

EVALUATION OF THE IMPACT OF THE SOURCE (PATIENT VERSUS STAFF) ON NOSOCOMIAL NOROVIRUS OUTBREAK SEVERITY

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ABSTRACT

OBJECTIVE: To study the dependence of infection risk and outbreak size on the type of index case (ie, patient or staff).

METHODS: Nosocomial outbreaks were reviewed and categorized into those started by patients and those started by staff. Infection risks and outbreak sizes were evaluated taking into account the index case category.

RESULTS: Of the 30 nosocomial outbreaks of norovirus with person-to-person transmission, 20 (67%) involved patients as the index cases. Patient-indexed outbreaks affected significantly more patients than did staff-indexed outbreaks (difference in means, 16.25; 95% confidence interval [CI₉₅], 5.1 to 27.0). For the numbers of affected staff, no dependence on the index case category was detectable (difference in means, -1.05; CI₉₅, -9.0 to 6.9). For patients exposed during patient-indexed outbreaks, the risk

of acquiring a norovirus infection was approximately 4.8 times as high as the corresponding risk for patients exposed during staff-indexed outbreaks (odds ratio [OR], 4.79; CI₉₅, 1.82 to 8.28). The infection risk for exposed staff during patient-indexed outbreaks was approximately 1.5 times as high as the corresponding risk during staff-indexed outbreaks (OR, 1.51; CI₉₅, 0.92 to 2.49).

CONCLUSIONS: Patient-indexed norovirus outbreaks generally affect more patients than do staff-indexed outbreaks. Staff appear to be similarly affected by both outbreak index category groups. This study demonstrates the importance of obtaining complete outbreak data, including the index case classification as staff or patient, during norovirus outbreak investigations. Such information may be useful for further targeting prevention measures (*Infect Control Hosp Epidemiol* 2005;26:268-272).

During the winter of 2002–2003, more norovirus outbreaks were observed than ever before in Germany and elsewhere.^{1,2} In hospitals and long-term-care facilities, many staff members were affected and staff shortage complicated patient care.³ Wards had to be closed either completely or to new admissions; if many staff were affected, reliable patient care became impossible. Patients had to be transferred to other wards in other departments with staff who were not knowledgeable about the relevant specific diagnostics and therapies.

Thus, implementing appropriate prevention measures is essential, especially because the infectivity and potential spread is great for the currently circulating genetic variants of norovirus. Currently, we lack an understanding of norovirus outbreak dynamics that could enable us to recommend prevention measures adaptable to specific situations. The primary mode of transmission is from person to person in 85% of nosocomial norovirus outbreaks.⁴ The influence on outbreak occurrence or severity of the index source (ie, patient or staff) is unknown.

Our study investigated the possible differences between outbreaks in wards depending on the index case

category. Furthermore, outbreaks affecting more than one ward in the same hospital were analyzed.

METHODS

All published nosocomial norovirus outbreaks with proven or suspected person-to-person transmission were included (ie, Medline search of studies published from 1962 to 2004 using the terms “norovirus,” “Norwalk virus,” “small-round structured virus,” and “outbreak”), as were data obtained from Outbreak Worldwide Database,⁵ German data published in *Epidemiologisches Bulletin*, data from personal communication with another German teaching hospital, and our own data.⁶

Inclusion criteria for statistical analyses were outbreaks with epidemic curves for each ward and outbreaks for which the index case could be identified. For infection risk analyses, outbreaks were included if attack rates were available separately for each ward. Authors of studies of outbreaks published since 1994 were contacted but could not supply further data meeting our inclusion criteria.

For the infection risk analyses, Epi-Info software

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TABLE 1
STUDIES ON NOSOCOMIAL OUTBREAKS: INDIVIDUAL WARDS

| Study | Month and Year of Outbreak | Country | Department | No. of Outbreak Wards | No. of Infected Individuals | Index Case | Included in Statistical Analyses | Included in Attack Rate Analyses |
|-----------------------------------|-------------------------------|-------------|---|-----------------------|-----------------------------|------------------------------------|------------------------------------|----------------------------------|
| Kaplan et al. ⁷ | December 1980 | US | Nursing home | 2 | 72 | P, P | - | - |
| Gustafson et al. ⁸ | April 1981 | US | Chronic care | 1 | 53 | U | - | - |
| Riordan and Wills ⁹ | September to October 1983 | UK | Elderly care unit | 4 | 97 | S, S, S, U | - | - |
| Leers et al. ¹⁰ | April 1983 | Canada | Internal medicine | 6 | 126 | P, S, U, U, U, U | - | - |
| Spender et al. ¹¹ | January to February 1985 | UK | Pediatrics | 4 | 48 | U, U, U, S | - | - |
| Gellert et al. ¹² | December to January 1988–1989 | US | Elderly care unit | 3 | 181 | S, U, U | - | - |
| Pegues and Woernle ¹³ | July 1991 | US | Nursing home, two wings | 1 | 91 | P | P | P |
| Chadwick and McCann ¹⁴ | November 1992 | UK | Elderly care unit | 2 | 126 | U, U | - | - |
| Cunney et al. ¹⁵ | February 1993 | Ireland | Elderly care unit, internal medicine | 2 | 95 | U, U | - | - |
| Green et al. ¹⁶ | January 1994 | UK | Internal medicine | 1 | 50 | P | P | P |
| Green et al. ¹⁷ | May 1994 | UK | Elderly care unit | 4 | 81 | P, U, U, U | - | - |
| Green et al. ¹⁷ | May 1994 | UK | Psychiatry | 1 | 29 | U | - | - |
| Russo et al. ¹⁸ | October 1995 | Australia | Elderly care unit, internal medicine | 2 | 98 | P, S | P, S | - |
| Caceres et al. ¹⁹ | January 1996 | US | Not described | 1 | 37 | S | S | S |
| Marx et al. ²⁰ | February 1996 | US | Elderly care unit | 1 | 86 | P | P | - |
| O'Neill et al. ²¹ | June 1999 | UK | Elderly care unit | 1 | 16 | P | P | - |
| O'Neill et al. ²¹ | April 1999 | UK | Internal medicine | 1 | 30 | P | P | - |
| Khanna et al. ³ | February to March 2001 | Switzerland | Dermatology, internal medicine, BMT | 3 | 63 | P, S, S | P, S, S | - |
| Sinn ²² | January to February 2001 | Germany | Internal medicine, elderly care unit | 2 | 68 | P, S | P, S | - |
| McCall and Smithson ²³ | January 2001 | UK | Acute elderly care unit | 1 | 58 | P | -* | - |
| Mattner et al. ⁶ | November to January 2002–2003 | Germany | Psychiatry, two in internal medicine, pediatrics, internal medicine, trauma | 6 | 165 | P, P, P, S, S, U | P, P, P, S, S | P, P, P, S |
| Borck [†] | November to January 2002–2003 | Germany | Four in internal medicine, neurology, obstetrics, surgery, two in the elderly care unit, neurology, internal medicine, surgery, elderly care unit | 13 | 366 | P, P, P, P, P, P, P, P, S, S, S, U | P, P, P, P, P, P, P, P, S, S, S, S | - |
| Total | | | | 62 | 2,036 | P = 25; S = 16; U = 21 | 30 | 7 |

P = patient; S = staff; U = unknown; US = United States; UK = United Kingdom; BMT = bone marrow transplant unit.

*Study was excluded because the staff group comprised a subgroup not belonging to the ward.

[†]H. U. Borck, MD, personal communication, 2003.

TABLE 2
NOSOCOMIAL NOROVIRUS OUTBREAK SIZES DIFFERENTIATED BY THE INDEX CASE: PATIENT OR STAFF*

| | Mean No. of Affected Patients | Mean No. of Affected Staff | Mean No. of All Affected Individuals |
|---|----------------------------------|-------------------------------|---|
| Observed means for patient-indexed outbreaks | 27.75 | 11.75 | 39.5 |
| Observed means for staff-indexed outbreaks | 11.5 | 12.8 | 24.3 |
| 95% confidence interval for difference in mean [†] | 5.1 to 27.0 | -9.0 to 6.9 | 1.1 to 29.0 |
| <i>P</i> [‡] | .006 | .78 | .036 |

*Thirty wards included.

[†]Using Welch's approximate *t* test (two sided).

TABLE 3
INFECTION RISK OF PATIENTS DEPENDING ON THE INDEX CASE: PATIENT OR STAFF*

| Index Case | No. of Patients Infected | No. of Patients Not Infected | Total | OR | CI ₉₅ | <i>P</i> |
|-------------------|-----------------------------|---------------------------------|-------|------|------------------|----------|
| Patient (5 wards) | 154 | 202 | 356 | 4.79 | 1.82 to 8.28 | < .0005 |
| Staff (2 wards) | 21 | 132 | 153 | | | |
| Total | 175 | 334 | 509 | | | |

OR = odds ratio; CI₉₅ = 95% confidence interval.

*Denominator population was available from only 7 wards.

TABLE 4
INFECTION RISK OF STAFF DEPENDING ON THE INDEX CASE: PATIENT OR STAFF*

| Index Case | No. of Staff Infected | No. of Staff Not Infected | Total | OR | CI ₉₅ | <i>P</i> |
|-------------------|--------------------------|------------------------------|-------|------|------------------|----------|
| Patient (5 wards) | 79 | 145 | 224 | 1.51 | 0.92 to 2.49 | .08 |
| Staff (2 wards) | 36 | 100 | 136 | | | |
| Total | 115 | 245 | 360 | | | |

OR = odds ratio; CI₉₅ = 95% confidence interval.

*Denominator population was available from only 7 wards.

(version 6; Centers for Disease Control and Prevention, Atlanta, GA) was used. Further statistical analysis (Welch's approximate *t* test) was performed using Mathematica software (version 4.2; Wolfram Research, Inc., Champaign, IL).

RESULTS

From 19 publications and 1 personal communication, 62 outbreak wards including 2,036 individuals were included for analyses (Table 1).^{3,6-23} In 25 (40%) of the outbreaks, patients were the index; in 16 (26%), staff were the index. The index could not be identified in 21 (34%) of the outbreaks. The quality of data has improved during the past 20 years. The first outbreak included in our statistical analyses occurred in 1991.¹³ Thirty of these outbreaks (between 1991 and 2003) were included in our study. A total of 1,033 individuals (670 patients and 363 staff members) were involved as cases. The number of affected wards in a given hospital ranged from 1 to 13 (mean, 15 individuals per outbreak ward). Twenty (67%) of the outbreaks were started by patients, whereas 10 (33%) of the

outbreaks were started by staff. On internal medicine wards (with the neurology and pediatrics departments included), 11 of 18 outbreaks were patient indexed. In contrast, in elderly care units and psychiatry units, 7 of 8 outbreaks were patient indexed.

Only seven wards could be included in the infection risk analyses because only these studies included the denominator population.

A detailed analysis yielded the following results: (1) outbreaks started by patients affected more patients and individuals than did outbreaks started by staff (Table 2); (2) outbreaks started by staff affected as many staff as did outbreaks started by patients (Table 2); (3) the risk of a patient being affected was more than twice as high in an outbreak started by a patient compared with an outbreak started by staff (Table 3); and (4) the risk of staff members being affected was independent of the index source category group (Table 4).

Analysis of all available nosocomial outbreaks revealed that 14 (23%) of 62 ward outbreaks were proved

or suspected to have been started by staff from the same hospital but from another affected ward.

DISCUSSION

Norovirus outbreaks emerged during the past few years in Central Europe. In Germany during the winter of 2002–2003, up to 150 outbreaks per week were reported to the nationwide surveillance system. The majority (85%) of these outbreaks were nosocomial.^{1,2} In Europe, hospital outbreaks, compared with outbreaks in other settings such as schools and hotels, were reported more often to surveillance systems and seemed to involve fewer individuals.⁴ In contrast, outbreaks in Japan reported to its national surveillance systems demonstrated that hospital outbreaks involved more than 20 to 50 individuals, respectively.²⁴ Norovirus spread is facilitated by its transmission mode (contact transmission and possibly by aerosols when handling patient emesis), complicating the termination of outbreaks.²⁵ Until now, little was known about the severity of such outbreaks based on the source or index case as a patient or staff member. Some data support transmission through food, water, and contact,^{4,24,26,27} but to our knowledge, no investigation had been conducted to assess the impact of index case category on the severity of nosocomial outbreaks.

Our study demonstrates that outbreak patterns depend on the index case category. Patient-indexed outbreaks involve more individuals and more patients than do staff-indexed outbreaks. On the other hand, staff affection was independent of the index case category. These observations provide evidence for a faster and more effective spread of noroviruses within the patient group in patient-indexed outbreaks. There are several probable reasons for this. Patients may have poorer hygiene than do staff. It is possible that patient-source illness is not recognized as quickly as staff illness, so the virus has more time to spread before control measures are instituted. Furthermore, patients may have a weaker immune response to the virus, and therefore excrete much larger numbers of virus than do younger staff.

The observation that patient-indexed outbreaks are more severe contradicts the common assumption that mostly staff are responsible for the person-to-person transmission of norovirus in the hospital. Additionally, when patients transmitting the virus to other patients (by either aerosol or physical contact) is taken into account, more aggressive measures are required to prevent nosocomial transmission, such as those recommended by the Centers for Disease Control and Prevention, the National Disease Surveillance Center in Ireland, or the Robert-Koch-Institut in Germany.²⁸⁻³⁰ Isolation procedures, immediate environmental decontamination of soiled areas, frequent handwashing^{28,29} or hand antisepsis with a virus-active alcoholic disinfectant,³⁰ or staff and patients wearing masks when contact with feces or vomitus is expected should be effective in stopping further spread between patients in patient-indexed outbreaks.

Although it may be difficult to identify the index case while an outbreak is ongoing, one should try to do so

as early as possible. Indeed, Table 1 illustrates that in approximately two-thirds of all published nosocomial norovirus outbreaks, the index cases were determined.

In contrast, although staff were affected to approximately the same extent in both patient- and staff-indexed outbreaks, it may be prudent to apply similar prevention measures for staff and patients, such as minimizing contacts among staff and applying appropriate hand antiseptic procedures not only after patient contact but also after contact with other staff members.

The statistical analysis of attack rates of patient-indexed outbreaks supports the closing of a ward to new admissions as a prevention measure.

For staff-indexed outbreaks, the corresponding prevention measure would consist of reducing contact with infected staff by sending staff home until at least 48 hours after their symptoms resolve.³¹

On the other hand, when the less severe course of staff-indexed outbreaks is considered, it is possible that under certain circumstances (eg, high compliance with hand hygiene and prevention measures and a low attack rate), closing the ward to new admissions might be avoided.

Unfortunately, little is known about the dynamics of norovirus outbreaks. It is important to analyze the dynamics of an outbreak to devise more specific prevention measures. To this end, it is necessary to collect complete outbreak data, such as ward-specific epidemic curves regarding all involved groups of individuals, and to perform surveillance of individuals at risk (attack-rate calculation) as recommended by Beck-Sague et al. (from the Centers for Disease Control and Prevention).³²

REFERENCES

1. Koch J SE, Schreier E. Norovirus infections [in German]. *Epidemiologisches Bulletin* 2003;6:39-41.
2. Anonymous. Norovirus activity: United States, 2002. *MMWR* 2003; 52:41-45.
3. Khanna N, Goldenberger D, Graber P, Battegay M, Widmer AF. Gastroenteritis outbreak with norovirus in a Swiss university hospital with a newly identified virus strain. *J Hosp Infect* 2003;55:131-136.
4. Lopman BA, Adak GK, Reacher MH, Brown DW. Two epidemiologic patterns of norovirus outbreaks: surveillance in England and Wales, 1992-2000. *Emerg Infect Dis* 2003;9:71-77.
5. Outbreak Worldwide Database [database online]. Norderstedt, Germany: Shulke & Mayr GmbH, Robert-Koch-Institut; 2003. Available at www.outbreak-database.com. Accessed on January 15, 2004.
6. Mattner F, Sohr D, Heim A, Gastmeier P, Vennema H, Koopmans M. Risk groups for clinical complications of norovirus infections: an outbreak investigation. *Clin Microbiol Infect*. In press.
7. Kaplan JE, Schonberger LB, Varano G, Jackman N, Bied J, Gary GW. An outbreak of acute nonbacterial gastroenteritis in a nursing home: demonstration of person-to-person transmission by temporal clustering of cases. *Am J Epidemiol* 1982;116:940-948.
8. Gustafson TL, Kobylik B, Hutcheson RH, Schaffner W. Protective effect of anticholinergic drugs and psyllium in a nosocomial outbreak of Norwalk gastroenteritis. *J Hosp Infect* 1983;4:367-374.
9. Riordan T, Wills A. An outbreak of gastroenteritis in a psycho-geriatric hospital associated with a small round structured virus. *J Hosp Infect* 1986;8:296-299.
10. Leers WD, Kasupski G, Fralick R, Wartman S, Garcia J, Gary W. Norwalk-like gastroenteritis epidemic in a Toronto hospital. *Am J Public Health* 1987;77:291-295.
11. Spender QW, Lewis D, Price EH. Norwalk like viruses: study of an outbreak. *Arch Dis Child* 1986;61:142-147.
12. Gellert GA, Waterman SH, Ewert D, et al. An outbreak of acute gas-

- troenteritis caused by a small round structured virus in a geriatric convalescent facility. *Infect Control Hosp Epidemiol* 1990;11:459-464.
13. Pegues DA, Woernle CH. An outbreak of acute nonbacterial gastroenteritis in a nursing home. *Infect Control Hosp Epidemiol* 1993;14:87-94.
 14. Chadwick PR, McCann R. Transmission of a small round structured virus by vomiting during a hospital outbreak of gastroenteritis. *J Hosp Infect* 1994;26:251-259.
 15. Cunney RJ, Costigan P, McNamara EB, et al. Investigation of an outbreak of gastroenteritis caused by Norwalk-like virus, using solid phase immune electron microscopy. *J Hosp Infect* 2000;44:113-118.
 16. Green SM, Lambden PR, Deng Y, et al. Polymerase chain reaction detection of small round-structured viruses from two related hospital outbreaks of gastroenteritis using inosine-containing primers. *J Med Virol* 1995;45:197-202.
 17. Green J, Wright PA, Gallimore CI, Mitchell O, Morgan-Capner P, Brown DW. The role of environmental contamination with small round structured viruses in a hospital outbreak investigated by reverse-transcriptase polymerase chain reaction assay. *J Hosp Infect* 1998;39:39-45.
 18. Russo PL, Spelman DW, Harrington GA, et al. Hospital outbreak of Norwalk-like virus. *Infect Control Hosp Epidemiol* 1997;18:576-579.
 19. Caceres VM, Kim DK, Bresee JS, et al. A viral gastroenteritis outbreak associated with person-to-person spread among hospital staff. *Infect Control Hosp Epidemiol* 1998;19:162-167.
 20. Marx A, Shay DK, Noel JS, et al. An outbreak of acute gastroenteritis in a geriatric long-term-care facility: combined application of epidemiological and molecular diagnostic methods. *Infect Control Hosp Epidemiol* 1999;20:306-311.
 21. O'Neill HJ, McCaughey C, Wyatt DE, Mitchell F, Coyle PV. Gastroenteritis outbreaks associated with Norwalk-like viruses and their investigation by nested RT-PCR. *BioMed Central Microbiol* 2001;1:14.
 22. Sinn G. Norwalk-virus Ausbruch in einem Krankenhaus. *Epidemiologisches Bulletin* 2001;33:251-253.
 23. McCall J, Smithson R. Rapid response and strict control measures can contain a hospital outbreak of Norwalk-like virus. *Commun Dis Public Health* 2002;5:243-246.
 24. Inouye S, Yamashita K, Yamadera S, Yoshikawa M, Kato N, Okabe N. Surveillance of viral gastroenteritis in Japan: pediatric cases and outbreak incidents. *J Infect Dis* 2000;181(suppl 2):S270-S274.
 25. Sawyer LA, Murphy JJ, Kaplan JE, et al. 25- to 30-nm virus particle associated with a hospital outbreak of acute gastroenteritis with evidence for airborne transmission. *Am J Epidemiol* 1988;127:1261-1271.
 26. Koopmans MP. Outbreaks of viral gastroenteritis, in particular due to the Norwalk virus: an underestimated problem. *Ned Tijdschr Geneesk* 2002;146:2401-2404.
 27. Lopman BA, Reacher MH, Van Duynhoven Y, Hanon FX, Brown D, Koopmans M. Viral gastroenteritis outbreaks in Europe, 1995-2000. *Emerg Infect Dis* 2003;9:90-96.
 28. Centers for Disease Control and Prevention. "Norwalk-like viruses": public health consequences and outbreak management. *MMWR* 2001;50(RR-9):1-17. Available at www.cdc.gov/ncidod/dvrd/revb/gastro/rr5009.pdf. Accessed on February 15, 2004.
 29. Viral Gastroenteritis Subcommittee of the Scientific Advisory Committee of the National Disease Surveillance Center. *National Guidelines on the Management of Outbreaks of Norovirus Infection in Healthcare Settings*. Dublin, Ireland: National Disease Surveillance Center; 2003. Available at www.ndsc.ie/Publications/Norovirus/d819.PDF. Accessed on July 20, 2004.
 30. Anonymous. *Norwalk-Like Infections*. Berlin-Wedding, Germany: Robert Koch Institut; 2000. Available at www.rki.de/INFEKT/INF_A-Z/RAT_MBL/NORWALK.PDF. Accessed on January 3, 2004.
 31. Cowden JM. Winter vomiting. *BMJ* 2002;324:249-250.
 32. Beck-Sague C, Jarvis WR, Martone WJ. Outbreak investigations. *Infect Control Hosp Epidemiol* 1997;18:138-145.