Norwalk-like Virus Infection in Military Forces: Epidemic Potential, Sporadic Disease, and the Future Direction of Prevention and Control Efforts

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The impact of Norwalk-like virus (NLV) infection on military forces is evaluated in this report. NLVs were a major cause of both outbreaks and sporadic disease among crowded US ground troops in the 1991 war with Iraq. NLVs also have been found to be a cause of acute gastroenteritis in other ground and shipboard deployments. Four large outbreaks of acute gastroenteritis were investigated aboard US Navy aircraft carriers between 1992 and 1997. In these outbreaks, NLVs were identified as the probable cause, and crowding was a major risk factor for transmission. An evaluation of a routine shipboard deployment also suggests that NLVs cause sporadic gastroenteritis. These data indicate that NLV infection is a major cause of acute morbidity in military forces. Because of the limitations of available prevention and control methods, development of a vaccine against these viruses may be the best solution in the military environment.

Norwalk virus (NV) is a common cause of acute gastroenteritis outbreaks worldwide [1, 2]. In both developed and developing countries, NV infections begin in infancy, and by adulthood, a large proportion of the population has been infected [3–6]. Since the time this RNA virus was identified in 1972 [7], other morphologically related, small round structured viruses also have been found to cause outbreaks of gastroenteritis [8]. These viruses recently have been classified in a separate, provisionally named genus, “Norwalk-like viruses” (NLVs), within the family Caliciviridae [9].

NLV infection typically presents with rapid-onset of acute vomiting, diarrhea, nausea, and abdominal cramps. Although symptoms are self-limited after 1–2 days, a substantial proportion of infected individuals are incapacitated and may require medical care [1]. Challenge studies with NV have demonstrated high infection rates, frequent subclinical infections, and viral shedding in stools as early as 15 h after exposure, with prolonged excretion for 7–14 days [10, 11].

Transmission of NLVs often occurs via the fecal-oral route and involves contaminated food and water [12]. Epidemic gastroenteritis, which can occur in crowded populations, is characterized by large numbers of secondary cases due to person-to-person spread [13], possibly through aerosolized vomitus [14–17]. Infected food handlers can be responsible for large outbreaks [18], and contaminated ice has been implicated in widespread transmission [19].

Deployed military personnel are at particularly high risk of epidemic gastroenteritis because of crowded conditions that facilitate rapid person-to-person transmission of viral pathogens. Furthermore, high levels of sanitation are difficult to maintain in hurried combat deployments. In this review, the role of NLVs in causing acute morbidity among military forces is reviewed, and results are presented from investigations of outbreaks and sporadic gastroenteritis among deployed troops.

Materials and Methods

Literature review. A medical literature search for articles related to NV infection among military populations was conducted using MEDLINE and various MESH headings (calicivirus, Norwalk virus) and key words (gastroenteritis, military medicine). In addition, a comprehensive search of the reference section of publications related to this subject was conducted to identify relevant articles.

Medical record review. To determine how extensive a problem acute gastroenteritis poses for shipboard personnel, a review of the medical logs of all eight US Atlantic Fleet aircraft carriers was conducted for 1991–1994. US aircraft carriers typically deploy for 180 days about every 18 months. Until 1995, the medical staff of each Atlantic Fleet carrier was required to file a tally of the number of patients evaluated in sick call for a variety of illnesses. The medical logs containing these data were reviewed, and the number of episodes of acute vomiting seen per month was analyzed.

Sick-call visits for acute gastroenteritis usually were diagnosed clinically, without laboratory confirmation to rule out other infectious causes of vomiting or seasickness. However, seasickness is not a common problem on aircraft carriers, and viral pathogens
frequently are implicated in outbreaks of vomiting aboard large military ships.

Serologic investigation. A large outbreak of acute gastroenteritis was investigated aboard a US Navy aircraft carrier in 1992 [20]. Subsequent to this outbreak, a study was initiated to investigate outbreaks of vomiting aboard other carriers. The medical officers of aircraft carriers were contacted prior to departure for 6-month deployments to the Mediterranean and Western Pacific during the period 1995–1998. The ships’ senior medical officers were instructed to implement an outbreak investigation if they noted ≥25 cases of acute gastroenteritis within a 48-h period. Patients seen in sick call for acute vomiting were asked to donate an acute-phase serum specimen and to return in 10–14 days to provide a convalescent sample.

Because of a previously planned and unrelated study, laboratory capabilities were available in the initial shipboard outbreak to evaluate patients for bacterial causes of acute gastroenteritis [20]. In later shipboard investigations, it generally was not possible to conduct this kind of analysis because of limited clinical laboratory facilities on combat ships. However, evidence of NV infection was found in all investigated outbreaks of vomiting aboard US aircraft carriers.

In addition to investigations of acute outbreaks, a shipboard population deployed to the Mediterranean in 1991 was evaluated for the causes of acute diarrhea. This deployment, which began in August on the East Coast of the United States and lasted 6 months, was not associated with a recognized outbreak of acute gastroenteritis. However, sporadic cases of diarrheal disease were frequently evaluated in sick call after shore leave, which is customary in deployments to this region of the world. A serum sample was collected at the beginning and end of the deployment from 2000 personnel. Also, a questionnaire survey was administered after the deployment, which elicited information about any episode of diarrhea (defined as ≥3 loose or watery stools within a 24-h period), but data on acute vomiting was not obtained.

In shipboard investigations, paired serum samples collected at least 10 days apart were evaluated by a broadly reactive enzyme immunoassay for antibodies to the recombinant NV capsid antigen (anti-NV) [21]. A ≥4-fold rise in antibody level was considered evidence of recent NLV infection [22, 23].

Results

Literature review. Surveillance investigations indicated that NLVs were a major cause of both outbreaks and sporadic cases of acute gastroenteritis among crowded US ground forces deployed to Saudi Arabia during the war with Iraq in 1991 [24, 25]. NLVs also have caused acute gastroenteritis in other ground deployments [26], among deployed shipboard personnel [27], and during routine garrison duties [28].

In addition to military ships, commercial cruise ships often have experienced outbreaks of gastroenteritis caused by Norwalk and related enteric viruses [29–34]. These shipboard outbreaks have sometimes recurred during subsequent cruises [29, 30, 34]. Investigations of other non-military populations indicate that NLVs also may have a role in causing sporadic cases of traveler’s diarrhea [35, 36].

Medical record review. The review of the medical logs of eight Atlantic Fleet aircraft carriers revealed that acute vomiting has been a common problem. During a total of 159 months of active service between 1991 and 1994, there were 10,398 sick-call visits for acute vomiting. For each ship, which had average crew sizes of 3000 individuals in port and 5000 while deployed, the median number of cases evaluated per month was 41 (range, 0–775). The data also suggested that 10 outbreaks of acute gastroenteritis (defined as ≥200 cases of acute vomiting in a single month) may have occurred aboard six of the eight aircraft carriers during this 4-year period.

Shipboard outbreaks. In the spring of 1992, a large outbreak of gastroenteritis occurred on a US aircraft carrier with 4500 personnel 1 day after departing from the East Coast of the United States [20]. Gastroenteritis, defined as acute vomiting or diarrhea, was reported in all areas of the ship by 13% of the surveyed crew. Fifty-eight percent of affected sailors sought medical care, depleting all intravenous rehydration fluids aboard ship. In addition, routine operations were adversely affected because 7% of the crew missed ≥1 day of work because of illness. Half of 32 sailors with gastroenteritis seroconverted to anti-NV, and NLV particles were found in 2 stool samples by immune electron microscopy [20].

This outbreak persisted over a 5-week period. Although the number of new cases decreased substantially during the first port visit in the Mediterranean, a rapid increase of cases recurred after the port call. By the second port visit, the epidemic had ended. Of note, crew members were widely dispersed just before the deployment began, and during the outbreak, crew members living in the most crowded sleeping compartments were at more than a two times higher risk of developing illness.

In June 1996, another US aircraft carrier experienced an outbreak of gastroenteritis beginning 6 days after a 4-day port visit to Singapore. This outbreak lasted 2 weeks and affected >800 (14%) of the 5600 crew members. Seroconversion to NLV antibody was found among 45 (67%) of 67 evaluated cases of acute gastroenteritis.

In September 1996, a third US aircraft carrier experienced an outbreak of gastroenteritis that began during a port call in Rhodes, Greece. Approximately 450 cases occurred in 13 days among ~5600 personnel. One-half of patients seen in sick call were lost to routine duties. Many cases of gastroenteritis received intravenous fluids because of dehydration. Seroconversion to anti-NV was found among 22 (73%) of 30 paired serum samples.

A fourth large outbreak of probable Norwalk gastroenteritis aboard a US aircraft carrier was researched separately from the preceding shipboard investigations [37]. This outbreak occurred in September 1997, 8 days after a port visit in Japan, and lasted 2 weeks. Forty-four percent of the 4200-member
crew may have been affected. Eleven percent of the crew sought medical attention, with >50% receiving rehydration therapy.

A likely source of NLV infection was not found in any of these shipboard outbreaks. Adequate chlorination was present in potable water supplies, and all shipboard food was obtained from previously inspected and approved sources. It was concluded at the end of these outbreaks that >1 crew members probably had acquired the infection during shore leave and then returned to the ship where crowding facilitated transmission. No particular season of the year was associated with the occurrence of these shipboard outbreaks.

Because of high operational tempos aboard combat ships and the increased risk of accidents among sick crew members, intravenous fluids often were used to treat dehydrated sailors so that they could recover more quickly. These outbreaks compromised operational activities by preventing key personnel from carrying out critical tasks, such as assisting in aircraft landing operations.

**Routine shipboard deployment.** During a routine 6-month deployment to the Mediterranean, 40% of 2000 surveyed personnel reported at least one episode of acute diarrhea. Among 100 randomly selected individuals with acute diarrhea, 29% developed a >4-fold rise in titer to NLV antibody, compared with seroconversion among 14% of 100 sailors who did not develop diarrhea ($P < .05$).

**Discussion**

A review of the medical literature and studies of shipboard personnel indicate that NLVs are a major cause of acute morbidity among US military forces. Outbreaks have compromised routine military operations among both shipboard and ground personnel [20, 24, 38]. In addition to disruptive outbreaks, a study of a routine shipboard deployment suggests that NLVs may cause sporadic disease in crowded military populations. Studies of other military populations and travelers also suggest that NLVs cause sporadic gastroenteritis [39].

In military outbreaks, the major risk factor for NV infection appears to be crowding, which limits the options that can be taken to control transmission. Obviously, shipboard personnel cannot be dispersed. Transmission may be interrupted if a port visit has been scheduled, although outbreaks can recur [20]. Some separation may be possible among ground personnel, but during wartime deployments, dispersal of combat troops is not feasible. The effectiveness of any temporary measures to reduce crowding is limited because of the ease of transmission of NLVs and prolonged shedding after both symptomatic and asymptomatic infection [40].

Besides alleviating crowding, there are few alternatives for controlling NLV transmission. Sending sick troops home during garrison duty may be helpful, although removing symptomatic workers and food handlers has not consistently ended outbreaks [41]. Stringent clean-up of toilets, food preparation facilities, and living quarters also is important but has not reliably controlled transmission [42, 43]. Increased chlorination of potable water and heating food may be of limited benefit [30, 44, 45].

Without adequate methods of prevention and control, development of a vaccine against NLVs may be the best solution to this infectious disease risk in the military environment [46]. However, there are a number of potential problems with the development of a vaccine. Challenge studies suggest that there is short-term but not consistent long-term immunity after infection [47, 48], and some individuals are repeatedly susceptible to symptomatic infection, whereas others never develop symptoms, even after direct challenge [47, 49].

It is also important to note that numerous studies have demonstrated that natural immunity is not widespread [50] and that prior exposure to NV, as evidenced by pre-existing IgA or IgG serum antibody to NV, is not consistently protective [51–54]. However, no serologic assay has been developed to measure neutralizing antibody titers to NLVs because these viruses cannot be cultivated in vitro. Therefore, it remains possible that neutralizing antibodies will correlate with protective immunity.

In addition to questions about long-lasting immunity, there are problems that arise due to the considerable genetic diversity among NLVs [2, 55, 56]. Infection with 1 NLV strain may not provide cross-protection against other strains [57], a factor that could make it difficult to develop a broadly effective vaccine [58]. A candidate NV vaccine has been developed, although it is not known whether it induces homotypic or heterotypic protective immunity [59, 60]. And, even if NLV transmission is prevented, there are other enteric viruses that could cause acute gastroenteritis among military forces [61].

**References**


