Viral Gastroenteritis

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Overview

- Acute infectious gastroenteritis is a common illness seen globally.
- Viral pathogens cause most of these cases.
- Acute viral diarrheal disease is generally self-limiting in developed countries but can have significant morbidity for young and older adult patients.
- In developing countries, viral diarrheal diseases are a significant cause of death, especially in infants.
- According to the CDC, viral gastroenteritis infections can account for over 200,000 deaths of children per year and are the third leading cause of death in children younger than 5 worldwide.

Overview

- Viral gastroenteritis commonly causes nausea, vomiting, diarrhea, abdominal pain, anorexia, weight loss, dehydration
- Cases may occur sporadically or as outbreaks in closed communities such as daycare centers, nursing homes, cruise ships
- Multiple viruses can cause gastroenteritis, but the exact viral agent is usually not identified in routine clinical practice.
- Rapid symptom onset and prominent vomiting may help distinguish viral gastroenteritis from bacterial or protozoal diarrhea. Also, viral gastroenteritis usually involves non-bloody diarrhea

people sick with vomiting bug on Princess Cruises ship in Caribbean

A CRUISE ship in the Caribbean has had to cut its voyage short after hundreds onboard were struck down by gastroenteritis. More than 300 people began suffering from diarrhoea and vomiting on the Caribbean Princess ship.

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By Harriet Mallinson

18:38, Tue, Feb 11, 2020 | Updated: 18:39, Tue, Feb 11, 2020

Cruise: At least 345 passengers and 26 crew members suffered from vomiting and diarrhoea

(Image: Getty Images/Princess Cruises)

Viral Gastroenteritis - Management

- Most cases of non-severe viral gastroenteritis do not require specific medical therapy. The mainstay of treatment include:
- Hydration and electrolyte replacement
- **Oral rehydration solution (ORS): Balanced sodium-glucose solution that significantly reduces mortality from infectious diarrhea, especially in developing countries**
- Antidiarrheal drugs may reduce symptoms by decreasing secretion, reducing intestinal motility
- Ondansetron may help tp reduce vomiting

Etiology of Viral Gastroenteritis

DEFINITIVE

- Rotavirus
- Norovirus
- Adenovirus
- Astrovirus
- Sapovirus

Less Common / Uncertain Viral Causes of Gastroenteritis

- Aichivirus: Increasingly identified in stool samples Member of Picornaviridae
- Bocavirus: Detected in children with diarrhea Exact pathogenic role remains uncertain
- Coronavirus: Certain non-respiratory strains may cause GI symptoms Distinct from SARS-CoV-2 respiratory infection
- Enterovirus: Occasionally associated with diarrhea
- Parvovirus: Sometimes implicated in gastroenteritis
- Pestivirus: Associated with sporadic gastroenteritis cases
- Picobirnavirus: Frequently detected in immunocompromised patients
- Torovirus: Linked to sporadic gastroenteritis cases

Rotavirus Gastroenteritis

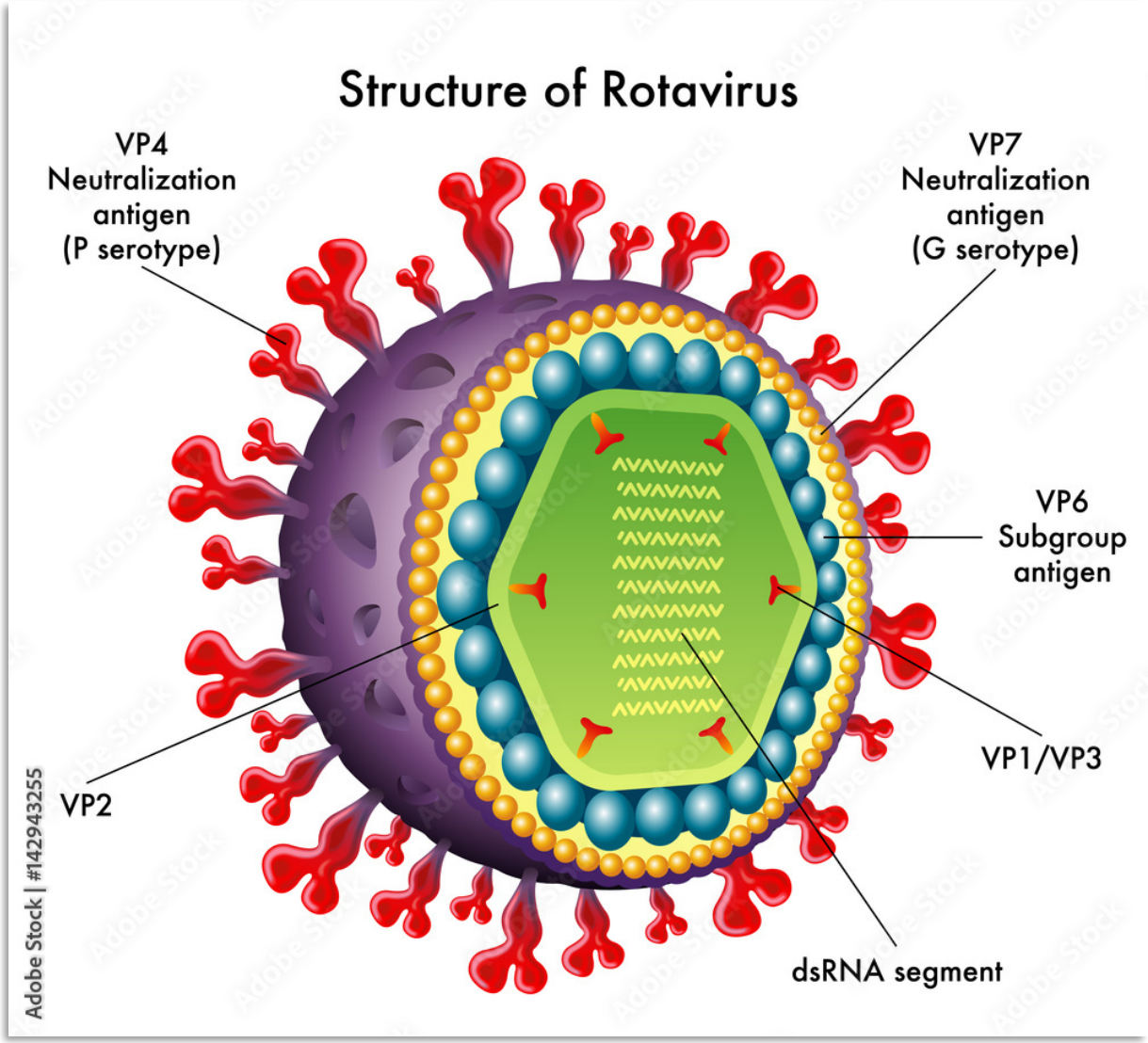
- Rotavirus is a non-enveloped, double-stranded RNA virus about100 nm in size. Member of *Reoviridae* family
- Rotavirus genome is composed of 11 RNA segments
- Rotavirus has a triple-layered structure with an outer capsid composed of VP4 (P protein) and VP7 (G protein), an inner capsid containing VP6, and a central core; VP4 and VP7 determine serotype specificity and induce neutralizing protective antibodies.
- Electron microscopy appearance reveal a wheel-like structure with radiating spokes. “rota” = wheel
- Rotaviruses are environmentally stable and resistant to elimination by routine handwashing

Rotavirus Gastroenteritis

- Worldwide, **rotavirus is the most common viral gastroenteritis in children**
- The most common cause of severe diarrhea amongst infants and young children in the United States before the rotavirus vaccine was introduced in 2006
- Rotavirus infection is seasonal, with its **peak in the winter** from November-April.
- The peak incidence is between 3 months when maternal antibody levels of protection may wane with most infants impacted by the age of 2 years
- It can be asymptomatic or symptomatic with an incubation period of 1-3 days and illness lasting for 5-7 days.
- Immunocompromised adults, the elderly, travelers are at risk of illness.

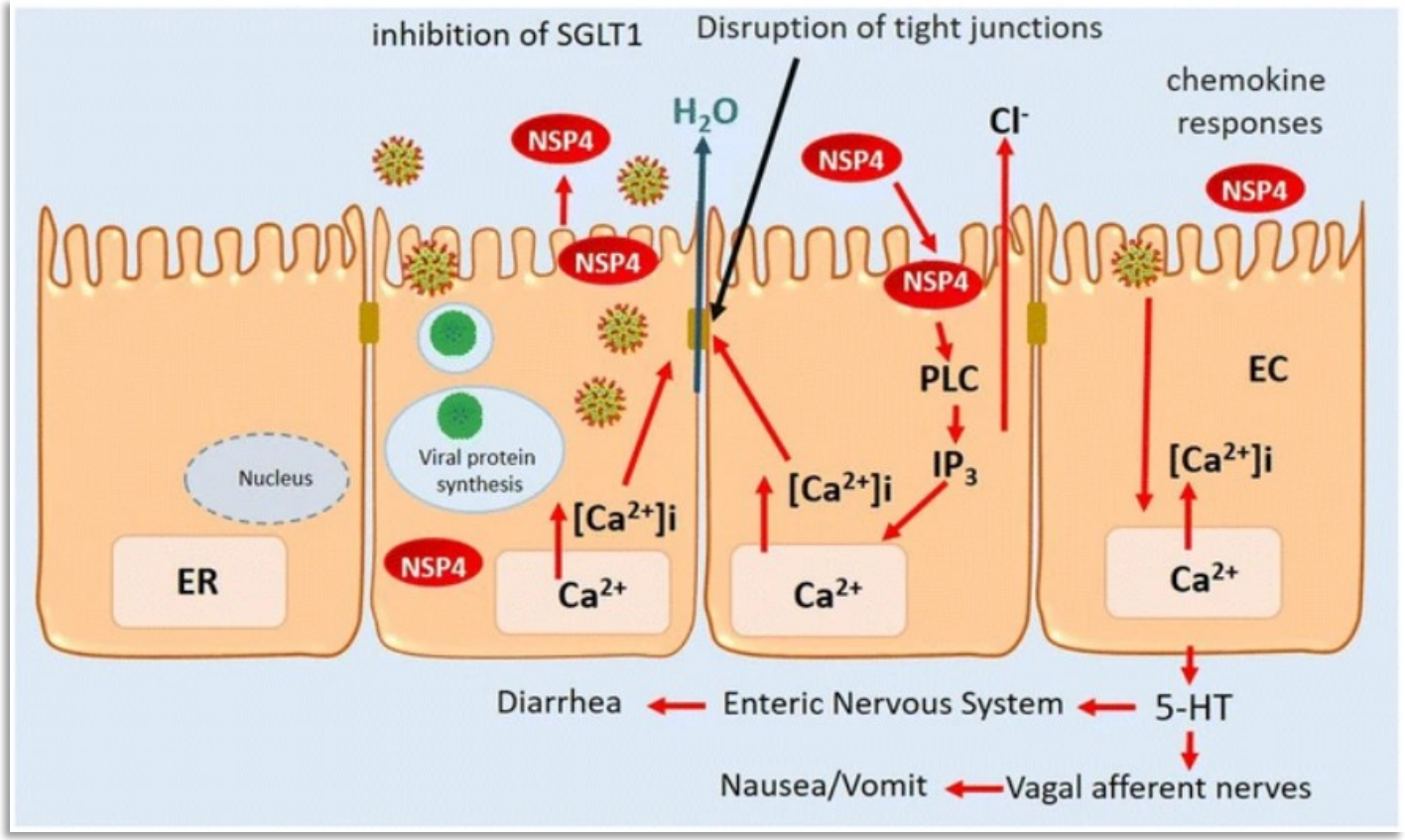
Rotavirus Gastroenteritis – Pathophysiology

- Disease mechanisms include malabsorption, secretory diarrhea, and enteric nervous system (ENS) activation
- Infection begins after oral ingestion and targets small intestinal enterocytes. VP4 spike protein is cleaved by trypsin into VP8 which binds host receptors (sialic acid and histo-blood group antigens HBGAs) and VP5 that mediates membrane penetration
- After entry into enterocytes the outer capsid is removed and viral replication begins. Viral replication occurs in cytoplasmic structures called viroplasms.



Rotavirus Gastroenteritis – Pathophysiology

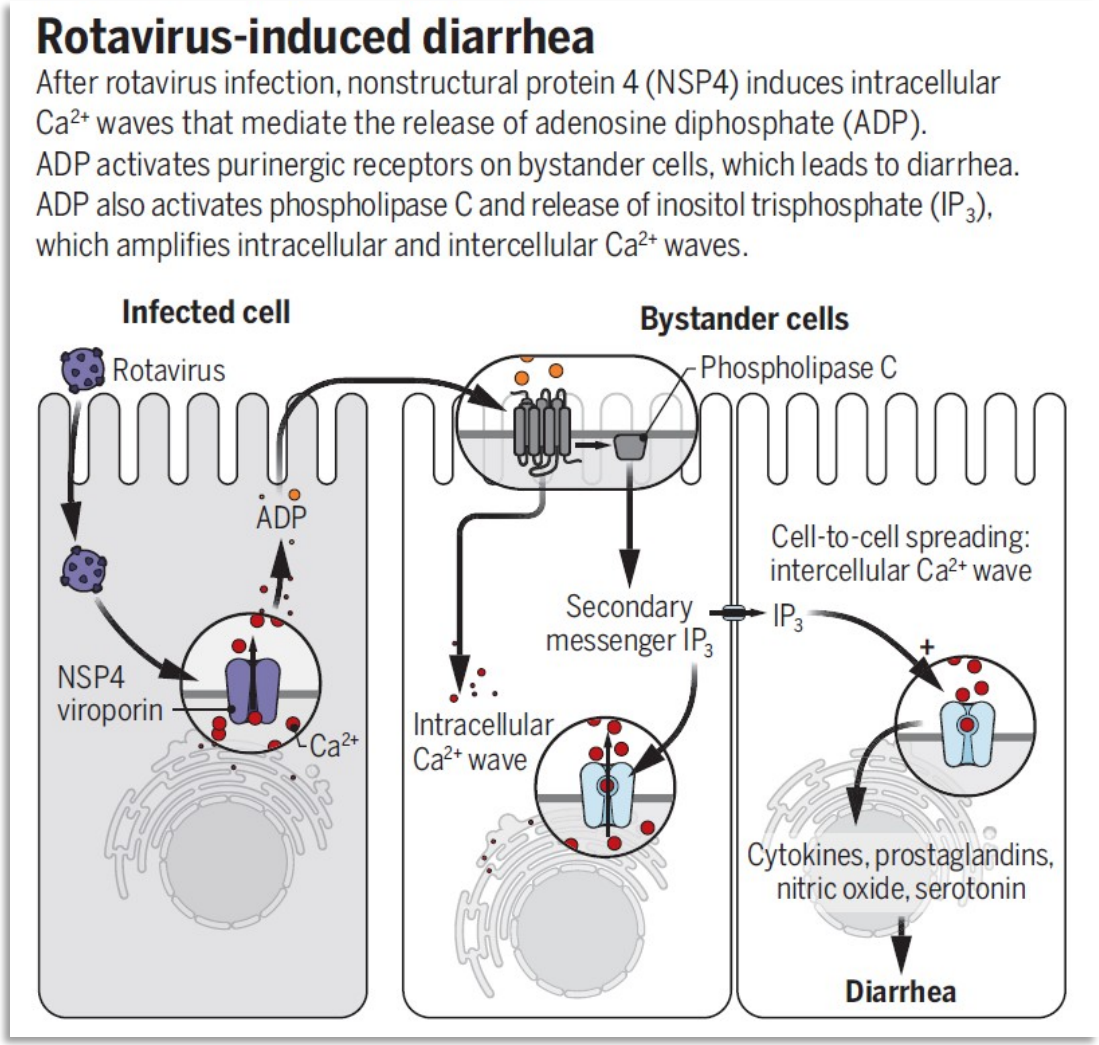
- Rotavirus enterotoxin (NSP4) is the major pathogenic enterotoxin of rotavirus. It functions as a viroporin forming a calcium-conducting ion channel causing release of Ca2+ from the endoplasmic reticulum leading to increased intracellular Ca2+.
- Increased intracellular Ca+2 causes microvillus damage and reduced disaccharidase enzyme activity with inhibition of Sodium-Glucose Cotransporter 1 function leading to enterocyte dysfunction and necrosis.



Source: Gonzalez-Ochoa, G., Flores-Mendoza, L.K., Icedo-Garcia, R. et al. Modulation of rotavirus severe gastroenteritis by the combination of probiotics and prebiotics. Arch Microbiol 199, 953–961 (2017).

Rotavirus Gastroenteritis – Pathophysiology

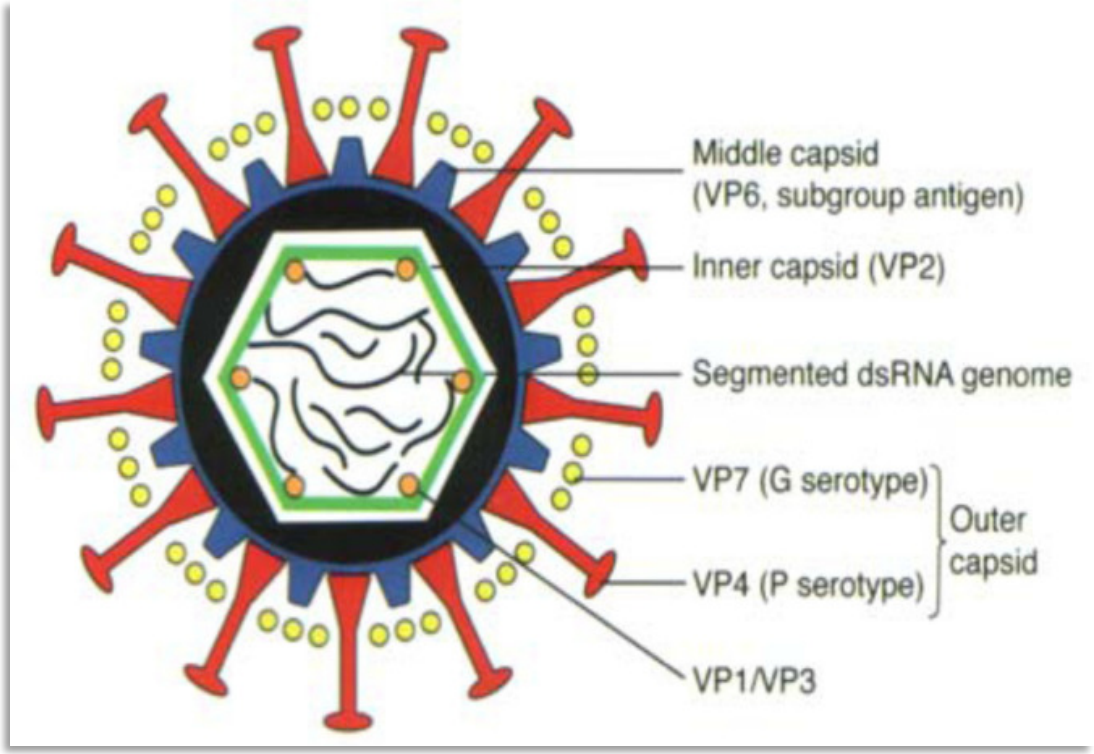
- Malabsorption occurs due to destruction of enterocytes which leads to reduced absorptive capacity, decreased Na+ and water absorption, and reduced digestive enzymes which results in osmotic diarrhea.
- Secretory component of diarrhea is mediated by NSP4 enterotoxin with ENS activation causing increased intestinal secretion and fluid loss into intestinal lumen
- ENS contributes to diarrhea, vomiting, and intestinal hypermotility. Mechanisms involve serotonin pathways and nitric oxide signaling



Source: Stanifer M, Boulant S. The origin of diarrhea in rotavirus infection. Science. 2020 Nov 20;370(6519):909-910

Rotavirus Gastroenteritis – Pathophysiology

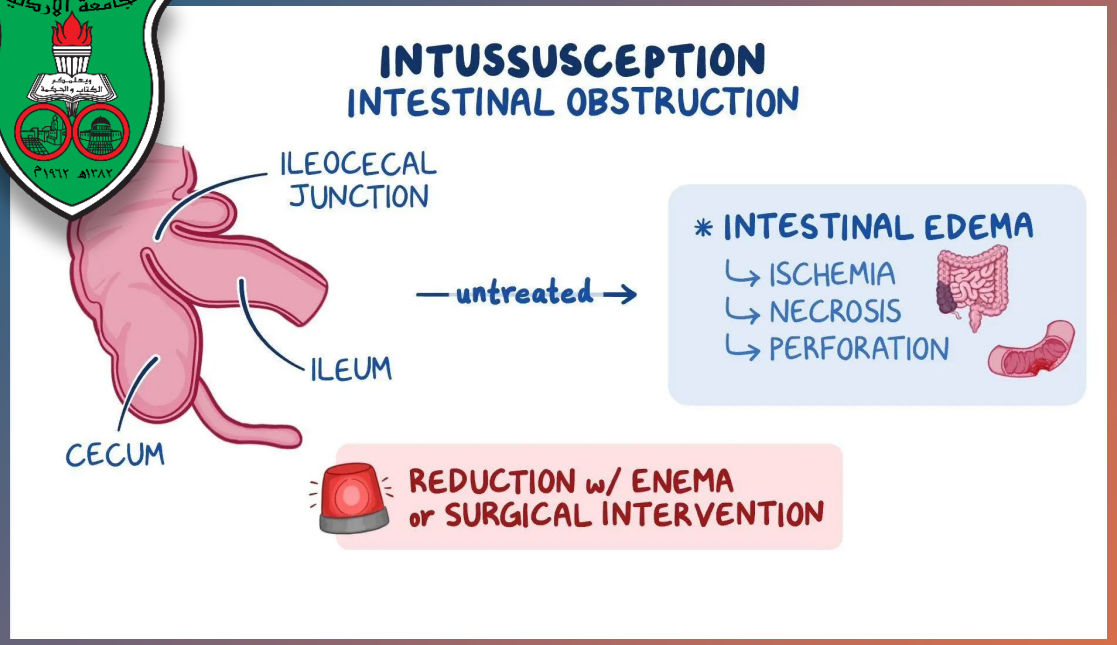
- Immune response involves innate immunity, cellular immunity, and humoral immunity. Protective antibodies develop mainly against VP4 and VP7.
- A single infection does not provide lifelong immunity. Repeated asymptomatic infections help maintain long-term protection.
- After first infection 38% protected from reinfection 77% protected from diarrhea 87% protected from severe disease Repeated exposures increase immunity and protection.



Source: Omatola, Cornelius A, and Ademola O Olaniran. "Rotaviruses: From Pathogenesis to Disease Control-A Critical Review." Viruses vol. 14,5 875. 22 Apr. 2022

Rotavirus Gastroenteritis

- Rotavirus mainly affects infants and young children
- Clinical presentation includes high fever, nausea and vomiting that precede watery diarrhea
- Compared with Norovirus infection, Rotavirus diarrhea lasts longer and typically persists for 3–9 days. Severe prolonged diarrhea and dehydration are major contributors to mortality.
- Diagnosis involves stool antigen testing commonly used for rotavirus detection.



Rotavirus Gastroenteritis – Vaccination

- Due to high infant morbidity, rotavirus vaccination is recommended for all infants without contraindications.
- First vaccine: Rotashield (licensed in 1998) was effective but associated with increased risk of intussusception 3–20 days after vaccination
- Withdrawn from market in 1999
- Current vaccines introduced in 2006: RotaTeq and Rotarix

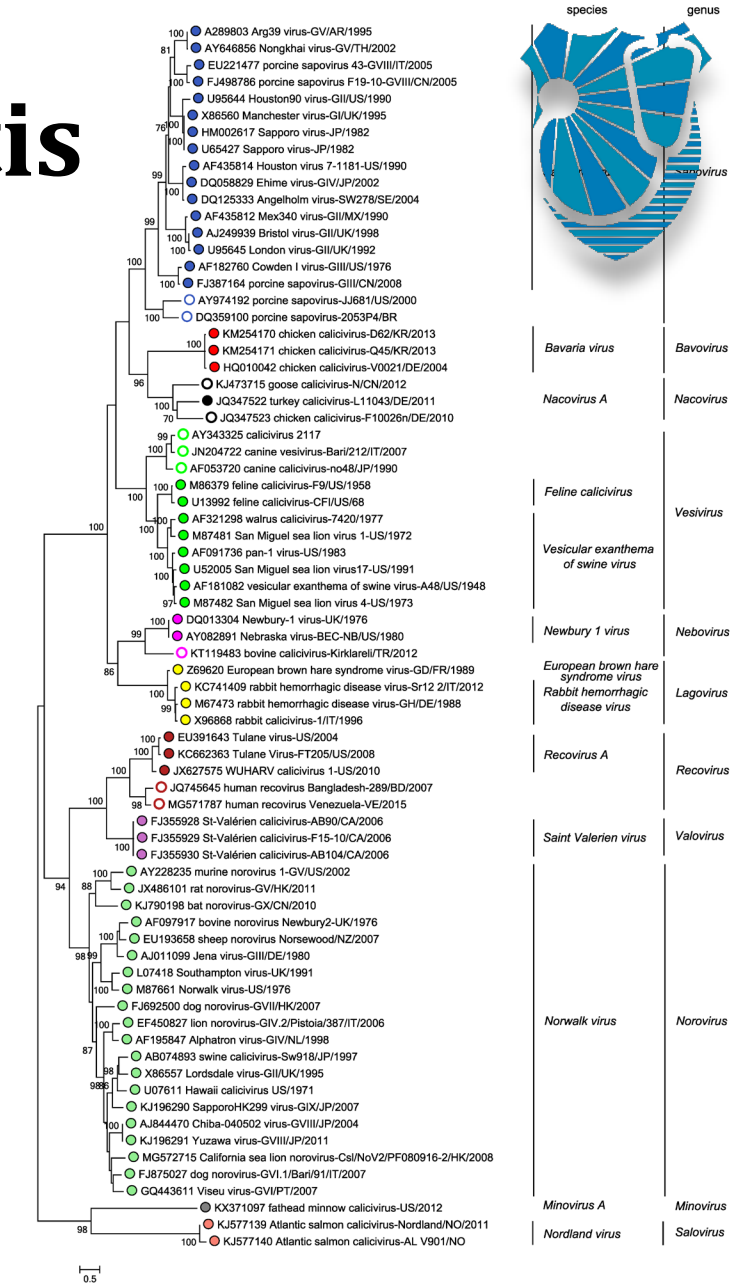
Rotavirus Gastroenteritis - Vaccination

- RotaTeq: Live oral reassortment vaccine containing 5 viral strains. Administered at 2 months, 4 months, 6 months. Effectiveness: 98% reduction in severe rotavirus gastroenteritis 74% protection against any severity gastroenteritis in first year 96% reduction in hospitalizations

- Rotarix: Live oral vaccine containing 1 strain Given as 2 oral doses at 2 months, 4 months. Provides: 85–96% protection against severe disease 96% reduction in hospitalizations over two seasons.

Norovirus Gastroenteritis

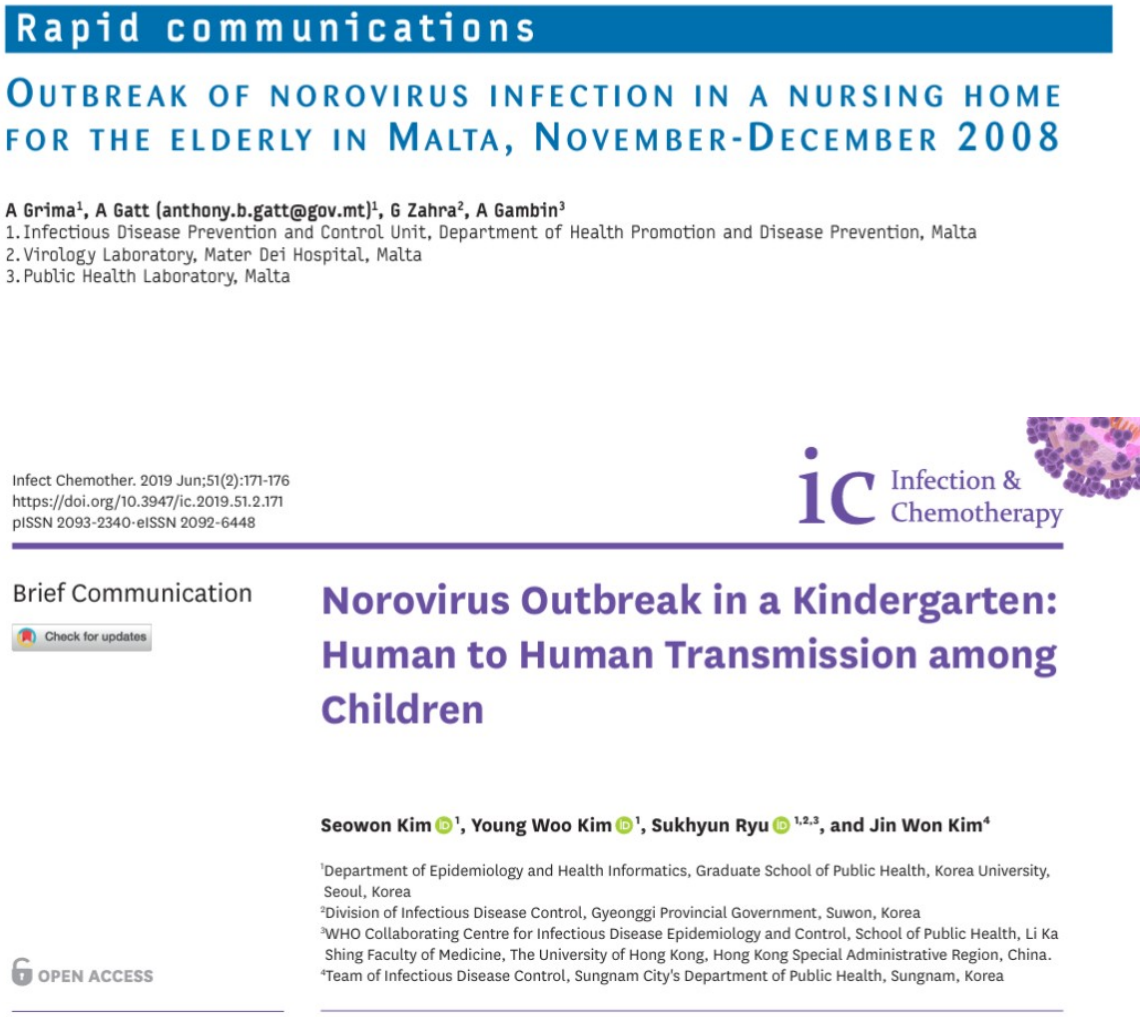
- Norovirus was the first viral agent proven to cause gastroenteritis.
- Noroviruses belong to the *Caliciviridae* family with single-stranded RNA positive-sense genome. The virus is non-enveloped about 37-41 nm in size
- Includes noroviruses and sapoviruses
- Noroviruses are major pathogens because of the very low infectious dose required for transmission, prolonged viral shedding, and the ability to survive in the environment.
- It cause about 18% of gastroenteritis cases worldwide and is the leading cause of foodborne illness in the United States.



https://ictv.global/report/chapter/caliciviridae/caliciviridae

Norovirus Gastroenteritis – Epidemiology

- According to the CDC, Norovirus causes annually 19–21 million illnesses, 56,000–71,000 hospitalizations, 570–800 deaths.
- GII strain is the most common norovirus genotype. Common outbreak settings include cruise ships, nursing homes, schools, workplaces.
- Outbreaks occur most commonly in winter ("winter vomiting disease"), but infection can occur year-round.



Rapid communications

OUTBREAK OF NOROVIRUS INFECTION IN A NURSING HOME FOR THE ELDERLY IN MALTA, NOVEMBER-DECEMBER 2008

A Grima[1], A Gatt (anthony.b.gatt@gov.mt)[1], G Zahra[2], A Gambin[3]
1. Infectious Disease Prevention and Control Unit, Department of Health Promotion and Disease Prevention, Malta
2. Virology Laboratory, Mater Dei Hospital, Malta
3. Public Health Laboratory, Malta

Infect Chemother. 2019 Jun;51(2):171-176
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pISSN 2093-2340-eISSN 2092-6448

ic Infection & Chemotherapy

Brief Communication

Check for updates

Norovirus Outbreak in a Kindergarten: Human to Human Transmission among Children

Seowon Kim[1], Young Woo Kim[1], Sukhyun Ryu[1,2,3], and Jin Won Kim[4]

[1]Department of Epidemiology and Health Informatics, Graduate School of Public Health, Korea University, Seoul, Korea
[2]Division of Infectious Disease Control, Gyeonggi Provincial Government, Suwon, Korea
[3]WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China.
[4]Team of Infectious Disease Control, Sungnam City's Department of Public Health, Sungnam, Korea

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Norovirus Gastroenteritis – Clinical Features

- Incubation period is short (12-48 hours) followed by acute onset of nausea, vomiting, and watery diarrhea.
- Usually lasts <48 hours but viral shedding may continue for weeks, even in asymptomatic individuals.
- Prolonged diarrhea may occur in children and chronically immunosuppressed patients.
- Vomiting results from delayed gastric emptying and abnormal gastric motor function

Norovirus Gastroenteritis – Outbreaks & Infection Control

- Outbreak control is difficult and requires aggressive environmental cleaning, bleach-based disinfectants, strict soap-and-water hand hygiene
- Norovirus is not effectively inactivated by alcohol-based hand sanitizers.
- Factors contributing to explosive outbreaks:
  - Close-contact environments
  - High infectivity
  - Environmental persistence
  - Prolonged viral shedding
  - Lack of long-lasting immunity
- Most worldwide outbreaks in the past decade have been associated with the GII.4 strain of Norovirus.

Norovirus Gastroenteritis – Pathophysiology

- Norovirus primarily targets immune cells—including macrophages, dendritic cells, B cells, and T cells
- Microfold (M) cells are specialized epithelial cells in gut-associated lymphoid tissue (GALT).
- Norovirus exploits M cells to cross intestinal epithelium and reach immune target cells
- It avoids enterocyte damage since the virus crosses epithelium by transcytosis
- Productive epithelial infection is not required
- Norovirus VP1 binds to HBGAs, influencing susceptibility to infection.

Norovirus Gastroenteritis – Pathophysiology

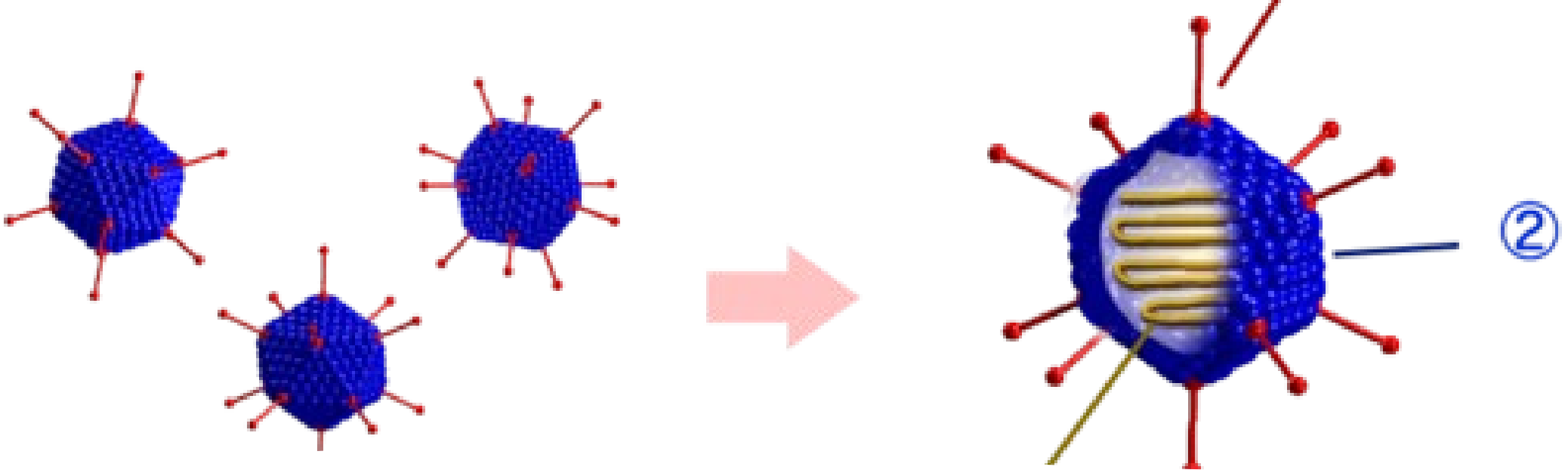
- Gut microbiota strongly influence norovirus infection.
- Commensal bacteria express HBGA-like molecules and promote norovirus infection of B cells
- Antibiotic treatment in mice decreased norovirus replication
- Restoring microbiota restores infectivity. Therefore, gut bacteria facilitate viral replication. Gut microbiota suppress type III interferon antiviral activity. This promotes viral persistence in the colon and prolonged viral shedding which may explain chronic shedding after symptoms resolve.

Norovirus Gastroenteritis – Diagnosis & Infection Control

- Specific stool antigen tests are available for identification of Norovirus.
- Noroviruses are among the most contagious enteric viruses because of the very low infectious dose and high environmental stability
- Hospitalized patients should be placed in contact isolation. Have rooms disinfected with chlorine bleach 1000–5000 ppm Approximately 1:50–1:10 dilution of household bleach.
- Alcohol-based hand sanitizers may work against some enteric viruses but are ineffective against norovirus.
- Recommended hand hygiene: Handwashing with soap and water for at least 20 seconds.

Astrovirus Gastroenteritis

- Astrovirus is a member of *Astroviridae* family, and it is a small, non-enveloped, single-stranded RNA virus 25-30 nm in size with characteristic five- or six-pointed star appearance on electron microscopy
- Astrovirus causes 2-10% of viral gastroenteritis in children
- Eight serotypes exist with type 1 as the most common.
- Usually causes mild gastroenteritis and hospitalization is rarely required
- Identified using multiplex molecular testing of stool samples



Adenovirus Gastroenteritis

- Human adenovirus is a non-enveloped double-stranded DNA virus, 70-90 nm in size
- Adenoviruses commonly cause respiratory and ocular infections
- **Gastroenteritis is mainly associated with adenovirus species F, serotypes 40 and 41**
- Adenoviruses cause 1.5-5% of viral gastroenteritis in children <2 years
- Unlike rotavirus, adenovirus gastroenteritis does not show clear seasonality

Adenovirus Gastroenteritis

- Adenovirus gastroenteritis has a longer incubation period than rotavirus or norovirus at about 8-10 days
- The illness duration is usually 5-12 days
- Diagnosis is based mostly using multiplex PCR testing of stool samples
- Adenovirus gastroenteritis occurs most commonly in children, immunocompromised patients
- Adenoviruses are often resistant to common disinfectants and may remain infectious for prolonged periods on medical instruments and surfaces

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Viruses
Adenovirus F 40/41
Astrovirus
Norovirus GI/GII
Rotavirus A
Sapovirus (I, II, IV and V)

Sapovirus Gastroenteritis

- Sapoviruses cause acute gastroenteritis in humans and animals. They belong to the genus Sapovirus within the family *Caliciviridae*.
- The incubation period ranges from less than 1 day to 4 days. Major clinical symptoms include diarrhea and vomiting; however, additional constitutional symptoms (i.e., nausea, stomach/abdominal cramps, chills, headache, myalgia, or malaise) are also frequently reported. Similar to the case for norovirus illness, fever is a rare clinical symptom. Diarrhea usually resolves within 1 week; however, individuals showing symptoms for a longer time (i.e., from over a week to up to 20 days) were also reported
- In general, the severity of sapovirus gastroenteritis is milder than that for rotavirus and norovirus

Thank You!

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