A NOROVIRUS OUTBREAK AT A LONG-TERM–CARE FACILITY: THE ROLE OF ENVIRONMENTAL SURFACE CONTAMINATION

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ABSTRACT

BACKGROUND: The role of environmental surface contamination in the propagation of norovirus outbreaks is unclear. An outbreak of acute gastroenteritis was reported among residents of a 240-bed veterans long-term–care facility.

OBJECTIVES: To identify the likely mode of transmission, to characterize risk factors for illness, and to evaluate for environmental contamination in this norovirus outbreak.

METHODS: An outbreak investigation was conducted to identify risk factors for illness among residents and employees. Stool and vomitus samples were tested for norovirus by reverse transcription polymerase chain reaction (RT-PCR). Fourteen days after outbreak detection, ongoing cases among the residents prompted environmental surface testing for norovirus by RT-PCR.

RESULTS: One hundred twenty-seven (52%) of 246 residents and 84 (46%) of 181 surveyed employees had gastroenteritis. Case-residents did not differ from non–case-residents by comorbidities, diet, room type, or level of mobility. Index cases were among the nursing staff. Eight of 11 resident stool or vomitus samples tested positive for genogroup II norovirus. The all-cause mortality rate during the month of the outbreak peak was significantly higher than the expected rate. Environmental surface swabs from case-resident rooms, a dining room table, and an elevator button used only by employees were positive for norovirus. Environmental and clinical norovirus sequences were identical.

CONCLUSION: Extensive contamination of environmental surfaces may play a role in prolonged norovirus outbreaks and should be addressed in control interventions (*Infect Control Hosp Epidemiol* 2005;26:802-810).

Noroviruses are a common cause of acute gastroenteritis and represent one of four genera of the virus family Caliciviridae.[1,2] The norovirus genome is composed of single-stranded, plus-sense viral RNA that is protected by a non-enveloped protein capsid. This capsid structure helps protect noroviruses from environmental degradation caused by elevated temperatures or desiccation and also provides increased resistance to chemical disinfection as compared with enveloped viruses or vegetative bacteria.[3,4] Many strains of noroviruses have been implicated in outbreaks of acute gastroenteritis in various settings, including cruise ships,[5] hotels,[6,7] rehabilitation centers,[8] restaurants,[9] public gathering places,[10] hospitals,[11-13] and long-term–care facilities (LTCFs).[1,14-17]

Norovirus outbreaks in LTCFs and other healthcare institutions typically spread rapidly, have high attack rates, and are difficult to control.[14,15,17] Furthermore, the elderly and chronically ill are particularly vulnerable to complications resulting from gastroenteritis, such as dehydration, electrolyte disturbances, and aspiration of vomitus. Studies have linked diarrheal disease to increased mortality rates in the elderly.[18,19] Given that vomiting and diarrhea are typical symptoms of norovirus gastroenteritis, norovirus outbreaks in LTCFs may contribute to an increased rate of mortality among residents, although this has not been well studied.

Transmission of noroviruses during institutional outbreaks can occur via multiple routes, including person-to-person contact[17,20] and aerosolization of viral particles during vomiting.[9,11] Contaminated fomites in the environ-

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ment have also been suggested as a possible source of infection[7,8,10,12]; however, the role of environmental contamination in outbreaks remains unclear. Among LTCF residents and hospitalized patients, fecal incontinence, dementia, and immobility are common conditions that may facilitate extensive contamination of the environment with fecal pathogens.

During the fall and winter of 2002, an increased number of gastroenteritis outbreaks consistent with norovirus, particularly in LTCFs, were reported to the Centers for Disease Control and Prevention.[14] From January through February 2003, an extensive and prolonged outbreak of norovirus acute gastroenteritis affected the residents and employees of a 240-bed veterans LTCF. An outbreak investigation was conducted using epidemiologic and molecular diagnostic methods to identify the likely mode of transmission, to characterize risk factors for illness, and to evaluate for environmental contamination. In this article, we report the findings of our investigation and highlight the role of widespread environmental contamination in the propagation and persistence of this norovirus outbreak.

METHODS

Epidemiologic Investigation

Following the identification of the outbreak, nursing staff were interviewed to identify possible case-residents. A resident was considered to be a case-resident with acute gastroenteritis if at least one of the following criteria had been documented between January 1 and February 10, 2003: (1) three or more occurrences of loose stools in a 24-hour period; (2) one or more episodes of unexplained vomiting; or (3) a physician diagnosis of acute gastroenteritis. Residents with symptoms attributable to a chronic underlying condition or another cause of diarrhea (eg, *Clostridium difficile* colitis or laxative use) were considered non–case-residents.

Medical records were reviewed to find case-residents not identified by staff and to collect demographic and clinical information, including diet (ie, standard vs dysphagia), number of comorbid conditions, medication history, laboratory test results, and all transfers to the affiliated acute care hospital emergency department and deaths (in either the LTCF or the hospital) during the outbreak period. Seven categories of comorbid conditions were considered for the analysis: cardiovascular disease, diabetes, chronic lung disease, gastroesophageal reflux disease, other gastrointestinal disorders, organic brain disease or dementia, and psychiatric disorders. Medications investigated included antibiotics, proton pump inhibitors, histamine 2 receptor antagonists, laxatives, and psyllium used during the 7 days prior to the onset of symptoms for case-residents. For non–case-residents, medication use during the week preceding and inclusive of the outbreak peak was ascertained for comparison (January 6 to 12). This period was chosen because it correlated with the periods investigated for the largest number of case-residents.

Nursing staff were interviewed to obtain resident data regarding dining locations, self-feeding ability, presence of a feeding tube, and ambulatory status (ie, self-mobile by foot or wheelchair, mobile with assistance, or strictly bed bound). The all-cause mortality rates of LTCF residents during the outbreak, the months immediately before and after, and the same months in the 2 previous years were abstracted from the discharge databases of the LTCF and the affiliated acute care hospital.

Self-administered questionnaires were distributed to all LTCF employees to screen for symptoms of gastroenteritis during the outbreak period, and food intake histories were recorded for the 4 days immediately before the outbreak peak (January 6 to 9, 2003). A case-employee was defined as an employee with self-reported diarrhea or vomiting during the outbreak period, excluding those who reported other likely causes for gastroenteritis. Employees who reported symptoms but not an onset date were considered non–case-employees, as were those who reported only nausea, fever, or chills. Employees who were based at the acute care hospital but routinely worked at the LTCF (eg, security staff) were included in the analysis. Employees from the acute care hospital who did not work regularly at the LTCF (eg, consulting physicians and maintenance staff) were excluded from the analysis.

Laboratory Investigation

To confirm the suspected norovirus etiology of the gastroenteritis outbreak, 8 samples of fresh stool and 3 samples of fresh vomitus were collected from case-residents on January 10 and stored in sterile containers at 4°C. Aliquots were sent to the Pennsylvania Department of Health State Laboratory for initial norovirus testing by reverse transcription polymerase chain reaction (RT-PCR). The QIA amp Viral RNA Mini Kit (QIAGEN, Inc., Valencia, CA) was used for viral RNA extraction, and the Light Diagnostics Calicivirus Genotype 1&2 Typing Oligo-Detect (CHEMICON International, Inc., Temecula, CA) assay with the QIAGEN OneStep RT-PCR Kit (QIAGEN, Inc.) was used for the qualitative detection of noroviruses. Stool and vomitus samples with sufficient remaining volume were subsequently sent to the Johns Hopkins University Bloomberg School of Public Health for independent norovirus analysis. Viral RNA was recovered using heat release[21] and amplified using RT-PCR as described below. Additional testing for rotavirus, adenovirus, and *C. difficile* toxins A and B was also performed on some stool specimens. Testing for rotavirus and adenovirus types 40 and 41 was performed by enzyme immunoassay.

Because of ongoing resident cases 2 weeks after the outbreak peak and after an initial terminal cleaning of the LTCF environmental surfaces with the routinely used phenolic agent (Ready-To-Use Wex-Cide, Wexford Labs, Inc., Kirkwood, MO), swabs from 10 environmental fomites (surfaces) were collected on January 24 from various sites in the LTCF for norovirus analysis. An area of each fomite surface of approximately 100 cm^2 (except for elevator buttons, which were approximately 25 cm^2) was wiped with 2 sterile cotton-tipped swabs moistened in 0.85% sterile

normal saline. The swabs were placed in 15-mL polypropylene tubes containing 2 mL of normal saline, stored at 4°C, and shipped to the Johns Hopkins University Bloomberg School of Public Health for norovirus recovery and subsequent analysis by RT-PCR, Southern oligoprobing hybridization, and sequencing.

The following process was developed to isolate noroviruses from the fomite samples. Each sample (2 swabs plus 2 mL of normal saline) was transferred to a reusable 50-mL polypropylene oakridge centrifuge tube. Norovirus RNA was extracted by adding 20 mL of the phenol-guanidinium–based compound TRIzol (Invitrogen, Carlsbad, CA) to each sample and vortexing for 5 minutes. TRIzol degrades viral protein capsids and protects liberated viral RNA by degrading RNases. The swabs were then removed, and viral RNA loss was minimized by pressing the swabs against the inside of the tube with a plastic RNase–DNase-free microspatula (Corning, Inc., Corning, NY) during removal. Chloroform (0.2 mL/mL of TRIzol) was added to the viral RNA–containing solution, mixed by hand for 15 seconds, and centrifuged at 10,000 × g for 20 minutes at 4°C. The aqueous phase containing the viral RNA was transferred to a clean oakridge centrifuge tube. Sodium acetate (final concentration, 0.3 M) and a volume of isopropanol equal to the volume of the recovered aqueous phase were added to precipitate the RNA, and the solution was mixed by hand for 30 seconds, incubated at room temperature for 10 minutes, and centrifuged at 10,000 × g for 20 minutes at 4°C. The supernatant was discarded, and the remaining pellet was washed with 70% ethanol and centrifuged at 7,500 × g for 15 minutes at 4°C. The resulting supernatant was discarded, and the RNA-containing pellet was air dried for 10 minutes and suspended in 100 µL of molecular-grade water (Barnstead Nanopure Diamond Water System, Dobuque, IA) containing 0.4 U/µL of RNasin (Perkin-Elmer, Foster City, CA).

Twenty microliters of suspended RNA from each cotton swab sample or RNA recovered from heat-released stool samples were tested by RT-PCR in three separate reactions containing genogroup I primers, genogroup II primers, or Norwalk virus internal standard primers (to test for sample inhibition).[22] Briefly, samples were assayed for norovirus by single-enzyme, single-tube RT-PCR using rTth (Perkin-Elmer) in 50-µL reactions. An MJ thermal cycler (MJ Research, Inc., Cambridge, MA) and 200-µL, thin-walled PCR tubes without oil overlays were used for the reactions.

The RT-PCR reaction mix yielded a final solution containing 1 × EZ buffer; 0.2 mM of deoxynucleotide triphosphates; 0.6 µM of upstream and downstream primers; 2.5 mM of manganese acetate; 10 U of RNasin; 5 U of rTth; and 20 µL of the sample. The RT reaction was incubated at 50°C for 10 minutes for downstream primer annealing and at 60°C for 50 minutes for RT. cDNA was amplified as follows: initial denaturation at 94°C for 2 minutes; 40 cycles of template denaturation at 92°C for 15 seconds, primer annealing at 50°C for 30 seconds, and primer extension at 60°C for 30 seconds; and a final extension at 60°C for 5 minutes. Region B primers were used to amplify norovirus RNA.[22] These primers are composed of the genogroup I primer set Mon 432 sense (5'TGGACICGYGGICCYAAYCA3') and Mon 434 anti-sense (5'GAASCGCATCCARCGGAACAT3'), and the genogroup II primer set Mon 431 sense (5'TGGACIAGRGGICCYAAYCA3') and Mon 433 anti-sense (5'GAAYCTCATCCAYCTGAACAT3'). The expected PCR product size was 213 bp.

The Norwalk virus internal standard RT-PCR reaction mix was composed of the same components described above except that the primer set NVp35/NVp36 replaced the region B primers.[21] The RT-PCR reaction was the same as described above except that primer annealing temperatures were 55°C. The expected PCR product size using NVp35/NVp36 primers was 347 bp.

All norovirus PCR products were confirmed by Southern hybridization oligoprobing using genogroup I and II probes.[22] Southern hybridization and detection was performed according to methods described elsewhere.[23]

Norovirus-specific RT-PCR amplicons from positive fomites and five stool samples were ligated into pCR2.1-TOPO cloning vector and transformed into One Shot TOP10 Chemically Competent *Escherichia coli* cells using the TOPO TA Cloning Kit (Invitrogen). Clones with the proper insert were identified by restriction enzyme digestion and direct PCR amplification of transformed cells using norovirus-specific primers and the PCR amplification conditions described above with a Taq polymerase enzyme. The inserted norovirus nucleic acid in positive clones was sequenced on an automated sequencer at the Johns Hopkins University Core Sequencing Facility with M13 forward and reverse primers complementary to the plasmid sequence upstream and downstream of the insert.

Statistical Analysis

Analysis of potential resident and employee risk factors for gastroenteritis was performed using Epi-Info 2002 software (Centers for Disease Control and Prevention, Atlanta, GA). We calculated the *P* values of relative risks (RRs) using the chi-square method and Fisher's exact test (when indicated). The expected all-cause mortality rate during the outbreak period was calculated by using the ratio of the monthly mortality rates during the flanking months to the rates during the same months in the previous 2 years. With the use of this expected rate, an expected number of deaths was calculated and the *P* value for the difference between the observed and the expected number of deaths was calculated using a Poisson probability. *P* values of less than .05 were considered significant.

RESULTS

The LTCF is a 240-bed veterans institution located in an urban setting in Philadelphia, Pennsylvania. It is affiliated with an acute care hospital located across the street. There are 2 wards on each floor (1B, 1C, 2B, and 2C), each with 27 double and 6 single rooms (Fig. 1). Each ward has a nursing station and a dedicated nursing staff.

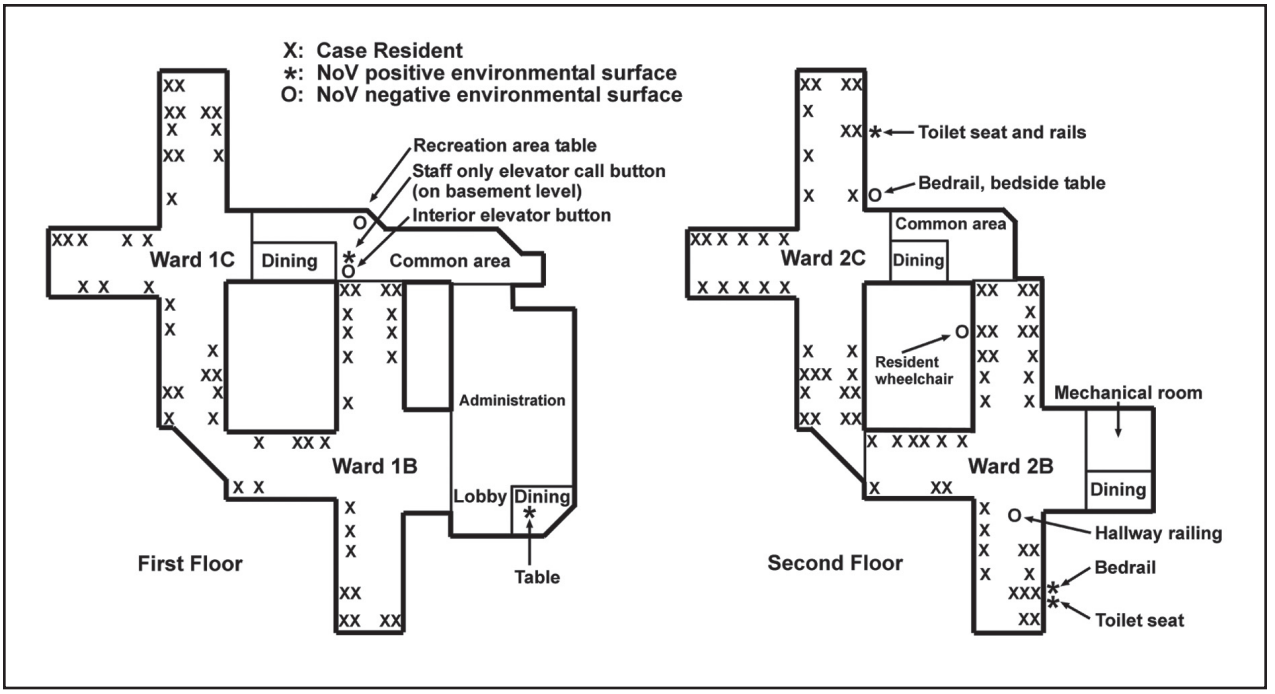

FIGURE 1. Floor plans of the long-term–care facility including the locations of the case-residents' bedrooms and the sites of the surfaces tested for norovirus (NoV).

During the outbreak period, there were a total of 246 residents at the LTCF. Most LTCF residents were long-term residents, with 74% admitted more than 6 months prior to the outbreak. The residents were 97% male and their ages ranged from 40 to 103 years (median age, 77 years), with only 15% younger than 60 years. Residents had a median of 2 comorbid conditions (range, 0 to 6), with 87% having a cardiovascular or chronic pulmonary condition, 28% with any gastrointestinal disorder, 24% with diabetes, and 70% with organic brain disease, dementia, or a psychiatric disorder.

Resident Cases

One hundred twenty-seven (52%) of the residents met the case definition for outbreak-specific gastroenteritis. The first case-resident became symptomatic on January 4, and the epidemic curve depicts an explosive outbreak with a prolonged period of ongoing incident cases (Fig. 2). The symptoms of the case-residents included nausea (36%), vomiting (75%), diarrhea (75%), and fevers or chills (1%).

Attack rates on individual wards ranged from 43% on ward 1B to 60% on ward 2B. Six of the first 7 case-residents were located on ward 2B. Resident characteristics, including ward, room type (single or double), ambulatory status, having a feeding tube, recent medications, diet type, and eating site, were not associated with being a case-resident (Table 1, not all data shown); however, there was a nonsignificant trend of non–case-residents having a feeding tube (16% vs 9%). Non–case-residents were more likely to have a nil per os (nothing by mouth) order than were case-residents (12% vs 4%; $P = .02$, Fisher's exact test).

Ninety-six case-residents had symptom onset before or during the peak of the outbreak (onset of symptoms before January 12, designated as "early" cases) and 31 had a later onset (on or after January 12, "late cases"). This represents an attack rate of 41% during the early period, whereas the attack rate was 21% during the late period among residents who were not previously ill. Of the 13 new LTCF admissions in the late period, 8 residents became case-residents (62%), representing one-fourth of all resident cases during the late period.

During the outbreak period, 37 residents were transferred to the emergency department of the acute care hospital (Table 2). Case-residents were more likely to be transferred than were non–case-residents (RR, 2.2; 95% confidence interval [CI_{95}], 1.1 to 4.3); however, when divided into early and late resident cases, only case-residents during the late period were significantly more likely than non–case-residents to be transferred (RR, 3.8; CI_{95}, 1.8 to 8.0). The rate of death among case-residents was not elevated compared with that among non–case-residents, although case-residents during the late period did have a nonsignificant increase in the rate of death compared with non–case-residents (16% vs 8%). However, the all-cause mortality rate at the LTCF increased in January, during the outbreak, to 24.8 deaths per 10,000 resident-days, resulting in a number of deaths significantly higher than the expected number (17 vs 5; $P < .01$; Fig. 3).

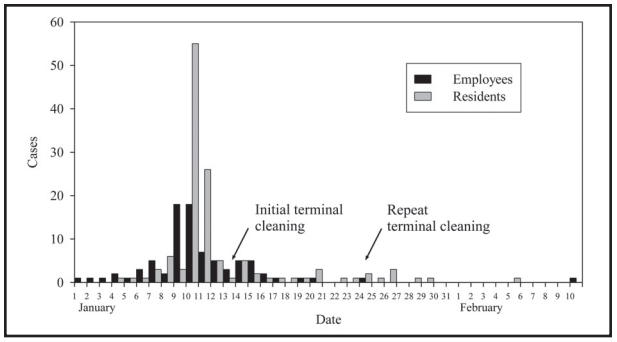

FIGURE 2. Onset of symptoms among the case-residents and case-employees of a long-term–care facility in Philadelphia during a norovirus outbreak from January to February 2003.

Employee Cases

Among 246 employees at the LTCF, 181 (74%) returned surveys, with 84 (46%) meeting the case definition. The first employee case of gastroenteritis occurred on January 1, and employee cases peaked 1 day before the resident cases did (Fig. 2). Three employees reported symptoms up to 3 days before the first case-resident; however, there was no documented contact between the initial case-employees and the earliest case-residents.

Employee symptoms included nausea (76%), vomiting (65%), diarrhea (88%), and fevers or chills (64%). Among departments with 15 or more employees, attack rates ranged from 21% among food workers to 73% among custodial staff (Table 3). Among ward-specific staff, attack rates ranged from 33% on ward 1C to 55% on wards 1B and 2B, although the differences were not significant. Departments with frequent direct resident contact (nursing, nurse practitioners, physicians, and physical and occupational therapists) had a combined attack rate of 45%, similar to employees without direct resident contact (49%). Prior to the implementation of infection control interventions, symptomatic employees were observed providing direct resident care.

Laboratory Investigation

Among samples collected from symptomatic residents on January 10, 2003, noroviruses were detected in all 8 stool samples and in 1 of 3 vomitus samples by RT-PCR. Assays for adenovirus and rotavirus (7 stool samples), as well as *C. difficile* toxins (3 stool samples), were negative. All 8 samples (7 stool and 1 vomitus) sent to the Johns Hopkins University Bloomberg School of Public Health were confirmed to be positive for genogroup II norovirus by RT-PCR. Five stool samples that were further characterized by sequencing the RT-PCR amplicons generated using primers to the conserved polymerase region were identical to the norovirus genogroup II strain designated as Hu/NoV/Farmington Hills/2002/USA.

Of the 10 environmental samples tested, 5 were positive for norovirus by RT-PCR and Southern oligoprobe hybridization (Table 4). Positive swabs were obtained from two toilet seats in bathrooms used by case-residents, a bed rail from a case-resident's bed, a dining room tabletop, and an elevator button in the basement near a staff entrance (Fig. 1). Sequencing of norovirus RNA showed an identical match to sequences from the clinical isolates.

TABLE 1
COMPARISON OF CASE-RESIDENTS AND NON–CASE-RESIDENTS OF A LONG-TERM–CARE FACILITY IN PHILADELPHIA DURING A NOROVIRUS OUTBREAK FROM JANUARY 1 TO FEBRUARY 10, 2003*

	Case-Residents (n = 127)	Non–Case-Residents (n = 119)
Male	122 (96%)	116 (97%)
Female	5 (4%)	3 (3%)
Median age, y (range)	79 (41–98)	76 (40–103)
Median no. of chronic conditions† (range)	2 (0–6)	2 (0–4)
Ward of residence		
1B	26 (20%)	34 (29%)
1C	30 (24%)	30 (25%)
2B	37 (29%)	25 (21%)
2C	34 (27%)	30 (25%)
Room type		
Single	11 (9%)	12 (10%)
Double	116 (91%)	107 (90%)
Ambulatory status		
Mobile with assistance only or strictly bed bound	39 (31%)	40 (34%)
Self-mobile	88 (69%)	79 (66%)
Diet		
Standard	86 (68%)	71 (60%)
Dysphagia	36 (28%)	34 (29%)
Nil per os‡	5 (4%)	14 (12%)
Use of a feeding tube	12 (9%)	19 (16%)
Eating site		
Dining room	56 (44%)	57§ (50%)
Resident room	71 (56%)	58§ (50%)
Require feeding assistance	18 (14%)	15 (13%)

*$P > .05$ for all comparisons of characteristics between case-residents and non–case-residents unless otherwise noted.
†Seven categories of chronic illnesses were considered: cardiovascular disease, diabetes, chronic lung disease, gastroesophageal reflux disease, other gastrointestinal disorders, organic brain disease or dementia, and psychiatric disorder.
‡Nothing by mouth. $P = .02$, Fisher's exact test.
§Eating site data were not available for 4 non–case-residents.

Outbreak Control Measures

On January 8, 2002, LTCF staff reported the acute increase in residents with gastroenteritis to the infection control team. Within 24 to 48 hours, initial infection control strategies were instituted including the reinforcement of hand hygiene, implementation of contact precautions for all case-residents, use of masks when assisting vomiting resi-

TABLE 2
TRANSFERS TO THE EMERGENCY DEPARTMENT OF THE ACUTE CARE HOSPITAL AND DEATHS* AMONG THE RESIDENTS OF A LONG-TERM–CARE FACILITY IN PHILADELPHIA DURING A NOROVIRUS OUTBREAK FROM JANUARY TO FEBRUARY 2003†

	Transferred		Died	
	No. (%)	RR‡ (CI_{95})	No. (%)	RR‡ (CI_{95})
All case-residents	26 (20)	2.2 (1.1–4.3)§	12 (9)	1.2 (0.5–2.9)
Case-residents during the early period‖	15 (16)	1.7 (0.8–3.5)	7 (7)	1.0 (0.4–2.5)
Case-residents during the late period¶	11 (36)	3.8 (1.8–8.0)#	5 (16)	2.1 (0.8–5.9)
Non–case-residents	11 (9)	-	9 (8)	-

RR = relative risk; CI_{95} = 95% confidence interval.
*Includes deaths in both the long-term–care facility and the acute care hospital.
†$P > .05$ unless otherwise specified.
‡All comparisons made with non–case-residents.
§$P = .01$.
‖Onset of symptoms before January 12.
¶Onset of symptoms on or after January 12.
#$P < .001$, Fisher's exact test.

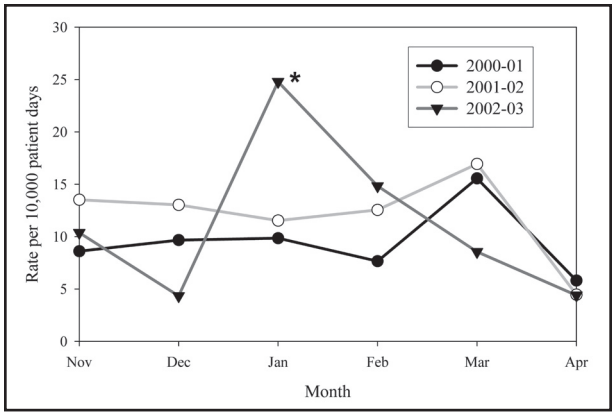

FIGURE 3. All-cause mortality rates among residents of the long-term–care facility, November to April 2000 to 2003. *$P < .01$ for the observed number of deaths compared with the expected number.

TABLE 3
ATTACK RATES AMONG THE EMPLOYEES OF A LONG-TERM–CARE FACILITY IN PHILADELPHIA DURING A NOROVIRUS OUTBREAK FROM JANUARY 1 TO FEBRUARY 10, 2003

	Case-Employees	Non–Case-Employees	Attack Rate (%)
All employees	84	97	46
Department*			
Nursing	42	57	42
Food service	5	19	21
Custodial	11	4	73
Security	16	10	62
Direct patient contact			
Yes	48	59	45
No	36	38	49

*Only departments with at least 15 employees were included in this table.

dents or cleaning soiled fomites, and exclusion of symptomatic employees from work until 48 hours after the resolution of their symptoms. During the week following the outbreak discovery, terminal cleaning of the LTCF was performed using the routine phenolic cleaning agent (Ready-To-Use Wex-Cide). Because of ongoing incident cases during the first 3 weeks of the outbreak, infection control staff supervised a systematic repeat terminal cleaning of all LTCF environmental surfaces from January 24 to February 6 (started after the collection of environmental samples) using an alternate phenolic agent (Microbac II, Ecolab, St. Paul, MN) at a 1:128 dilution, which has been experimentally shown to be effective against cultivable feline calicivirus.[24] A moratorium on new admissions was also instituted on January 27. Following the completion of the second terminal cleaning, there was only one case of gastroenteritis (employee, norovirus etiology unconfirmed).

DISCUSSION

We have described an explosive and prolonged outbreak of acute norovirus gastroenteritis affecting residents and employees of an LTCF. Similar to other LTCF outbreaks, the outbreak spread rapidly and had high attack rates. Insufficient clinical documentation at the LTCF combined with limited ability to conduct direct resident interviews may have resulted in an underestimate of the attack rate among residents. Participation bias may have overestimated the attack rate for employees; however, if all non-responders were non–case-employees, the attack rate would still have been substantial (34%).

Introduction of norovirus from the community is highly plausible given reports of numerous norovirus outbreaks in the northeastern United States during this period and emergence of the norovirus Farmington Hills strain as a frequent cause of outbreaks in the United States since July 2002.[14] Because initial cases occurred among employees, it can be hypothesized that an employee introduced the virus into the LTCF, although introduction by other individuals from the community such as visitors or volunteers must also be considered. Other investigations of LTCF norovirus outbreaks have implicated employees in the spread of no-

TABLE 4
RESULTS OF NOROVIRUS TESTING PERFORMED WITH REVERSE TRANSCRIPTION POLYMERASE CHAIN REACTION ON ENVIRONMENTAL SURFACE SAMPLES COLLECTED ON JANUARY 24, 2003

Specimen No.	Site	Ward	Result on Norovirus RT-PCR–Oligoprobing	Comment
1	Toilet seat	2B	Positive	Bathroom attached to case-resident's room, sampled 2 days after onset of symptoms
2	Dining room table	1B	Positive	Common dining room table
3	Table	1C	Negative	Resident recreation area table
4	Elevator button	Basement	Positive	Exterior elevator call button in basement used only by staff
5	Elevator button	-	Negative	Interior elevator button
6	Bed rail	2B	Positive	Bed rail of case-resident bed, sampled 2 days after onset of symptoms
7	Handrail	2B	Negative	Railing located in hallway in central area of ward
8	Wheelchair	2B	Negative	Wheelchair of case-resident, sampled 19 days after onset of symptoms
9	Bed rail, bedside table	2C	Negative	Bed rail and table associated with case-resident, sampled 14 days after onset of symptoms
10	Toilet seat and handrails	2C	Positive	Bathroom attached to room of 2 case-residents who had onset of symptoms on the day of sampling

RT-PCR = reverse transcription polymerase chain reaction.

rovirus to multiple residents.[15,17] In this outbreak, we could not directly link initial employee cases to initial resident cases; however, we believe that employees played an amplification role given that (1) the initial cases were employees, (2) bed-bound residents were as likely to be case-residents as were ambulatory residents, and (3) prior to infection control interventions, several ill employees were observed providing direct patient care.

Residents of this LTCF who had acute gastroenteritis were more likely than non–case-residents to be transferred to the emergency department. Case-residents during the late period were particularly at risk for transfer, perhaps the result of increased caution among staff following the outbreak peak. We also observed a significant increase in the all-cause mortality rate during the first month of the outbreak, more than double the rate observed in previous years (Fig. 3); however, except for a nonsignificant trend toward a higher risk of death in late cases, case-residents did not have a higher risk of death compared with non–case-residents. This may be explained by the possible misclassification of case-residents as non–case-residents due to limited clinical documentation. Another factor may be the adverse effect of employee illness on resident care. Although usual nurse-to-resident ratios were maintained during the outbreak, the staff replacing the ill caregivers may have been less familiar with the residents.

Although we suspect that the norovirus outbreak was the primary cause of the increase in all-cause mortality, other possible causes should be considered, including outbreaks of respiratory infections, especially influenza. During the outbreak period there were no observed increases in influenza-like illnesses in the LTCF, and influenza surveillance data from the Philadelphia Department of Public Health for January 2003 indicated a low level of influenza A activity that did not peak until the following month.[25] Although unlikely, we are unable to completely exclude the possibility that other illnesses may have caused the observed increase in all-cause mortality among residents.

We believe that environmental surface contamination may have played a significant role in the persistence of this outbreak, particularly given the high attack rate among new admissions in the late outbreak period. There is significant epidemiologic evidence that environmental surface contamination can be a source for new infections in outbreaks.[10,26-28] RT-PCR is a sensitive method for detecting norovirus from stool[29] and water,[30] and it has been used to implicate shellfish,[31] delicatessen foods,[32] drinking water,[33] and recreational water[34] as sources of norovirus outbreaks. However, there is little research regarding the use of RT-PCR in detecting caliciviruses on fomites.[35,36]

Previous norovirus outbreak investigations have used RT-PCR to investigate environmental surface contamination,[7,8,12,16,37,38] and some have isolated noroviruses.[7,8,12,38] Two prior investigations isolated norovirus RNA from environmental surfaces and concluded that environmental contamination likely played a major role in prolonging the outbreaks.[7,8] Nucleotide sequencing was not performed on the environmental strain in either study, although one concluded that the environmental strain was identical to the strain from clinical cases using hybridization probes.[8] Sequence analysis is the preferred method to establish an association between environmental and clinical strains, especially given the possibilities of multiple circulating strains or cross-contamination in the laboratory.[38]

In our investigation, we used novel norovirus recovery techniques on fomite swab samples to identify environmental surfaces contaminated with noroviruses. Sequence analyses determined that the noroviruses detected in the fomite samples were identical to those isolated from the stool samples. The norovirus sequence information obtained from these fomite samples corresponded to the conserved polymerase region of the norovirus genome; however, there was insufficient extracted norovirus RNA remaining to attempt RT-PCR analysis of these samples using primers from the less-conserved capsid region of the norovirus genome. Nonetheless, our findings indicate that contamination was not limited to fomites associated exclusively with case-residents. The isolation of noroviruses from areas far from bedrooms and commodes (including an elevator button used exclusively by staff) suggests that widespread environmental contamination was likely.

Noroviruses have been detected in the stool samples of experimentally infected adults up to 13 days after inoculation.[39] Further study on the duration of viral shedding among the elderly and chronically ill with norovirus gastroenteritis is needed. Prolonged shedding, along with resident factors including dementia, incontinence, and immobility, may have contributed to the extensive environmental contamination.

Recent studies have also demonstrated that norovirus on experimentally contaminated surfaces can be readily transferred to other fomites via hands and washcloths.[36] In our study, the environmental samples were collected 2 weeks after the outbreak peak, raising the possibility that environmental contamination may have been previously more extensive. Furthermore, at the time of collection, the LTCF had already undergone the initial institution-wide cleaning with a phenolic cleaning agent. Clearly, contamination can persist for long periods despite routine decontamination efforts, due to either viral resistance or recontamination from prolonged shedding.

Our investigation underscores the importance of a multilateral infection control strategy during a norovirus outbreak at an LTCF, particularly the exclusion of ill employees, moratoria on new admissions to limit the pool of susceptible individuals, and terminal cleaning of all surfaces. Because caliciviruses are resistant to many surface disinfectants at commonly used concentrations, care must be taken to use cleaning agents with evidence of efficacy against caliciviruses.[24,36,40]

Similar to norovirus outbreaks in hotels and on cruise ships, outbreaks in LTCFs may be prolonged because of the potentially high level of environmental contamination and regular introduction of susceptible individuals. In our study, we have demonstrated that RT-PCR testing of environmental surfaces along with clinical samples can lead to further understanding of the role of fomites in propagating norovirus outbreaks in LTCFs and ultimately help focus and evaluate outbreak control measures, particularly cleaning efforts. Further study is needed to define the role of environmental analysis in investigating norovirus outbreaks in healthcare institutions.

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CORRECTION

In the September issue of the Journal, the following elements of the article "A Large Nosocomial Outbreak of Hepatitis C Virus Infections at a Hemodialysis Center" by Savey et al. were incorrect.

On page 752, the first sentence of the second paragraph below the Abstract should have concluded as follows: ". . . and the use of blood transfusion has decreased with the introduction of erythropoietin to treat anemia.[16,17]"

On page 754, the second sentence of the first paragraph below the heading Assessment of Infection Control Practices and Procedures should have read as follows: "The French Ministry of Health recommends one nurse for every four patients and one additional nurse (or auxiliary nurse) for every 8 patients in a dialysis center, for a total nurse-to-patient ratio of 0.375."

Regarding Table 2 on page 757, there were 22 (35.5%) female control-patients and 40 (64.5%) male control-patients.

On page 758, the first sentence of the last paragraph should have read as follows: "The hemodialysis unit had spontaneously adopted double filters (which were changed for each patient) on both arterial and venous lines, as internal transducers are considered as a critical point in the dialysis machine.[14,24]"