

Noroviruses

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. 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.

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.

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.

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