woman who developed “numbness, fatigue, weakness, aches, [and] fever” 1 day after she received meningococcal, measles, mumps, rubella, and tetanus vaccines and who had peripheral polynuropathy with some persistent symptoms diagnosed 60 days after the event. The second case was in a 20-year-old man who was hospitalized because of “numbness” on the right side of his body that began 24 h after receipt of meningococcal, influenza, diphtheria, and tetanus vaccines. A specific diagnosis for this condition was not reported.

Two reports of optic neuritis were also included in VAERS. One case was in a 40-year-old man, which occurred 10 days after he received meningococcal, influenza, and inactivated poliovirus vaccines, and the other was in an 8-year-old girl, which occurred 4 days after administration of meningococcal and hepatitis B vaccines. The final serious neurological event after vaccination with meningococcal vaccine in combination with others was diplopia that developed in a 49-year-old man 10 days after receipt of meningococcal, tetanus, diphtheria, yellow fever, typhoid, and inactivated poliovirus vaccines, concomitantly with the administration of mefloquine for malaria prophylaxis. Serious reports after vaccination with the meningococcal vac-
cine in combination with other vaccines also included 3 men, aged 31–38 years, with similar symptoms (joint pain, fatigue, rash, and abdominal pain) that resulted in hospitalization. Time to onset was 31 days after immunization in 1 case and was not given in the other 2. There was an injection site reaction in a 7-year-old boy that began the day of vaccination and resulted in hospitalization and another report of an injection site reaction in a 53-year-old man that lasted 8 weeks and was treated with prednisone. The 5 reports of nausea and vomiting were in men 20–61 years of age, 4 of whom developed symptoms within 1 day of vaccination and one of whom developed symptoms 5 days after vaccination. All 5 patients required hospitalization. The other reports included a case of fever and pulmonary edema in a 54-year-old man with history of hypertrophic cardiomyopathy which occurred 1 day after vaccination; dyspnea and fatigue which occurred at an unknown time after vaccination in a 40-year-old woman who was later diagnosed with polyclonal gammopathy; and fevers that began 1–2 days after vaccination that required hospitalization in both a 32-year-old man and 29-year-old woman.

**Other clinically significant events.** In addition to the serious events listed in table 3, several clinically significant events were submitted to VAERS, but the reporters did not indicate that any of the criteria for a “serious” event were met. A 2.5-year-old girl with a history of seizures related to fever was reported to have fever (temperature above 40°C) and seizures related to fever 3 days after she received meningococcal vaccine alone. A tonic clonic seizure followed by a post-ictal state occurred immediately after vaccination with hepatitis A and meningococcal vaccines in a 31-year-old man with a history of seizures. Finally, there was 1 report of anaphylaxis in an 18-year-old man who developed difficulty breathing, tachycardia, edema, and urticaria 1 min after simultaneous administration of meningococcal, influenza, and hepatitis B vaccines.

**Reports from Rhode Island, the military, and foreign sources.** Sixty events were reported from Rhode Island in 1998 in connection with a statewide immunization campaign in which 275,000 doses of vaccine were distributed (Susan Shepardson, Rhode Island Department of Health, personal communication), for a reporting rate of 21.8 adverse events reported per 100,000 doses distributed. Nine of these events were classified as serious and 51 were classified as less serious. The serious reports consisted of 5 cases of injection site reactions, 2 reports of urticaria and difficulty breathing, and the report of Guillain-Barré syndrome in an aforementioned 9-year-old boy, all of which occurred after receipt of meningococcal vaccine alone. There was also 1 report of optic neuritis in an 8-year-old girl 4 days after she received the meningococcal and hepatitis B vaccines, previously discussed. The 5 most common adverse event coding terms were as follows: fever (34; 57%), headache (19; 32%), dizziness (16; 27%), injection site hypersensitivity (15; 25%), and urticaria (13; 22%). All but 2 adverse events were in the age group that contained people targeted in the immunization campaign (i.e., people aged 2–22 years). Fifty-seven events were associated with the meningococcal vaccine alone.

All military recruits (~180,000 per year) receive the meningococcal vaccine [1]. In addition, another 1–2 times the number of doses administered to recruits are administered to other military personnel. A total of 4,075,250 doses were distributed to the military during the years 1991–1998 (David Trump, Office of the Assistant Secretary for Health, Department of Defense, personal communication). There were 25 events (16 during 1991–1998, 10 (40%) of which were serious and 15 (60%) of which were less serious events, reported to VAERS during the period under study. The adverse event reporting rate for 1991–1998 in the military was 0.4 reports per 100,000 doses distributed. The serious events included 3 cases of Guillain-Barré syndrome; 3 cases of joint pain, fatigue, rash, and abdominal pain; 2 cases of fever; 1 case of nausea and vomiting; and 1 case of IgA nephropathy, previously discussed. The 5 most commonly reported COSTART terms were chills (8; 32%), asthenia (7; 28%), fever (7; 28%), headache (6; 24%), and dyspnea (5; 20%). The case of IgA nephropathy was reported after receipt of meningococcal vaccine alone; all other events occurred after simultaneous administration of multiple vaccines. Other simultaneously administered vaccines in this group included typhoid (11; 44%), anthrax (9; 36%), influenza (7; 28%), hepatitis B (4; 16%), adenovirus (3; 12%), cholera (3; 12%), hepatitis A (3; 12%), tetanus/diphtheria (3; 12%), and yellow fever (3; 12%).

No reports of death were made to VAERS for meningococcal vaccines administered in the United States. There was only 1 death report in VAERS after meningococcal vaccination: an 18-year-old died of meningitis during an outbreak of group C meningococcal disease in Ontario, Canada [21]. The patient received the vaccine as part of an immunization campaign and fell ill 4 days later. No other details were available on this case. There were also 4 foreign reports of failure of the vaccine to protect against nonfatal meningococcal disease. Two of the 4 cases were reported as being caused by group C N. meningitidis and the other 2 cases did not report the type. Of 11 serious reports from outside the United States, only 3 described events that occurred after meningococcal vaccination alone, including persistent paresthesia in a 35-year-old woman that began 31 days after immunization, myocarditis the day after immunization in an 8-year-old boy, and atypical pneumonia 1 day after vaccination in a 50-year-old woman. The remaining 8 reports of serious events occurred after simultaneous administration of multiple vaccines and were clinically heterogeneous. There was also 1 report of diplopia 1 day after vaccination with meningococcal vaccine alone in an 8-year-old boy, which was
classified as “less serious” because the reporter did not indicate that any of the criteria for a “serious” event were met.

**DISCUSSION**

Here, we summarize the reports of adverse events to VAERS during a period when >6 million doses of meningococcal vaccine were distributed in the United States. Compared with the number of doses distributed, relatively few serious adverse events were reported, and no patterns of previously unrecognized reactions clearly related to the vaccine were found in our review. However, as evidenced by the reports of the vaccines most commonly administered simultaneously with meningococcal vaccine, many meningococcal vaccinations are administered to travelers. Underreporting to VAERS may be greater among travelers than among the general population, because many of the adverse events in travelers will occur while those persons are out of the country [22]. More complete information on the safety of vaccines among travelers may be available from a consortium of travel clinics such as the Geosentinel sites [23].

There was some variability in reporting rates by year, with 1998 having the highest rate. The increase in reporting in 1998 is primarily because of 60 reports from Rhode Island after a statewide meningococcal immunization campaign that reached 60%–70% of people aged 2–22 years in the state [3]. The reporting rate in the military is lower than the reporting rate from nonmilitary populations during the period of 1991–1998. Because the role of meningococcal vaccine in adverse events reported after simultaneous administration of multiple vaccines is difficult to interpret, we focus our discussion on adverse events reported after meningococcal vaccination alone.

Guillain-Barré syndrome was not seen in previous studies of meningococcal vaccination but was reported once to VAERS after meningococcal vaccination alone and 4 times after administration of meningococcal vaccine simultaneously with other vaccines. The increased risk of Guillain-Barré syndrome after influenza vaccination has been noted primarily in the second week after vaccination, although the period of increased risk may be as long as 6 weeks [24]. The 1 case of Guillain-Barré syndrome after meningococcal vaccination alone occurred 32 days after vaccination after 2 weeks of worsening paresthesias, although this might occur in temporal association with the vaccine by chance alone. The cases of Guillain-Barré syndrome reported after simultaneous administration of multiple vaccines occurred 7–16 days after vaccination. The role of vaccination in these cases is difficult to assess because respiratory infections were associated with 3 of the 4 cases, and respiratory infections have been shown to predispose to development of Guillain-Barré syndrome [25].

There were 10 reports of paresthesia after meningococcal vaccination alone. Similar adverse reactions have been reported after mass vaccination campaigns [11, 14], although a causal relationship with the vaccine has not been established. An immunologically mediated process has been hypothesized as an explanation of both central and peripheral neurological events after vaccination [26]. All other serious neurological adverse events occurred after meningococcal vaccine was administered in combination with other vaccines, making the role of the meningococcal vaccine in these events difficult to determine.

The serious report of vomiting and diarrhea involved a 1-year-old child 96 days after the child had received the vaccine and was unlikely to be related to vaccination. The few serious adverse events in the “other” category were clinically heterogeneous and lacked a clear biological link to the vaccine.

The reported intervals for the injection site and allergic reactions after meningococcal vaccination alone were all within 24 h of vaccination. This close temporal relation makes a causal association with the vaccine more likely. Vaccine components that might contribute to these reactions include residual endotoxin [10, 27] or protein not removed during the purification of the vaccine, the preservative thimerosal [28], or the meningococcal polysaccharide antigens. However, no specific information is available from VAERS reports to identify the cause of the reactions.

The adverse events of fever and injection site reactions reported after receipt of meningococcal vaccine alone were consistent with what was found in the safety and immunogenicity trials during the development of the quadrivalent vaccine [29, 30]; they provide further support for a causal link. Systemic adverse events, such as headache and dizziness, may be linked to the vaccine, although such events are routinely reported following administration of placebo in clinical trials, and the high background prevalence of these conditions prevents supporting a causal link in all cases.

The sole report of death after meningococcal vaccination occurred outside the United States and was related to failure of the vaccine to prevent meningococcal disease. The death occurred during an epidemic of meningococcal type C disease, and illness began just 4 days after vaccination. Four other cases of failure of the vaccine to protect against meningococcal disease 97–378 days after vaccination were also reported from foreign sources. The vaccine has been shown to be 85%–95% effective against meningococcal subgroups A and C [5], so 100% effectiveness is not expected, especially if insufficient time is allowed between vaccination and exposure to *N. meningitidis*. The vaccine provides maximal protection at 10–14 days after immunization [5].

Other safety evaluations of the meningococcal polysaccharide vaccines have noted similar adverse events after meningococcal vaccination [10–14]. Fever and injection site and allergic reactions, which include serious cases, are likely to be causally linked to the vaccine. However, the relatively few reports of
serious adverse events with >6 million doses of meningococcal polysaccharide vaccines distributed, and the lack of previously unrecognized events with a clear causal relationship to the vaccine, are reassuring with regard to the safety of the meningococcal vaccine. The likely expansion of meningococcal vaccination to even larger numbers of people provides additional opportunity for safety surveillance. We encourage reports of adverse events after vaccination to VAERS. Information on VAERS and the VAERS reporting form is available on the Internet at http://www.vaers.org or http://www.fda.gov/cber/vaers/vaers.htm or at (800) 822-7967.

**VAERS WORKING GROUP**

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**Acknowledgments**

We thank Diane Erwin, for assistance with computer programming for the analysis of the VAERS database, and Carl Frasch and Leslie Ball, for helpful suggestions and manuscript review.

**References**


