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Popular Article

Norovirus: From Historic Outbreaks to Modern Challenges and Future Solution

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Introduction

When an outbreak of gastroenteritis occurred in Norwalk, Ohio, back in the day, norovirus—formerly known as Norwalk virus—first appeared on the scene (1). Being the first viral troublemaker to wreak such damage, it earned its stripes. The sickness, which was first called "winter vomiting disease" in 1929, got its moniker from how people clutch their stomachs and rush to the nearest bathroom during the festive season (2). In 1968, a Norwalk elementary school was the epicenter of yet another norovirus outbreak. Imagine that half of the student body had diarrhea, vomiting, nausea, and possibly even a fever. It was an enormous stomach bug feast! Almost all of those affected initially reported feeling queasy (98%) and vomiting (92%), along with a long list of additional symptoms including fever, tiredness, and cramping in the abdomen (3).

Etiology

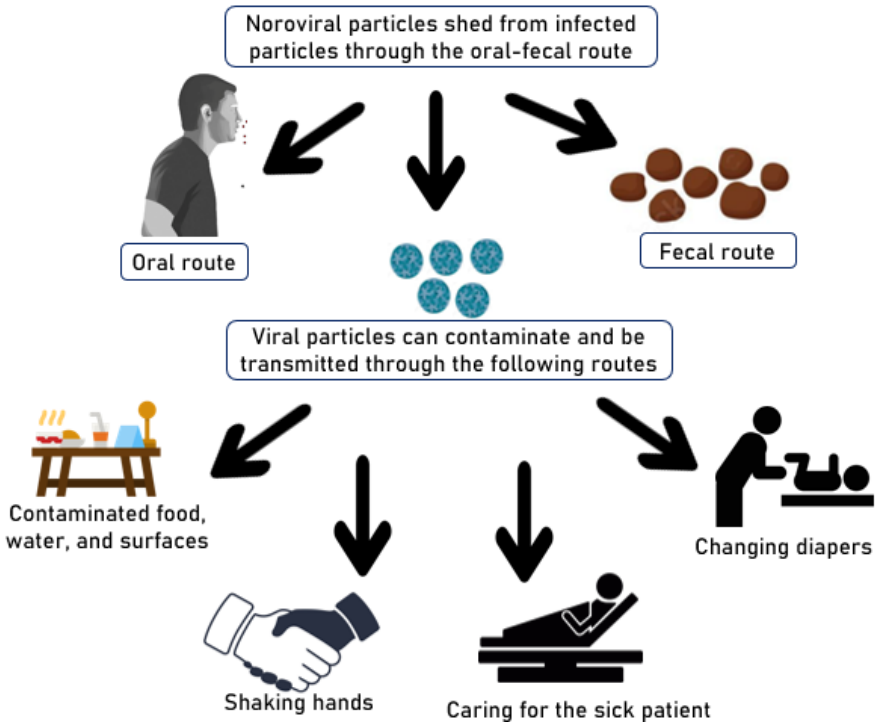
Norovirus (NoV) is a non-enveloped virus belongs to the Caliciviridae family and genus Norovirus. Its virion is small, 27–35 nm in diameter, and highly stable in various harsh environments, which makes difficult to eliminate the virus (4).

Epidemiology

Norovirus (NoV) outbreaks pose a significant burden globally, with an estimated 400,000 infectious cases and 56 mortality incidents annually in the UK alone (5). However, underreporting is common, impacting epidemiological estimates and control measures. The COVID-19 pandemic has

exacerbated this issue, leading to decreased surveillance and testing for diseases like NoV. Recent observations indicate a rise in NoV outbreaks post-pandemic, possibly due to "immunity debt" from lockdown restrictions. Children under 5 years old bear a substantial NoV burden, with around 200 million cases globally and 50,000 annual deaths. Healthcare facilities are particularly vulnerable, accounting for 40% of all NoV outbreaks. Research conducted in India between 2017 and 2019 on hospital-based norovirus surveillance among children under age of 5 years highlights how close physical proximity and frequent interaction in healthcare environments contribute to the transmission of norovirus, resulting outbreaks within hospital settings. This surveillance initiative aimed to gather comprehensive data on norovirus infections among young children admitted to hospitals across the country (4).

***Fig* 1. Transmission Modes of NoV reported by CDC**



Symptoms

Norovirus most commonly cause vomiting, diarrhea, and foodborne illness. It triggers the inflammation in stomach or intestines known as acute gastroenteritis with symptoms appear 12 to 48 hours post exposure. Most individuals recover within 1 to 3 days, but they can transmit the virus several days thereafter. Norovirus infected individuals often experience severe symptoms, including frequent vomiting and diarrhea which can lead to dehydration, particularly in young children, elderly and those people underlying with health conditions. It is important to monitor children with norovirus for signs of dehydration, such as reduced tear production, unusual sleepiness (6).

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The most common symptoms	Other symptoms
• Diarrhea • Vomiting • Nausea • Stomach pain	• Fever • Headache • Body aches

Diagnosis:

Specimen collection for norovirus includes stool, serum, vomitus, food, water, and environmental swabs (e.g., doorknobs, handrails, kitchen counters). Diagnostic methods focus on detecting viral RNA or antigens. RT-qPCR assays are the preferred choice due to their high sensitivity and specificity. Multiplex gastrointestinal platforms can also detect norovirus along with other pathogens. Enzyme immunoassays (EIAs) rapidly detect norovirus antigens in stool but have lower sensitivity than RT-qPCR and should be confirmed using RT-qPCR, especially for outbreak investigations. Genotyping of norovirus strains helps link cases and identify common sources. Surveillance networks like CaliciNet use dual typing methods to track and understand the spread of norovirus outbreaks (6).

How You Treat Norovirus

For individuals with norovirus illness, there isn't a specific medication available. The primary focus is on staying hydrated by drinking plenty of fluids to replace those lost through vomiting and diarrhea, which helps prevent dehydration. Sports drinks, caffeine-free beverages, and oral rehydration fluids available over the counter can aid in mild dehydration. However, these drinks may not provide all the necessary nutrients and minerals. It's essential to address dehydration promptly, as severe cases may require hospitalization for intravenous fluids. Antibiotics are not effective against norovirus infections, as they target bacteria, not viruses. As such, providing supportive care and ensuring proper hydration continue to be the primary approach for managing norovirus infection (6).

Future Treatment

Holds promise with the development of vaccine candidates primarily based on virus-like particles (VLPs). Challenges such as NoV's heterotypic nature and rapid mutation rate necessitate a bivalent vaccine targeting multiple genotypes, akin to strategies used against Influenza. Clinical trials of VLP-based vaccines, including HIL-214, show potential for cross-protection against different NoV variants. Additionally, small molecule inhibitors targeting viral and host factors offer another avenue for treatment. Despite promising results in preclinical studies, the challenge lies in improving their

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bioavailability for clinical efficacy. Nitazoxanide, an FDA-approved drug, shows promise in reducing symptom duration in NoV patients but requires further evaluation (4).

Prevention and Control

- **Identifying transmission modes:** Focus on contaminated food, water, and person-to-person contact.
- **Controlling contamination:** Ensure food and water safety, maintain hygiene among food handlers, and limit person-to-person spread.
- **Preventing oyster-related outbreaks:** Monitor water quality and restrict fecal waste dumping.
- **Using molecular assays:** Detect NoV in food and water, but availability is limited.
- **Practicing personal hygiene:** Exclude sick food handlers, disinfect surfaces, and consider alternative work arrangements.
- **Preventing person-to-person spread:** Encourage strict personal hygiene and disinfect contaminated surfaces.
- **Closure of facilities:** If outbreaks persist, consider temporarily closing affected areas to halt transmission.

Conclusion

Noroviruses (NoVs) remain a significant cause of epidemic and endemic acute gastroenteritis worldwide, particularly with current healthcare pressures. The dominant GII.4 genotype, along with recent increases in cases, underscores the need for effective control measures. Healthcare facilities are especially at risk because people there are often in close contact, and some patients have weakened immune system. Existing control measures rely heavily on basic practices like hand hygiene and surface disinfection, but recent data questions their effectiveness, highlighting the need for better protection against hand-to-hand transmission of viruses like NoV. Developing new hand hygiene products or vaccines is crucial, leveraging the success of mRNA COVID-19 vaccines for potential NoV vaccines. Exploring mRNA vaccines targeting NoV VP1 or its receptor-binding P-domain, akin to SARS-CoV-2 spike protein, shows promise. Additionally, small molecule inhibitors offer an alternative method for controlling NoV spread. Continued research offers hope for future prevention and protection against NoV outbreaks globally.

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