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UNDER SECRETARY FOR HEALTH'S INFORMATION LETTER

THE ROLE OF NOROVIRUS IN OUTBREAKS OF GASTROENTERITIS

1. **Background.** Norovirus (Norwalk-like viruses), a frequent cause of outbreaks of gastroenteritis, is transmitted by multiple modes: ingestion of contaminated food or water, swimming in contaminated water, person-to-person by the fecal-oral route, and by aerosolization of viral particles from vomitus. These outbreaks of disease occur any place where persons congregate including military settings, cruise ships, group homes, schools, and nursing home care units. The latter is of particular interest to the Veterans Health Administration (VHA) with its past and future emphasis on long-term care. Since acute gastroenteritis can be a serious disease in the elderly or those with co-morbid illness, it is reasonable to provide information on the virus, diagnosis, treatment, and most important, prevention strategies to mitigate the possible effects of a norovirus cluster of cases in VHA long-term care units.

2. **The Virus.** Noroviruses are members of the family *Caliciviridae* and are well recognized etiologies of non-bacterial acute gastroenteritis. Noroviruses cause approximately 23 million cases of acute gastroenteritis each year and are likely the leading cause of outbreaks of gastroenteritis in the United States. Since such outbreaks are not uncommon, they present an opportunity for an active prevention program to prevent spread of infection in a congregate setting.

3. **Diagnosis.** The key to diagnosis of norovirus disease is suspecting acute viral gastroenteritis when a patient becomes ill, or when an outbreak of acute gastroenteritis becomes apparent. Molecular techniques are used for the specific diagnosis of norovirus disease. The usual test is reverse transcription polymerase chain reaction (RT-PCR) on stool. Norovirus RT-PCR testing is usually initiated after it is determined that an evaluation of an outbreak is necessary. Actual testing is usually done in specialized laboratories at the municipality, State, or Centers for Disease Control and Prevention level. Specimen collection needs to be coordinated with the receiving laboratory to ensure proper collection and transport. Ideally, the stool sample needs to be collected within the first day of onset of symptoms since the yield is greatest at this point. Rectal swabs are of less value compared to stool specimens. Vomitus can also be collected. Paired serum for acute and convalescent testing are also useful; the convalescent specimen needs to be collected 3 to 6 weeks after resolution of symptoms. Therefore, this is primarily a retrospective diagnosis. Environmental specimens may be of use and need to be collected after it has been determined that an evaluation is necessary and that such specimens are going to be of benefit to outbreak mitigation.

4. Treatment. There is no specific antiviral treatment for norovirus. Therefore, goals of treatment are supportive with particular emphasis on hydration and electrolyte balance. This may be particularly difficult in the elderly and chronically ill, and may require dosage adjustments of regular medications if renal dysfunction occurs. In general, the disease is self-limited after approximately 36 to 72 hours and is of minimal risk to a younger, healthier population.

5. Prevention. Prevention of spread of norovirus infection and disease is particularly difficult because of certain characteristics of the organism. The virus requires a very low infectious dose of less than 100 viral particles for spread of infection. The low infectious dose facilitates person-to-person transmission by the fecal-oral route (usually contaminated hands to mouth) and perhaps by droplet formation or aerosolization of viral particles in vomitus. There may be asymptomatic shedding in the stool for 2 days before and can last up to 2 weeks after acute illness. This obviously increases the risk of secondary spread and increases the chance of transmission when a food handler is infected. The virus is particularly environmentally stable and can survive up to 10 parts per million (ppm) chlorine, freezing, and heating to 60° Centigrade. This makes it difficult to eliminate from contaminated water and on environmental surfaces. In addition, the usual cleaning solutions used in hospitals are not particularly effective against norovirus. There is substantial strain diversity with multiple genetic and antigenic types. This requires complex diagnostics, and allows for repeated infections by multiple strains. Lastly, the lack of long-lasting immunity allows infections to occur more than once in the same patient.

a. **Specific Prevention Strategies.** Specific prevention strategies include:

(1) Early identification of patients with possible infectious diarrhea.

(2) When a patient with potential infectious diarrhea is identified, appropriate precautions need to be taken. Standard precautions alone may not be sufficient. If norovirus is suspected, confirmed, or during an outbreak situation, increased rigor may be necessary. Droplet precautions may be warranted in the event of vomiting as evidence exists for transmission due to aerosolization of vomitus that presumably results in droplets contaminating surfaces or entering the oral mucosa and being swallowed. Considering norovirus is an enteric infection with a low-infectious dose and that there are environmental implications for transmission, contact precautions need to be instituted.

(3) Persons who clean areas substantially contaminated by feces or vomitus need to consider wearing masks (not respirators) to prevent unintended ingestion of viral particles.

(4) Patient hygiene. Whenever possible, it is appropriate for patients to wash their hands before eating or other congregate activities. Soap and water is appropriate for washing hands.

(5) Staff needs to wash their hands with soap and water before food handling, between patients, and before and after any other duties where soiling may spread virus from patient-to-staff, staff-to-staff or staff-to-patient. **NOTE:** *A recommendation for the specific use of an alcohol-based hand-hygiene product in abatement strategies for norovirus was not identified.*

(6) Patients with norovirus acute gastroenteritis need to be left in contact precautions at least 48 hours after symptoms abate.

(7) Employees who have norovirus acute gastroenteritis should be off-duty for approximately 48 hours after symptoms abate.

(8) Because of the residential quality of long-term care facilities, food discipline needs to be maintained at all times. This includes issues regarding the sharing of food among patients, the sharing of food from patients to staff, the sharing of food from staff to patients, and other potential mechanisms for spreading the infection among the long-term care site community.

(9) Patients and staff need to receive specific training and education on acute gastroenteritis (epidemic diarrheal disease) to include causes, risks, and prevention techniques with emphasis on the hygienic issues in the prevention of the spread of the disease.

(10) If there is acute gastroenteritis in the community, it is prudent to educate visitors regarding issues of food discipline and handwashing.

b. **Environment of Care.** In the long-term care setting, cleanliness is not a luxury, but rather a necessity. Because of the proximity of groups of elderly and/or chronically ill patients, some of whom may be incontinent, attention to details of rigorous cleaning of the environment is critical. In the best of circumstances, however, norovirus presents a particular challenge. When there is evidence of norovirus activity in the long-term care setting, the usual cleaning routine may not suffice because of the low-infectious dose of the organism and its stability in the environment. Therefore, more frequent cleaning, using an Environmental Protection Agency (EPA)-registered hospital detergent or disinfectant designed for general housekeeping purposes, in patient-care areas is appropriate. Considering environmental surfaces have been implicated in health care-associated transmission of norovirus, additional disinfection of environmental surfaces in patient care areas may be prudent. Suitable disinfectants for this purpose include freshly prepared chlorine solutions at concentrations of equal to or greater than 1000 ppm, phenol-based compounds, and accelerated hydrogen peroxide products. The most practical disinfectant is a 1 to 50 (ratio) solution of domestic bleach (an EPA-registered sodium hypochlorite product is preferred). Disinfectants need to be used with care. Potential shedders of virus need to be removed from the environment by appropriate precautions or work restrictions, and, if possible, new persons should not be moved into the setting until the outbreak has abated. Contaminated linens need to be handled as little as possible with the minimum of agitation and need to be laundered with detergent at the maximum available cycle length and then need to be machine dried.

6. Conclusion. While norovirus disease can be a major inconvenience in such places as cruise ships, in long-term care units the consequences of this disease are considerable and can be fatal. Therefore, it is prudent to maintain vigilance in routine infection control practices and prepare for the contingency of a patient becoming ill with acute viral gastroenteritis. If prepared, the facility should be able to address the first such case and prevent spread to other residents and staff. The keys to success for prevention of infection and spread of infection with viral gastroenteritis agents are:

- a. A clean environment of care,
- b. Early detection of patients who may have viral gastroenteritis,
- c. Rapid intervention with appropriate precautions, and
- d. Meticulous attention to handwashing, food discipline, and specialized cleaning, as needed.

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8. Inquiries

a. For questions related to clinical issues of the norovirus illness, contact the Office of the Program Director for Infectious Diseases, Dr. Gary Roselle at (513) 475-6398.

b. For questions regarding sanitation and linen contact the Environmental Program Service at (202) 565-8525.

c. For questions regarding general programmatic and broader safety issues, contact the National Center for Patient Safety at (734) 930-5890.

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Norovirus: Technical Fact Sheet

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Noroviruses (genus *Norovirus*, family *Caliciviridae*) are a group of related, single-stranded RNA, nonenveloped viruses that cause acute gastroenteritis in humans. Norovirus was recently approved as the official genus name for the group of viruses provisionally described as “Norwalk-like viruses” (NLV). This group of viruses has also referred to as caliciviruses (because of their virus family name) and as small round structured viruses, or SRSVs (because of their morphologic features). Another genus of the calicivirus family that can cause gastroenteritis in humans is *Sapovirus*, formerly described as “Sapporo-like virus” (SLV) and sometimes referred to as classic or typical calicivirus.

Noroviruses are named after the original strain “Norwalk virus,” which caused an outbreak of gastroenteritis in a school in Norwalk, Ohio, in 1968. Currently, there are at least four norovirus genogroups (GI, GII, GIII and GIV), which in turn are divided into at least 20 genetic clusters.

Clinical Presentation

The incubation period for norovirus-associated gastroenteritis in humans is usually between 24 and 48 hours (median in outbreaks 33 to 36 hours), but cases can occur within 12 hours of exposure.

National Immunization Program

- ▶ [Rotavirus Vaccine Announcement](#)
(Oct 22, 1999)

Norovirus infection usually presents as acute-onset vomiting, watery non-bloody diarrhea with abdominal cramps, and nausea. Low-grade fever also occasionally occurs, and vomiting is more common in children. Dehydration is the most common complication, especially among the young and elderly, and may require medical attention. Symptoms usually last 24 to 60 hours. Recovery is usually complete and there is no evidence of any serious long-term sequelae. Studies with volunteers given stool filtrates have shown that asymptomatic infection may occur in as many as 30% of infections, although the role of asymptomatic infection in norovirus transmission is not well understood.

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Virus Transmission

Noroviruses are transmitted primarily through the fecal-oral route, either by consumption of fecally contaminated food or water or by direct person-to-person spread. Environmental and fomite contamination may also act as a source of infection. Good evidence exists for transmission due to aerosolization of vomitus that presumably results in droplets contaminating surfaces or entering the oral mucosa and being swallowed. No evidence suggests that infection occurs through the respiratory system.

Noroviruses are highly contagious, and it is thought that an inoculum of as few as 10 viral particles may be sufficient to infect an individual. During outbreaks of norovirus gastroenteritis, several modes of transmission have been documented; for example, initial foodborne transmission in a restaurant, followed by secondary person-to-person transmission to household contacts. Although presymptomatic viral shedding may occur, shedding usually begins with onset

of symptoms and may continue for 2 weeks after recovery. It is unclear to what extent viral shedding over 72 hours after recovery signifies continued infectivity.

Immunity to Norovirus

Mechanisms of immunity to norovirus are unclear. It appears that immunity may be strain-specific and lasts only a few months; therefore, given the genetic variability of noroviruses, individuals are likely to be repeatedly infected throughout their lifetimes. This may explain the high attack rates in all ages reported in outbreaks. Recent evidence also suggests that susceptibility to infection may be genetically determined, with people of O blood group being at greatest risk for severe infection.

Disease burden of Norovirus Gastroenteritis

CDC estimates that 23 million cases of acute gastroenteritis are due to norovirus infection, and it is now thought that at least 50% of all foodborne outbreaks of gastroenteritis can be attributed to noroviruses.

Among the 232 outbreaks of norovirus illness reported to CDC from July 1997 to June 2000, 57% were foodborne, 16% were due to person-to-person spread, and 3% were waterborne; in 23% of outbreaks, the cause of transmission was not determined. In this study, common settings for outbreaks include restaurants and catered meals (36%), nursing homes (23%), schools (13%), and vacation settings or cruise ships (10%).

Most foodborne outbreaks of norovirus illness are likely to arise through direct contamination of food by a food handler immediately before its consumption. Outbreaks have frequently been

associated with consumption of cold foods, including various salads, sandwiches, and bakery products. Liquid items (e.g., salad dressing or cake icing) that allow virus to mix evenly are often implicated as a cause of outbreaks. Food can also be contaminated at its source, and oysters from contaminated waters have been associated with widespread outbreaks of gastroenteritis. Other foods, including raspberries and salads, have been contaminated before widespread distribution and subsequently caused extensive outbreaks.

Waterborne outbreaks of norovirus disease in community settings have often been caused by sewage contamination of wells and recreational water.

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Diagnosis of Norovirus

Human. In the last 10 years, diagnosis of norovirus illness in outbreaks has improved with the increasing use of reverse transcriptase polymerase chain reaction (RT-PCR). Currently, 27 state public health laboratories have the capability to test for noroviruses by RT-PCR. RT-PCR can be used to test stool and emesis samples, as well as to detect the presence of noroviruses on environmental swabs in special studies. Identification of the virus can be best made from stool specimens taken within 48 to 72 hours after onset of symptoms, although good results can be obtained by using RT-PCR on samples taken as long as 5 days after symptom onset. Virus can sometimes be found in stool samples taken as late as 2 weeks after recovery.

Older methods for diagnosis include direct and immune electron microscopy of fecal specimens, and detection of a fourfold increase of specific antibodies in acute- and convalescent-phase blood samples. An enzyme-linked immunosorbent assay

for detection of virus in stools is under development.

Sequencing of noroviruses found in clinical samples has helped in conducting epidemiologic investigations by linking cases to each other and to a common source and by differentiating outbreaks that were mistakenly connected. Sequences can be entered into CaliciNet, a database used to store the different sequences of norovirus that cause disease throughout the United States, thereby allowing rapid assessment of the relationships between strains.

In addition to microbiological techniques, several epidemiologic criteria have been proposed for use in determining whether an outbreak of gastroenteritis is of viral origin. Kaplan's criteria for this purpose are as follows: 1) a mean (or median) illness duration of 12 to 60 hours, 2) a mean (or median) incubation period of 24 to 48 hours, 3) more than 50% of people with vomiting, and 4) no bacterial agent previously found. Although quite specific, these criteria are not very sensitive, and therefore the possibility of a viral etiology should not be discarded if the criteria are not met.

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Environmental. Assays to detect virus in food need to be adapted for each food substance; these have been only rarely used, with the exception of assays to detect virus in shellfish. Water can be tested for noroviruses by using RT-PCR to detect virus when large volumes of water are processed through specially designed filters.

Management of Norovirus Infection

No specific therapy exists for viral gastroenteritis. Symptomatic therapy consists of replacing fluid losses and

correcting electrolyte disturbances through oral and intravenous fluid administration.

Prevention

Prevention of foodborne norovirus disease is based on the provision of safe food and water. Noroviruses are relatively resistant to environmental challenge: they are able to survive freezing, temperatures as high as 60°C, and have even been associated with illness after being steamed in shellfish. Moreover, noroviruses can survive in up to 10 ppm chlorine, well in excess of levels routinely present in public water systems. Despite these features, it is likely that relatively simple measures, such as correct handling of cold foods, frequent handwashing, and paid sick leave, may substantially reduce foodborne transmission of noroviruses.

Surveillance of Norovirus Infection in the United States

CDC currently does not conduct active surveillance to monitor outbreaks of gastroenteritis caused by noroviruses. Outbreaks are reported to CDC's Viral Gastroenteritis Section, Respiratory and Enteric Viruses Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases (NCID) when states send specimens for testing or sequencing, or outbreaks are reported directly by states to the database maintained by the Foodborne Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, NCID.

Recently, a system called CaliciNet has been developed on the basis of the PulseNet model. CaliciNet is a database of norovirus sequences identified from outbreaks of norovirus that can then help to determine links between outbreaks.

For further details please email calicinet@cdc.gov

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