Passenger Behaviors Associated With Norovirus Infection On Board a Cruise Ship—Alaska, May to June 2004

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Background. During May 2004, the Vessel Sanitation Program (VSP) investigated an outbreak of norovirus gastroenteritis on board a cruise ship sailing in Alaska waters. The objectives were to identify a common food item source and explore behavioral risk factors for person-to-person transmission among passengers.

Methods. A case was defined as three or more episodes of loose stools within 24 hours or two or fewer episodes of loose stools accompanied by one or more episodes of vomiting. Vomitus and stool samples from affected passengers were tested for norovirus by reverse transcriptase–polymerase chain reaction. Environmental health officers performed an environmental investigation following VSP protocol. Questionnaires about food items consumed and behavioral risk factors were placed in cabin mailboxes (n = 2,018). A case-control study design using multivariable logistic regression tested associations between risk factors and disease.

Results. A total of 359 passengers (24.1% of respondents) met the case definition. Four of seven clinical specimens tested positive for norovirus. No significant deficiencies in environmental health practices were identified, and no meal servings were associated with disease. Having a cabin mate sick with diarrhea or vomiting [odds ratio (OR): 3.40; 95% confidence interval (CI) = 1.80–6.44] and using a specific women's toilet that was contaminated with vomit (OR: 5.13; 95% CI = 1.40–18.78) were associated with disease. Washing hands before meals was protective (OR: 0.25; 95% CI = 0.12–0.54) against disease.

Conclusions. Widespread person-to-person norovirus outbreaks can occur on board cruise ships, even with appropriate environmental health practices. Programs to prevent and control norovirus outbreaks on board cruise ships should involve strategies that disrupt person-to-person spread and emphasize hand washing.

The cruise line industry has experienced record growth in recent years.[1] The Cruise Line International Association (CLIA), which represents >95% of the North American cruise market, reported 8 million passenger embarkations from North American ports in 2003 and an increase in sales among North American passengers of 6.8 and 14.7% during the first and second quarters of 2004, respectively. CLIA members introduced 62 new ships during 2000 to 2004, and passenger demand exceeded the industry's capacity for growth with occupancy rates above 102.3% since 2003.[1] Because outbreaks of gastrointestinal illness can occur on board cruises from consumption of contaminated water, ice, or food items or by person-to-person spread, the increase in the number of passenger days

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at sea also represents an expansion of a population at risk for disease.[2–6]

In 1975, the then Centers for Disease Control (CDC) established the Vessel Sanitation Program (VSP) to minimize the risk for gastrointestinal illness among passengers and crew on board ships arriving from foreign ports. In addition to conducting unannounced sanitation inspections, VSP operates the Gastrointestinal Illness Surveillance System (GISS), requiring ships to maintain a log of passengers and crew who experience gastroenteritis meeting a syndromal case definition.[2,7] Per GISS protocol, routine reporting of gastroenteritis cases is required when sailing into the United States from foreign ports and is required at any time when ≥2% of the passengers or crew on board are ill.[7]

During 1990 to 2000, VSP inspection scores steadily increased, whereas the proportion of vessels failing sanitation inspections decreased from 27.3% to 7.4%. The incidence of outbreaks of diarrheal disease subsequently decreased from 6.2 outbreaks per 1,000 cruises to 3.7 outbreaks per 1,000 cruises.[7] Despite these improvements, widespread outbreaks of gastrointestinal illness continue to occur on board cruise ships docking at ports in the United States. In 2002, a total of 21 outbreaks were reported to VSP; an infectious etiology was identified for 12 outbreaks, 9 (75%) of which were associated with noroviruses.[8]

During May 2004, VSP received an electronic report, through GISS, of an outbreak of gastrointestinal illness among 190 (9.4%) of 2,018 passengers and 20 (2.2%) of 896 crewmembers on board cruise ship A. The ship's original itinerary was an 8-day cruise, embarking from Vancouver, Canada, on May 29, 2004, touring the Alaska coast, visiting three ports of call, and disembarking at Whittier, Alaska, on June 5, 2004. Medical staff on board the vessel screened six clinical specimens by using enzyme-linked immunosorbent assay (ELISA). Five (83%) specimens were positive for norovirus. Because of the magnitude of the outbreak and continued evolution of cases, on May 31, 2004, VSP initiated an environmental and epidemiologic investigation on board the ship. Because previous outbreaks of norovirus on board cruise ships focused on but failed to identify common source risks associated with illness, despite appropriate methodology, the investigators of this outbreak added an additional focus to their investigation, in which behavioral risk factors for person-to-person transmission among passengers were explored.[8–12]

Methods

Epidemiologic Investigation

A passenger survey was designed to collect demographic information, symptom profiles, and possible exposures associated with illness from passengers and crew. From hypothesis-generating interviews with medical staff and early cases among passengers, staff from the CDC identified likely behavioral risks, including traveling with or sharing a cabin with an ill passenger; witnessing public vomiting episodes; hand washing and other personal habits (eg, smoking); participation in pre-embarkation tours, ports of call activities, or onboard cruise activities; and consumption of food, beverages, and ice. Passengers with diarrhea or vomiting were asked either during clinic visits or through the daily newsletter to voluntarily isolate themselves in their cabins until symptoms had resolved for ≥48 hours. The investigators included questions to determine the extent of compliance with isolation procedures recommended by the ship physician. To minimize the length of the survey and encourage survey completion, the investigators restricted questions about food items to meals served during the first 3 days of the cruise, consistent with the estimated exposure period.

Questionnaires were placed in the cabin mailboxes of each passenger (n = 2,018) the evening before disembarkation. Passengers were requested by letter and by announcement over the public address system to complete the questionnaires during the final morning of the cruise and to return the surveys to the reception desk as part of the checkout procedure.

A case of gastrointestinal illness was defined as three or more episodes of loose stools within a 24-hour period or two or fewer episodes of loose stools accompanied by one or more episodes of vomiting, occurring in a passenger who had sailed on cruise ship A during May 29 to June 4, 2004.

We performed a case-control study on a random sample of passenger surveys to test statistical associations between exposures and disease. Passengers who reported no symptoms or illness were considered eligible as control subjects. Those with indeterminate illness or uninterpretable questionnaires were excluded from further analysis. From the entire cohort of eligible completed questionnaires, the investigators selected every fifth case patient and every fifth control subject questionnaire, repeating this algorithm a second time to obtain a total of 100 case patients and 200 control subjects.

We limited our case-control analysis to events, exposures, meals, and food items served on board the vessel at all venues during the first 3 days of the

cruise, consistent with the exposure period. Persons with illness onset before a particular meal were removed from analyses for all meals subsequent to illness. The investigators performed univariate analysis, calculating odds ratios (ORs) and 95% confidence intervals (CIs) on individual exposures.[13] Multivariable logistic regression was performed, including the covariates determined as significant by univariate analysis and age and sex as a priori confounders. The investigators employed a backward selection procedure, whereby covariates with p values >0.2 were removed from the model.[14] All statistical analyses were performed by using SAS version 8.0 (SAS Institute, Cary, NC, USA).

Laboratory Analysis

Vomitus and stool samples from ill passengers were sent from the cruise ship to CDC's Respiratory and Enteric Viruses Branch for laboratory analysis. Samples were tested for norovirus by reverse transcriptase–polymerase chain reaction (RT-PCR) by using primers targeted for the polymerase (region B) and capsid genes (region GIID). Positive samples were sequenced for genogroup classification. Cultures for bacteria were not requested because of the high index of suspicion for norovirus as the etiologic agent of the outbreak and the positive onboard norovirus ELISA test results.

Environmental Health Investigation

Environmental health officers from CDC who sailed in the ship during the investigation reviewed the medical log for cases of gastroenteritis among passengers, the cruise line's outbreak prevention protocols, and the maintenance records for potable water, swimming pools, and whirlpool spas. They also performed daily manual tests of the potable water distribution system to verify the calibration of the chlorine analyzer and chart recorder. The housekeeping department, galley operations, and dining room service were inspected. Sanitizing solution buckets used in galleys, pantries, bars, and dining rooms were tested to assess whether chlorine concentrations were appropriate.

Results

Epidemiologic Investigation

Of the 2,018 surveys distributed to passengers, 1,489 (73.8%) were returned. Of these, 213 (14.3%) were excluded from further analysis because of being incomplete or reporting indeterminate illness that did not meet the case definition, 359 (24.1%) met the case definition for gastrointestinal illness, and 917 (61.6%) reported no symptoms for the duration of the voyage. The two systematically collected samples of 100/359 (27.9%) questionnaires from passengers who were case patients and 200/917 (21.8%) passengers who were control subjects were analyzed as part of the case-control study.

Sample demographic information for passengers was obtained from the 300 questionnaires selected for the case-control study. Of 291 passengers disclosing sex, 128 (44.0%) passengers were male and 163 (66.0%) were female. The mean age for passengers was 55.6 years. Of 286 passengers disclosing county or region of origin, 189 (66.1%) were from North America (United States or Canada), 26 (9.1%) were from Asia, and 71 (24.8%) were from Europe or Oceana (Australia or New Zealand).

Among all case patients, disease onset was clustered during the first 3 days of the cruise, with 227 (64.6%) having onset during this period (Figure 1). Among case patients sampled for the case-control study, 100 (100%) reported diarrhea, 74 (82%) nausea, 74 (74%) vomiting, 49 (59%) abdominal cramping, 50 (57%) headache, 40 (49%) myalgia, 24 (32%) fever, and 0 (0%) blood in stool. A total of 41 (41%) case patients reported illness duration of less than 1 day, 29 (29%) 1 to 2 days, 19 (19%) greater than 2 days, and 11 (11%) had unknown duration.

Seventy-seven (77%) case patients reported their symptoms to the clinic. Case patients who reported to the clinic were more likely to self-report compliance with the voluntary isolation period (49/77; 64%) than case patients who did not visit the clinic [4/17 (24%); OR: 2.06; CI = 1.16–3.67].

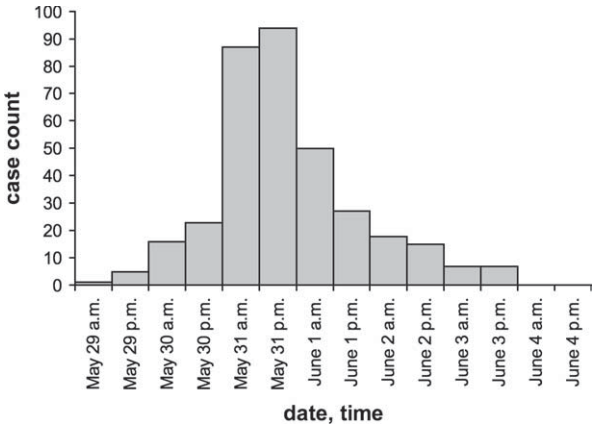

Figure 1 Epidemic curve of an outbreak of gastroenteritis among passengers on cruise ship A, May to June 2004 (n = 351).

In univariate analysis, North American residence (Canada and the United States) versus any other country of residence was significantly associated with disease (OR: 3.80; 95% CI = 2.07–6.98) (Table 1). No case patients occurred among the 26 passengers reporting residence in Asia. Sex was not significantly associated with illness. The mean age of cases and controls was 54.9 and 56.0 years, respectively, and the difference in age was not significant (*t*-test $p = 0.96$).

Beverages containing ice were associated with illness (OR: 11.8; 95% CI = 1.56–89.15). No significant association existed between illness and other beverages or any meal served during the first 3 days of the cruise. Using the swimming pool (OR: 3.48; 95% CI = 1.23–9.89), exercising in the gymnasium (OR: 2.02; 95% CI = 1.01–4.04), and using the whirlpool spas (OR: 2.95; 95% CI = 1.09–8.02) were associated with illness when performed during the first 2 days of the cruise. No other onboard cruise activities during any of the first 4 days were associated with illness. No significant association existed between illness and shoreside activities on day 2 of the cruise. Having participated in the pre-embarkation tour that started in city A was protective against illness (OR: 0.50; 95% CI = 0.25–0.99). No significant association existed with the tour that started in city B. Having cabin mates (OR: 4.27; 95% CI = 2.55–7.18) or travel mates (OR: 2.52; 95% CI = 1.51–4.21) symptomatic with diarrhea or vomiting was associated with disease. Of the public vomiting episodes, only use of the women's toilet contaminated during the captain's cocktail party was significantly associated with illness [OR: 6.03; 95% CI = 1.99–18.25 (analysis restricted to women)]. For any vomiting event, seeing or touching anyone else's vomitus was associated with disease (OR: 2.00; 95% CI = 1.12–3.56). Smoking while on the cruise was not associated with disease. Washing hands "always" versus "less than always" before meals was protective against illness (OR: 0.47; 95% CI = 0.26–0.87).

All 11 variables having significant associations with illness in univariate analysis were included in the multiple logistic regression model before backward selection. In the final model ($c = 0.78$; concordance = 78%), only four variables were significantly associated with disease: North American residence (OR: 2.61; 95% CI = 1.21–5.64), having a cabin mate sick with diarrhea or vomiting (OR: 3.40; 95% CI = 1.80–6.44), using the women's toilet at the captain's cocktail party (OR: 5.13; 95% CI = 1.40–18.78), and always washing hands before meals (OR: 0.25; 95% CI = 0.12–0.54), which was protective against illness.

Table 1 Case-control results and associations between exposure and gastroenteritis on board cruise ship A, May to June 2004 ($n = 300$)

	OR (CI)
Demographic	
Male sex	1.20 (0.73–1.95)
North American residence	3.80 (2.07–6.98)
Age (y)	0.99 (0.98–1.02)*
Beverages	
Unbottled, one or more	2.55 (0.55–11.90)
Bottled, one or more	1.48 (0.88–2.51)
With ice, one or more	11.80 (1.56–89.15)
Activity during first 2 d	
Used putting green	1.91 (0.75–4.86)
Gambled in casino	1.63 (0.93–2.88)
Exercised in fitness center	2.02 (1.01–4.04)
Visited spa salon	1.44 (0.56–3.70)
Used Internet cafe	0.98 (0.38–2.51)
Used pottery studio	Undefined
Swam in swimming pool	3.48 (1.23–9.89)
Used whirlpool spa	2.95 (1.09–8.02)
Watched movie at theater	1.34 (0.74–2.43)
Visited nightclub	0.91 (0.53–1.55)
Shopped in boutiques	1.22 (0.74–2.00)
Companions	
Sick cabin mate	4.27 (2.55–7.18)
Sick travel mate	2.52 (1.51–4.21)
Pre-embarkation	
From city A†	0.50 (0.25–0.99)
From city B†	1.25 (0.27–5.71)
Exposure to vomitus	
Attended lunch buffet, day 1	1.67 (0.93–2.99)
Attended safety drill, day 1	1.35 (0.83–2.21)
Used Internet cafe, day 1	0.52 (0.14–1.91)
Used toilet, party, day 2‡	6.03 (1.99–18.25)
Saw/touched vomitus	2.00 (1.12–3.56)
Personal hygiene habits	
Smoked on cruise	1.15 (0.44–3.03)
Always washed hands	0.47 (0.26–0.87)

CI = confidence interval; OR = odds ratio.
*Odds of disease per year of age calculated by using logistic regression.
†For example, referent value is no pre-embarkation tour.
‡Because this was a women's toilet, analysis was restricted to women. When unrestricted to women, result remained significant.

Laboratory Analysis

One vomitus and six stools collected by the ship's medical staff on May 31 and June 1 were tested for norovirus by RT-PCR. Three stool samples were positive at region B and region GIID, one stool sample was positive at GIID and negative at region B, and the remaining samples were negative at both regions. Investigators were able to successfully sequence GIID PCR products of three samples, all of which were identical and belonged to the Genogroup 2 to 6 Seacroft sequovar. Two of the region B PCR sequences were successfully sequenced and were identical, belonging to a nonspecific

Genogroup 2 subtype unresolved cluster (closest to groups 2–6, 2–7, and 2–9).

Environmental Health Evaluation

No abnormalities occurred in the use and maintenance of the ship's evaporators and potable water bunkering and evaporation systems. Onboard microbiological tests of potable water were negative for the presence of *Escherichia coli*. Halogen levels or residuals were within acceptable limits for potable water in all locations, the swimming pools, whirlpool spas, and sanitizing solutions. Housekeeping staff followed the written protocols of the ship's outbreak prevention document for their assigned tasks in passenger cabins and public areas (eg, the casino, dining rooms, or public toilets). Review of galley records and inspections revealed sound maintenance and food-handling practices.

The crew sanitation team responded to 330 separate vomiting accident episodes that were recorded during the first 4 days of the cruise. Five (2%) occurred on day 1, 11 (3%) on day 2, 205 (62%) on day 3, and 109 (33%) on day 4. A total of 312 episodes (94.6%) occurred in private cabins. The remaining 18 (5.4%) occurred in public places (eg, in or near public restrooms, bar areas, or dining rooms). According to the log, all episodes were cleaned up within an hour of report. No vomiting episodes or fecal accidents were recorded as occurring in the pools or whirlpools.

Discussion

Our investigation confirmed a widespread, rapidly progressing outbreak of norovirus among passengers and crew on board cruise ship A while sailing in Alaska waters during May to June 2004. The absence of deficiencies in environmental protocols and the lack of association with a single common source of infection combined with statistical associations between sick cabin mates and a public vomiting episode at the captain's cocktail party on the second day of the voyage support a person-to-person mode of transmission. One hypothesis for the cause of the outbreak as determined by passenger interviews and statistical findings is that multiple passengers embarked the vessel infected with a virus and subsequently infected others during public vomiting episodes or through the contamination of fomites. The epidemic curve (Figure 1) supports this hypothesis because it demonstrates that multiple passengers had disease onset within hours after embarkation. How primary case patients became infected prior to embarkation is beyond the scope of this study.

Widespread outbreaks of norovirus in which the most likely cause was person-to-person transmission or a point source with secondary person-to-person propagation have been previously documented on board cruise ships and aircraft carriers.[8–11,15–17] In the past, cruise ships with inadequate vessel sanitation have been more likely to be the site of an outbreak of gastrointestinal illness.[2,7] However, adequate vessel hygiene does not guarantee prevention of norovirus outbreaks specifically, as demonstrated by this and recent past outbreaks during which limited environmental deficiencies in food and water handling were noted by environmental health officers.[8,9,16,17] Therefore, the focus of intervention and response to outbreaks causally associated with person-to-person spread should extend beyond attempts to identify a point source to effective interventions that are successful at interrupting person-to-person transmission. Whether symptomatic crew or crew with subclinical illness might act as a reservoir of disease is unclear. What is clear, however, is that passengers put themselves, their cabin mates, and others at risk depending on their own behaviors and hygiene habits.

Rigorous hand washing has been well accepted as an effective means to prevent norovirus infection.[5] This study provides statistical evidence for the protective effects of hand washing during an outbreak of norovirus on board a cruise ship. Cruise ship companies should develop awareness campaigns to advise embarking passengers to practice adequate hand washing before meals and after activities in which contamination of hands is likely (eg, using the toilet). Hand-washing advisories should be posted in public lavatories throughout the ship. Health-care providers offering pretravel medical services should discuss the importance of hand washing with patients refilling medications or obtaining vaccinations as preparation for a cruise. Easy availability of hand-washing stations or alcohol-based hand sanitizers, for instance before buffet lines, may additionally help to reduce norovirus transmission.[18]

In our investigation, 95% of recorded vomiting episodes requiring cleanup occurred in private cabins, meaning that private cabins became the most common location with contaminated environmental surfaces. Sharing a cabin with a companion experiencing diarrhea or vomiting was associated with increased odds of acquiring infection. Other investigations have demonstrated positive associations between the risk for norovirus infection for

passengers staying in cabins with sick cabin mates, cabins that were previously contaminated with vomit or inhabited by a norovirus case patient, and crowded living quarters on aircraft carriers.[9,10,15–17] The cabin is therefore a likely location where norovirus transmission occurs, with infection resulting from contact with contaminated surfaces or directly from symptomatic persons. To prevent spread of disease, well passengers should be advised against personally cleaning the feces or vomit of others in their cabin. Trained housekeeping staff provided by the cruise ship performing these duties might reduce rates of transmission among passengers. A potential benefit also exists in early relocation of well cabin mates from cabins co-occupied by ill passengers to unoccupied cabins designated for use during outbreaks.

Toilet facilities are another location where norovirus transmission occurs. In our study, use of a specific toilet contaminated by vomit during a highly attended event (the captain's cocktail party) was associated with increased odds of illness. During a similar outbreak, use of communal toilet facilities was associated with illness, with risk for illness correlated with the number of persons sharing a given toilet. Conversely, access to a private toilet facility was protective against illness.[10] This is consistent with an investigation of a norovirus outbreak among cabin staff on an airplane that found that reportedly unsoiled toilets were the likely source of infection for passengers who subsequently became sick after disembarking.[19,20] To attenuate the propagation of norovirus during outbreaks, recommending that passengers restrict themselves to using the private toilet in their cabin as much as possible and to avoid using public toilets unless absolutely necessary might be advisable. Moreover, shared toilets should be the focus of particularly stringent disinfection with high-concentration bleach.

The voluntary 48-hour isolation period suggested to passengers by cruise line staff was intended to prevent symptomatic persons from exposing other passengers to norovirus by decreasing the number of contaminated public surfaces and fomites. In our study, case patients who visited the medical center self-reported higher compliance rates with the isolation period than those who did not attend the medical facility. The clinic is a location where important public health messages can be tailored to individual patients. Passengers with mild symptoms might not feel ill enough to seek the services of a health-care provider and might not understand that public health notices disseminated in the ship's newsletters or bulletins apply to themselves. To enhance compliance with voluntary isolation, at the time of embarkation, designated staff should request passengers to report illness to the clinic, regardless of the severity of symptoms, while removing any financial disincentives (eg, clinic fees) for doing so. Comprehensive reporting also allows medical staff to identify norovirus outbreaks earlier in their course, which might allow for earlier interventions to attenuate disease transmission.

Although thorough, the lengthy 14-page questionnaire may have limited the extent selected cases and controls truly represent the population at risk. The responder rate was nearly 74%; however, this value decreased to 63% when incomplete or improperly completed questionnaires were excluded from the study. We suspect that factors such as English language proficiency may have influenced response rates among subpopulations of travelers, but because characteristics of nonrespondents are unknown, we are uncertain whether or not travelers' decisions to not respond biased the study. In future investigations of cruise ship outbreaks of norovirus infection, we recommend that investigators limit questions about meals to meal times and locations rather than including specific food items. Though some data will be lost, this methodology will result in shorter questionnaires and will enhance responder rates.

In this case-control study, the investigators were unable to explain the association between illness and country of residence; Americans and Canadians had higher risks for disease, and no cases occurred among the 26 persons from Asia. Because this association persisted after controlling for hand washing and the presence of sick cabin mates, genetic differences, rather than behavioral factors, might be responsible for this finding. For example, previous studies have demonstrated decreased susceptibility to Norwalk virus infection and disease among persons with B blood type and immunity among persons homozygous recessive for the *FUT2* gene of the ABH histo-blood group. Both alleles are more common among Asian populations.[20–22]

This outbreak demonstrates that behavioral factors among passengers might be as important as environmental health practices in attenuating the risk for disease transmission during widespread outbreaks of norovirus on board cruise ships. Because such outbreaks are likely to continue and because epidemiologic investigations often fail in determining a point source of infection during outbreaks strongly indicative of a non–food borne mode of transmission,[8–12] these investigators recommend a continued focus on behavioral risk factors. Ultimately, such analytic work can result in

additional standardized recommendations for passengers and cruise line staff that might prevent outbreaks of norovirus from occurring in the presence of optimal environmental health practices.

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Declaration of Interests

Grant A. Tarling works for P&O Princess Cruises International. The other authors state that they have no conflicts of interest.

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