# Norovirus

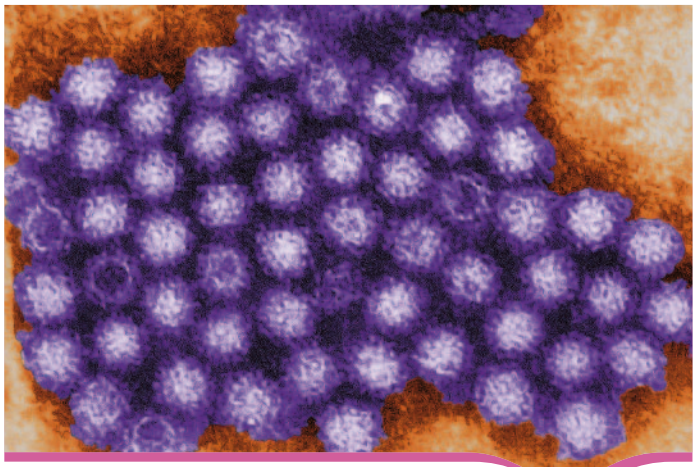
Norovirus
Family of *Caliciviridae*
Genus Norovirus

Virus

## Characteristics and sources of Norovirus

### Main microbial characteristics

Noroviruses (NoVs) are the principal causes of acute gastroenteritis (AGE) in humans of all age groups. They are small, non-enveloped viruses, with an icosahedral capsid, about 27 nm in diameter. Their single-stranded, positive-sense RNA genome is 7,500 to 7,700 bases in length and contains three Open Reading Frames (ORFs). NoVs vary widely regarding their antigenic and genetic characteristics. The absence of an *in vitro* cultivation system has led to classifying NoVs using genetic analysis. According to this criterion, NoVs are currently divided into five genogroups (G) with the 9, 19, 2, 2 and 1 sub-groups (sometimes called genotypes) belonging to GI through GV respectively. Only GI, GII and GIV have ever been observed in infected humans..



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### Sources of the hazard

Infected humans are the only reservoir of human noroviruses. Strains have been found in animals that are genetically similar to human strains, but there are no data on the risk of zoonosis. The sharing of glycan receptors, cellular ligands that are involved in the early stages of infection, seems to be a key factor in potentially facilitating the passage of NoVs between species.

Rates of faecal shedding can be high (up to $10^{11}$ particles/g of faeces) and shedding may last a considerable time (two to three weeks after disappearance of the symptoms). Asymptomatic subjects may also shed the virus in considerable quantities. Very large quantities of viral particles are therefore present in dejections during winter epidemics.

Regarding the physico-chemical properties of these viruses, they can resist purification treatment and thus remain in the environment for long periods. Viral loads are likely to be much heavier in the environment in the event of malfunction by sewage treatment plants or periods of heavy rain (causing overflow of lift stations).

### Transmission routes

Transmission occurs mainly by the faecal-oral route. It is often direct, from person to person, but can also be indirect, by ingestion of contaminated food or water or by contact with a contaminated environment. This foodborne transmission can then be amplified by person-to-person transmission. Contamination by aerial route (aerosols) has been proven, particularly during vomiting, and also contributes to viral dissemination.

**Recommendations for primary production**

- Good growing practices should be strictly observed in order to reduce the risk of contaminating raw materials (shellfish, fruits and vegetables) by potentially contaminated irrigation or sea water.
- The influence of weather events (heavy rain causing overflow of lift stations and sewage plants) on the pollution of water resources should be taken into account and preventive action plans should be set up to ensure their protection.
- In shellfish growing areas, this hazard should be taken into account in vulnerability profile studies and special attention should be paid to preventing contamination of water and to ensuring the traceability of produce. Local warning systems should be set up to give producers real-time information on any event likely to degrade water quality.

Data sheet on foodborne biological hazards
**May 2011**

# Human foodborne disease

## Nature of the disease

The characteristics of the disease are presented in Table 1.

**Susceptible population groups[1]:** Susceptibility to infection by NoVs varies depending on the individual. There are two known mechanisms that explain these differences in susceptibility: a genetic factor related to blood group antigens and acquired immunity. The blood group antigens in the intestinal wall are recognised differently by the different strains of NoV, leading to susceptibility that varies between individuals. As different strains have very different binding patterns, it is probable that each individual could be infected by at least one NoV. The second factor governing susceptibility is the acquisition of immunity after infection by a given strain. Such immunity is partial and of short duration because of the diversity of strains. The same individual can therefore be infected several times with different strains.

## Dose-effect[2] and dose-response[3] relationships

Infectiosity is high but varies between strains and according to the genetic susceptibility of the individual. Studies in volunteers have shown that the $ID_{50}$[4] for the Norwalk strain (GI.1) is between 18 and 1000 particles (assayed by RT-PCR). In some individuals, symptoms were observed after ingestion of fewer than five particles.

There is little information available concerning quantification of the virus in implicated foods. The only quantitative data available concern shellfish implicated in clusters of outbreaks (implicating strains GI and/or GII), with results varying from 50 to 16,000 copies per gram of digestive tissue.

## Epidemiology

In France, several systems provide mutually complementary surveillance of gastroenteritis: Inserm's *Réseau Sentinelles* network, the emergency services network of the InVS (Institute for Public Health Surveillance), mandatory notification of foodborne outbreaks and the National Centre of Reference (NCR) for enteric viruses.

Noroviruses are the major cause of acute gastroenteritis in all age groups and all countries. In Europe, a seasonal peak occurs in winter, but occasional outbreaks are observed in spring and summer. Sporadic cases are observed throughout the year. Variations in winter incidence have been linked with the appearance of variants or recombinant strains.

Noroviruses are the infectious agents most frequently responsible for gastroenteritis outbreaks in institutional settings (day-care centres, hospitals, schools, retirement homes, cruise liners, etc.). Virus dissemination in institutions is promoted by asymptomatic infected individuals. When a group is exposed to a common source of contamination, the attack rate is approximately 50%.

# Role of food

## Main foods to consider

Food can become contaminated at different stages of the food production process: growing and irrigation, harvesting, processing, packaging and preparation. Noroviruses are highly resistant and persistent after being released into the environment, which can lead to contamination of water.

Foods at risk can be divided into two categories:

- those that can become contaminated during production: foodstuffs cultivated with the use of irrigation (fruits and vegetables, mostly soft fruits) or immersion (bivalve shellfish), drinking water. Most foodborne norovirus outbreaks have been related to the consumption of shellfish contaminated during accidental overflows of wastewater or water from distribution systems where malfunctions have occurred;
- those that can become contaminated during handling by an infected person who does not take the appropriate hygiene precautions (potentially any type of handled food that is then consumed uncooked, or insufficiently cooked).

## Inactivation treatments in industrial environments

As human noroviruses cannot be cultivated *in vitro*, experiments are performed with canine calicivirus (CaCV), feline calicivirus (FCV) or murine norovirus (MNV). Generally speaking, virucidal treatments are only considered to be effective if they result in a 4-$log_{10}$ reduction in the number of infectious viral particles.

However, animal caliciviruses are unreliable surrogates as they do not have the same characteristics as human strains. The data given in the Table 2 should therefore be interpreted in the light of these reservations.

(1) Susceptible population groups: people with a higher than average probability of developing symptoms or serious forms of the disease, after exposure to a foodborne hazard [definition used for ANSES data sheets].

(2) Relationship between the dose (the quantity of microbial cells ingested during a meal) and the effect on an individual.

(3) For a given effect, the relationship between the dose and the response, i.e. the probability of this effect appearing, in the population.

(4) $ID_{50}$ is the dose causing the onset of infection in 50% of individuals exposed, while $LD_{50}$ is the dose causing the death of 50% of individuals exposed.

Table 1. **Disease characteristics**

| Mean incubation period | Main symptoms | Duration of infectious period (shedding) | Complications |
|---|---|---|---|
| 10– 50 hours | Acute gastro-enteritis: sudden onset of vomiting, nausea and/or diarrhoea, sometimes associated with abdominal cramps, discomfort, anorexia, fever (low-grade, and observed in fewer than 50% of cases), shivering, aches and headaches | Peak of viral shedding in faeces varies from 3 to 10 days depending on individuals, followed by reduced shedding that can last for up to 3 weeks | Dehydration with weight loss, electrolyte imbalance (hypokalaemia) and kidney failure that can lead to death. Observed most frequently in the elderly or in patients suffering from chronic diseases. Immunocompromised subjects can remain severely infected for long periods. |
| **Target population** | **Duration of symptoms** | **Asymptomatic forms** | |
| All age groups | 2 - 3 days<br>(sometimes longer, up to 6 days, in children and the elderly) | Yes<br>Observed in about 1/3 of volunteers during clinical studies | |

Table 2. **Inactivation treatments for animal caliciviruses in food**

| Virus | Inactivation treatment | Matrix | Number of $log_{10}$ reduction in viral titre |
|---|---|---|---|
| **Heat treatment** | | | |
| FCV CaCV | 71°C, 1 min | Cell-culture medium | 3 |
| | 56°C, 8 min | Cell-culture medium | 3 |
| MNV | 63°C, 0.44 min | Cell-culture medium | 1 |
| | 75°C, 15 sec | Raspberry purée, 9.2 °Brix | 2.8 |
| | 63°C, 1 min | Milk | 1.35 |
| **Disinfectants** | | | |
| FCV | Hypochlorite 200 ppm, 0.5 min | Raspberries (15 g in 200 ml of water) | 1.6 |
| | Peracetic acid 300 ppm, 10 min | Lettuce (10 g in 100 ml of water) | 3 |
| FCV CaCV | Ethanol at 70%, 30 min | Cell-culture medium | 3 |
| **High Pressure** | | | |
| FCV | 275 MPa/ambient temperature/5 min | Cell-culture medium | > 6 |
| | 500 MPa/20°C/5 min | Sausage | 3 |
| MNV | 400 MPa/5°C/5 min | Oyster | 4 |
| | 450 MPa/20°C/5 min | Cell-culture medium | 6.8 |
| **Irradiation** | | | |
| FCV | 200 Gy | Low-protein medium | 1,6 |
| **UV** | | | |
| FCV | 12 mJ/cm² | Low-protein medium | 3 |
| | 40 mJ/cm² | Lettuce | 3.5 |
| | 120 mJ/cm² | Lettuce | 3.8 |

The following drinking water treatments are considered to be effective against surrogate viruses (calicivirus in particular):

- chemical treatments at CT[5] values normally applied in the treatment of water intended for human consumption;
- UV radiation at a dose of 400 J/m² (4-log reduction) and ultrafiltration (6 $log_{10}$ reduction).

# Monitoring in food

### Regulations in force applicable to foods at a risk

There are currently no regulatory criteria. The *Codex alimentarius* Commission is preparing guidelines entitled *Application of general principles of food hygiene to the control of viruses in food* (currently at stage 3 of the procedure).

The virological quality of water is mainly assessed by screening for cultivable enteroviruses. In investigations of outbreaks of gastroenteritis due to norovirus, samples of suspect water and food can be sent to the National Reference Laboratories or to ANSES's laboratories for screening and characterisation at molecular level.

### Principles of methods of detection, counting and typing

As human noroviruses cannot be cultivated, only molecular biology techniques can be used to detect and quantify them. Concerning the method for analysis in foods (bottled waters, fresh fruits, vegetables, shellfish, etc.) and on food surfaces, standards are being developed at European level, based, following elution and concentration of the viruses, on one-step real-time RT-PCR using a hybridisation probe, either qualitatively or quantitatively.

(5) CT: product of the concentration of the disinfectant multiplied by the contact time. It varies depending on water quality (variable organic load).

**Recommendations to operators**

- **Kitchen staff or anyone else involved in handling foods, especially those intended to be eaten raw or lightly cooked, should be made aware of the risk of faecal-oral transmission and food hygiene measures. Personnel must be aware of the importance of not handling food if presenting symptoms of gastroenteritis.**
- **Compliance with cleaning and disinfection procedures and the conscientious choice of raw materials (origin, area of production, risk of viral contamination, etc.) contribute to better control of viral risk.**
- **Furthermore, it should be noted that European regulations include the obligation for certain categories of shellfish to undergo heat treatment.**

# Domestic hygiene

Noroviruses are resistant to conventional food storage methods (refrigeration and freezing) as well as heat treatment (30 min at 60°C) and variations in pH (3h at pH 3 at ambient temperature). The measures commonly recommended for preventing bacterial growth have no effect on viral contamination.

Hygiene rules must be respected scrupulously in the event of sickness in the household.

**Recommendations to consumers**

- **Personal and collective hygiene remains the basis for primary prevention. It is absolutely necessary to wash hands thoroughly after using the toilet and before preparing or eating food.**
- **People infected with noroviruses must not handle food.**
- **Avoid consuming shellfish that do not come from authorised and inspected areas of production, unless they have been thoroughly cooked.**

# References and links

### General references


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### Contact details for the reference laboratories (NCR, LCR, LNR)

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