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Norovirus Infection

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Case Study: Norovirus at Thanksgiving

In November, 2007, 24 family members gathered in Alpena Michigan to celebrate Thanksgiving with a family potluck. Nineteen of 24 attendees experienced vomiting and diarrhea 16–24 hours after the meal. Two care-givers became ill 24 hours after the onset of illness in their children. Symptoms lasted 24–48 hours and the 76 year old family matriarch was hospitalized and treated for dehydration. Upon further investigation, it was discovered that one attendee was caring for an infant with diarrhea prior to the meal. This attendee prepared food (Jello salad with whipped cream) for the potluck.

This case, taken from my personal family history, highlights many of the common features of norovirus infections — short incubation period, high attack rate, rapid onset of vomiting and diarrhea, typical duration of illness, and the high secondary attack rate among caregivers. More than 50% of all foodborne disease outbreaks can be attributed to noroviruses. Noroviruses are ubiquitous and they are the leading cause of acute gastroenteritis outbreaks worldwide. [1] Mead et al. reported that noroviruses cause 23 million infections, 50,000 hospitalizations and 310 fatalities in the United States each year. [2] These outbreaks affect people of all ages and they occur in a wide variety of settings including nursing homes, hospitals, restaurants, communities, schools, day care centers, military barracks, family gatherings, and cruise ships. [2] (Table 1)

Table 1. Outbreaks confirmed by CDC between 1994 and 2006 (n=660)

36%	**Long-term care facilities (e.g., nursing homes)**
31%	**Restaurants, parties, and events**
20%	**Vacation settings (including cruise ships)**
13%	**Schools and community settings**

Source: http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus-surv-diseaseburden.htm

Clinical Presentation/Treatment

Norovirus infection produces acute self-limiting gastroenteritis lasting 24–48 hours. Symptoms include nausea, vomiting, watery non-bloody diarrhea, abdominal pain, myalgia, headache, malaise, low grade fever or a combination of these symptoms. Diarrhea is more common than vomiting in children. Dehydration is the most common complication, especially among the young and elderly, and may require medical attention. Treatment is largely supportive with an emphasis on oral rehydration to replace fluids and electrolytes.

Epidemiology

Noroviruses (formerly Norwalk-like viruses) are nonenveloped RNA viruses and members of the Calicivirus family. Caliciviruses include two genera that cause human disease — noroviruses and sapoviruses. Noroviruses are separated into five genogroups on the basis of sequence comparison of the RNA polymerase and capsid region of the genome. Genogroups I, II, and IV are associated with infections in humans. **[3]** Most human norovirus gastroenteritis is caused by genogroup II viruses. Genogroup I infections are infrequent and genogroup IV infection is extremely rare. Multiple antigenic types circulate simultaneously in the same region.

Long-term and cross-strain immunity to noroviruses is limited. Short-term immunity lasting up to 14 weeks has been documented in volunteer studies after induced Norwalk virus illness but long-term immunity was variable. Some individuals became ill after re-challenge 27–42 months later. Levels of pre-existing norovirus antibody are not predictive of susceptibility or resistance to disease.

Incubation Period: 12–72 hours

Virus Transmission

Noroviruses replicate efficiently in the upper intestine and extremely high viral loads (>100,000 virus particles/gram of material) are present in stool and vomitus. Noroviruses are also among the most infectious viruses known to man. Ingestion of just 10 virus particles is sufficient to produce infection in normal healthy individuals. **[3]** Taken together, this means that frank exposure to stool may not be necessary for transmission because aerosols generated during vomiting and diarrhea may contain sufficient virus to infect another person. Contaminated fomites are also a significant source of infection **(Table 2)**. Caregivers and people who clean up after sick individuals are at high risk of infection. Infected individuals can shed virus in stools for two or more weeks but the highest virus concentrations are present for 72 hours after the symptoms subside.

Most norovirus contamination of food is thought to occur during preparation and service by food handlers who are infected with the virus **(Table 2)**. However, some foods can be contaminated with norovirus before being delivered to a restaurant or store. Several outbreaks have been caused by the consumption of oysters harvested from contaminated waters. Other food products, such as salads and fruit, have also been contaminated at their source.

Table 2. Norovirus Transmission

People can become infected with the virus by:	**Eating food or drinking liquids that are contaminated with norovirus,**	**Touching surfaces or objects contaminated with norovirus, and then placing their hand in their mouth, and**	**Having direct contact with another person who is infected and showing symptoms (for example, when caring for someone with illness, or sharing foods or eating utensils with someone who is ill).**
Food and drinks can become contaminated by:	**Direct contact with contaminated hands**	**Direct contact with work surfaces that are contaminated with infectious stool or vomit**	**Tiny droplets of vomitus that spray through the air when an infected person vomits**

Modified from: **http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus-foodhandlers.htm**

Noroviruses can also be transmitted in swimming pools and water parks. These recreational waters can be can be shared by dozens to thousands of people each day. The high incidence of diarrhea, fecal incontinence (particularly in young children) and the presence of residual fecal material on the bodies of swimmers (up to 10 g for young children) makes fecal contamination of swimming venues a common occurrence. [4] Chlorination of water at public swimming venues is one of the most common measures used to protect swimmers from infectious diseases. Unfortunately noroviruses are chlorineresistant and can survive for 30–60 minutes in water chlorinated at concentrations typically used in swimming pools. Maintaining adequate disinfectant levels at kiddie/ wading pools and interactive fountains can be especially challenging. The shallow depth, aeration, sunlight, and organic material (e.g., feces, urine, sweat, and dirt) from young children can rapidly diminish chlorine concentrations, particularly when bather load is high. [5] Decreased chlorine levels, the low number of viruses need to produce infection, and the high level of viral excretion in stool means that one or more ill individuals with diarrhea can contaminate large volumes of water and expose large numbers of coswimmers. [5]

Noroviruses are extremely hardy and difficult to destroy. Noroviruses can withstand freezing, heating to 140ºF (the temperature of a medium rare steak), and chlorine concentrations to 10 ppm, levels well above those found in public water systems. Soaps, alcohol hand sanitizers, and other detergents will not inactivate the virus but the mechanical washing process can reduce the amount of virus present on hands and other objects. When using these products, vigorous washing is recommended to reduce surface contamination.

Methods to prevent and control outbreaks

- Promote good hand hygiene, including frequent washing with soap and water and use of alcohol-based hand sanitizers (=62% ethanol) as a complement to (not a replacement for) to soap and water washing.

- Discourage sharing of eating utensils, toothbrushes, linens, or other personal items, especially when ill.

- Restrict ill individuals from food preparation activities until at least 72 hours after symptoms have resolved **(Table 3)**.

- Ill individuals should not use recreational water venues for 2 weeks after the symptoms resolve. **[4]**

- Encourage ill individuals to seek appropriate medical care and limit social activities if they have symptoms consistent with norovirus infection.

- Disinfect bathrooms and any areas possibly contaminated by ill persons, using a freshly made 1:10 dilution of chlorine bleach (5.25% hypochlorite) solution or another approved disinfectant. Agents registered as effective against norovirus by the Environmental Protection Agency are listed at **http://www.epa.gov/oppad001/list_g_norovirus.pdf**. Evidence for efficacy against norovirus usually is based on studies using feline calicivirus (FCV) as a surrogate. However, FCV and norovirus exhibit different physiochemical properties, and whether inactivation of FCV reflects efficacy against norovirus is unclear. **[6]**

- Caregivers and individuals who clean up after ill individuals are at higher risk of norovirus infection.
  To reduce the risk for norovirus transmission during cleanup:
  - remove vomitus and fecal material carefully to limit aerosolization (e.g., soaking up vomitus or diarrhea with paper towels or other disposable cloths with minimal agitation and removing those in impervious bags,
  - thoroughly clean surfaces and disinfect with freshly made 1:10 dilution of household bleach containing 5.25% hypochlorite or another EPA-registered norovirus disinfectant, and
  - wear appropriate personal protective equipment (PPE) (e.g., gloves, masks, and gowns) when cleaning vomitus or feces. **[7, 8]**

Table 3. Preventing the spread of noroviruses

Do not prepare food while ill:	**Noroviruses are present at highest concentrations for 72 hours after the symptoms resolve.**			
Practice proper hand hygiene:	**Noroviruses are present in the stool for as long as 2 to 3 weeks after an infected person feels better. Thus, continued care in washing hands is important in preventing the spread of this virus.**		**Alcohol-based hand sanitizers (containing at least 62% ethanol) may be a helpful addition to hand washing, but they are not a substitute for washing with soap and water.**	
Take care in the kitchen:	**Food items that might have become contaminated with norovirus should be thrown out.**	**Carefully wash fruits and vegetables, and cook oysters and other shellfish thoroughly before eating them.**	**Oysters should be obtained from reputable sources, and appropriate documentation should be kept in case trace back is needed.**	**Sick children and infants in diapers should be excluded from food preparation areas.**
Clean and disinfect contaminated surfaces:	**After an episode of illness, such as vomiting or diarrhea, immediately clean, disinfect, and rinse contaminated surfaces with a 10% bleach solution.** **To be effective, bleach solutions should be prepared daily.**			
Wash laundry thoroughly:	**Linens (towels, tablecloths, napkins) and clothing that are soiled to any extent with vomit or stool should be handled carefully — without agitating the item — to avoid spreading virus.**		**The items should be laundered with detergent at the maximum available cycle length and then machine dried.**	

Modified from: **http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus-foodhandlers.htm**

LABORATORY DIAGNOSIS

Virus Culture:

Virus culture is useless for the detection of noroviruses because these agents do not grow in routine cultures.

Electron Microscopy (EM) and Immune Electron Microscopy (IEM):

These methods have been used to detect noroviruses in stool specimens but the sensitivity of EM detection is low, requiring at least 10^6 viral particles per ml of stool. [9, 10] These procedures are not recommended because they will detect virus in less than 50% of infected individuals.

Antigen Detection Immunoassays:

Several antigen detection immunoassays are commercially available but these tests currently exhibit inadequate sensitivity (<50%) to be useful for diagnosis of sporadic cases. In addition, the wide antigenic variation among noroviruses makes it difficult for these assays to reliably detect norovirus infections.

Norovirus Serology.

Detection of norovirus antibodies in acute and convalescent sera is usually done for research studies. The wide antigenic variation and lack of cross-protection makes norovirus serologies problematic and they are not recommended for primary diagnosis. In addition, volunteer challenge studies have shown that antibody titers are not predictive of susceptibility or resistance to disease. [11]

Reverse-Transcriptase PCR (RT-PCR).

RT-PCR is the current method of choice for detecting norovirus infections in stool specimens. Identification of the virus can be best made from stool specimens obtained during the acute phase of illness (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.

RT-PCR testing of stool specimens for noroviruses will be available at Warde Medical Laboratory on January 10, 2011. This test will detect and differentiate genogroup I and II noroviruses. Genogroup IV norovirus infections are rare and testing for this genogroup is available through the Michigan Department of Community Health and the Centers for Disease Control and Prevention. Norovirus RT-PCR testing will also be included as part of the Comprehensive Virus Detection protocol when testing stool specimens.

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