

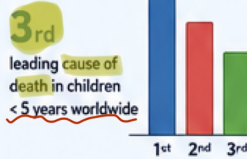
VIRAL GASTROENTERITIS

Overview, Symptoms, Management, and Etiology



GLOBAL IMPACT

>200,000 deaths of children per year



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 – CLINICAL FEATURES

Viral gastroenteritis commonly causes:



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.

Usually NON-BLOODY diarrhea. Not typically bloody.

Because usually the same management is made

VIRAL GASTROENTERITIS – MANAGEMENT

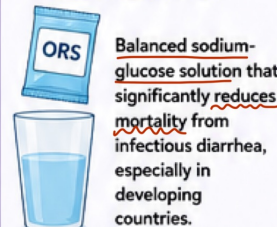
Most cases of non-severe viral gastroenteritis do not require specific medical therapy. The mainstay of treatment include:



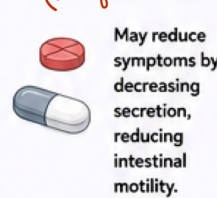
1. HYDRATION AND ELECTROLYTE REPLACEMENT



2. ORAL REHYDRATION SOLUTION (ORS)



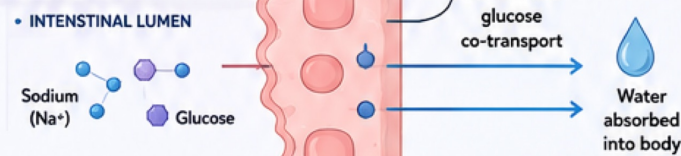
3. ANTIDIARRHEAL DRUGS



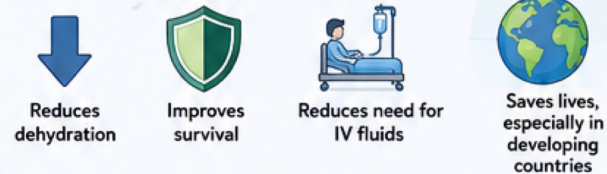
4. ONDANSETRON



HOW ORS WORKS



BENEFITS OF ORS



ETIOLOGY OF VIRAL GASTROENTERITIS

DEFINITIVE VIRAL CAUSES

	Rotavirus	Leading cause of severe diarrhea in infants and young children worldwide, especially in non-vaccinated regions.	~40%
	Norovirus	Most common cause of gastroenteritis outbreaks in all age groups.	~20-30%
	Adenovirus	Can cause diarrhea, especially in children and immunocompromised patients.	~5-10%
	Astrovirus	Common in children; usually causes mild to moderate diarrhea.	~5%
	Sapovirus	Causes sporadic cases and outbreaks of gastroenteritis.	~5%

Estimated contribution to viral gastroenteritis cases

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.

PREVENTION



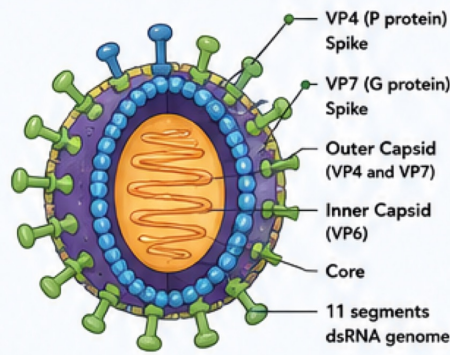
KEY TAKEAWAYS

- Viral gastroenteritis is common worldwide and a major cause of illness and death, especially in young children in developing countries.
- Usually self-limiting, but can cause severe dehydration.
- Management focuses on hydration, electrolyte replacement, and symptom relief.
- Multiple viruses can cause gastroenteritis; exact cause is often not identified.

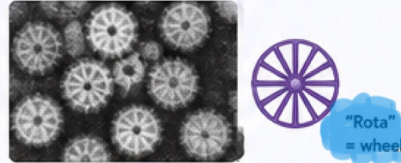
ROTAVIRUS GASTROENTERITIS - VIROLOGY & STRUCTURE

- Rotavirus is a **non-enveloped, double-stranded RNA virus** about **100 nm** in size. Member of **Reoviridae** family
- Rotavirus genome is composed of **11 RNA segments** *segmental genome*
- 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**

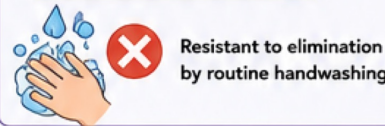
ROTAVIRUS STRUCTURE



ELECTRON MICROSCOPY APPEARANCE



ENVIRONMENTAL STABILITY



They bind receptors & they determine serotype specificity [Vaccine is composed of them]

ROTAVIRUS GASTROENTERITIS - EPIDEMIOLOGY & CLINICAL FEATURES

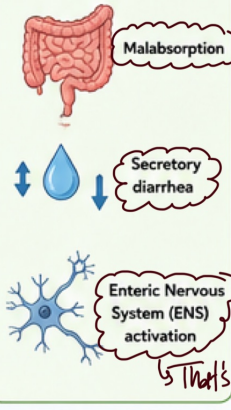
- Worldwide, rotavirus is the **most common viral gastroenteritis in children**
- The **most common cause of severe diarrhea** amongst **infants and young children** in the United States **before the rotavirus vaccine** was introduced in **2006**
- Rotavirus infection is seasonal, with its **peak** in 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 *At Risk*

CLINICAL MANIFESTATIONS



ROTAVIRUS GASTROENTERITIS - PATHOPHYSIOLOGY (PART 1) VIRAL ENTRY, REPLICATION & DISEASE MECHANISMS

DISEASE MECHANISMS INCLUDE

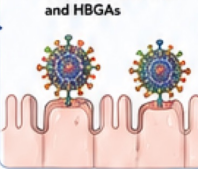


- Infection begins **after oral ingestion** and targets **small intestinal enterocytes**.
- VP4 spike protein** is **cleaved by trypsin** into **VP8** which binds host receptors (sialic acid and histo-blood group antigens HBGAs) and **VP5** that mediates membrane penetration *That means blood type plays a role in disease severity*
- After entry** into enterocytes the outer capsid is removed and **viral replication begins**.
- Viral replication occurs in cytoplasmic structures called **viroplasm**.

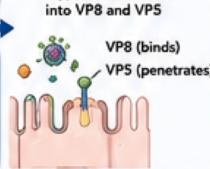
1 Oral ingestion



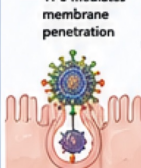
2 Attachment



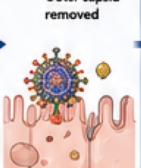
3 Protease activation



4 Penetration



5 Uncoating



6 Replication



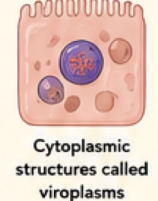
7 Assembly & release



TARGET CELL



SITE OF REPLICATION



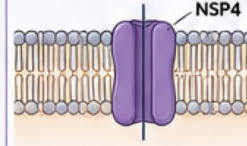
VP4 (P protein) VP7 (G protein) VP6 (inner capsid) Viral RNA (11 segments)

ROTAVIRUS GASTROENTERITIS - PATHOPHYSIOLOGY (PART 2) ENTEROTOXIN (NSP4) & MECHANISMS OF ENTEROCYTE INJURY

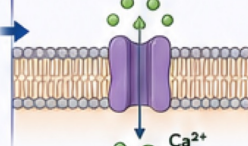
- Rotavirus **enterotoxin (NSP4)** is the major pathogenic enterotoxin of rotavirus.
- It functions as a **viroporin** forming a **calcium-conducting ion channel** causing **release of Ca²⁺ from the endoplasmic reticulum** leading to increased intracellular Ca²⁺.

NSP4 (Enterotoxin) as a Viroporin

1 NSP4 inserts into enterocyte membrane



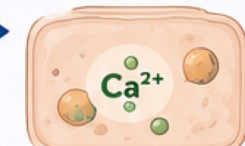
2 Forms calcium-conducting ion channel



3 Ca²⁺ released from endoplasmic reticulum



4 Increased intracellular Ca²⁺ concentration



Reason behind Malabsorption

EFFECTS OF INCREASED INTRACELLULAR Ca²⁺

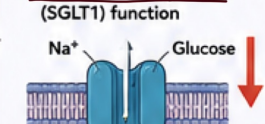
1 Microvillus damage



2 Reduced disaccharidase enzyme activity



3 Inhibition of Sodium-Glucose Cotransporter 1 (SGLT1) function



4 Enterocyte dysfunction and necrosis



RESULT

- Malabsorption, secretory diarrhea, and fluid loss



ROTAVIRUS GASTROENTERITIS – PATHOPHYSIOLOGY (PART 1)

- **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.

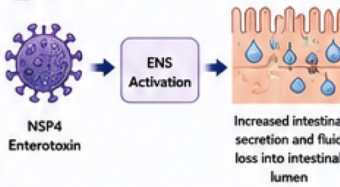
Secretory component of diarrhea is mediated by NSP4 enterotoxin with ENS activation causing increased intestinal secretion and fluid loss into intestinal lumen

- **ENS** contributes to diarrhea, vomiting, and intestinal hypermotility. Mechanisms involve serotonin pathways and nitric oxide signaling *as we already knew*

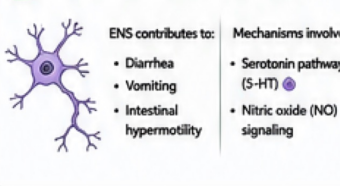
1 MALABSORPTION



2 SECRETORY DIARRHEA



3 ENTERIC NERVOUS SYSTEM (ENS)



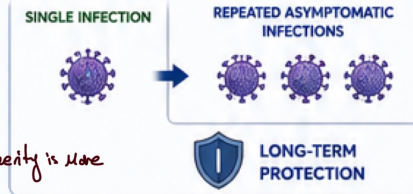
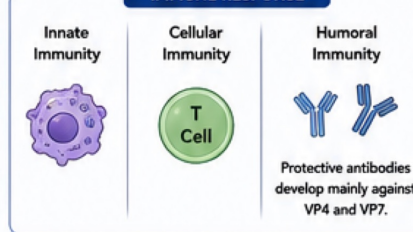
ROTAVIRUS GASTROENTERITIS – PATHOPHYSIOLOGY (PART 2)

- 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. *That's why the symptoms and severity is more in young pop.*

- After first infection **38%** protected from reinfection, **77%** protected from diarrhea, **87%** protected from severe disease. Repeated exposures increase immunity and protection.

IMMUNE RESPONSE



PROTECTION AFTER FIRST INFECTION		
38%	Protected from <u>reinfection</u>	
77%	Protected from <u>diarrhea</u>	
87%	Protected from <u>severe disease</u>	

ROTAVIRUS GASTROENTERITIS

Rotavirus mainly affects infants and young children

Clinical presentation includes high fever, nausea and vomiting that precede watery diarrhea + stool

Compared with Norovirus infection, Rotavirus diarrhea lasts longer and typically persists for (a week) 3-9 days. Severe prolonged diarrhea and dehydration are major contributors to mortality.

Diagnosis involves stool antigen testing commonly used for rotavirus detection *+PCR*

Illness lasts **3-9 days**

ROTAVIRUS GASTROENTERITIS – INTUSSUSCEPTION

REDUCTION w/ ENEMA or SURGICAL INTERVENTION

Normal intestine vs. Intussusception (intussusceptum enters distal bowel)

Reduction options: Enema OR Surgical intervention

* Due to high infant morbidity, rotavirus vaccination is recommended for all infants without contraindications.

ROTAVIRUS GASTROENTERITIS – VACCINATION (HISTORY)

- 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: RotaTaq and Rotarix

ROTAVIRUS GASTROENTERITIS – VACCINATION (CURRENT VACCINES)

1 RotaTaq® (Live oral reassortment vaccine)

- RotaTaq: Live oral reassortment vaccine containing **5 viral strains**.



ADMINISTRATION SCHEDULE



EFFECTIVENESS

- 98%** reduction in severe rotavirus gastroenteritis
- 74%** protection against any severity gastroenteritis in first year
- 96%** reduction in hospitalizations

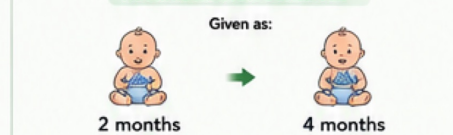
2 Rotarix® (Live oral vaccine)

- Rotarix: Live oral vaccine containing **1 strain**.



- Given as **2 oral doses** at 2 months, 4 months.

ADMINISTRATION SCHEDULE



EFFECTIVENESS

- 85-96%** protection against severe disease
- 96%** reduction in hospitalizations over two seasons
- Long-lasting protection with completed series

KEY TAKEAWAY SUMMARY

- Rotavirus** mainly affects infants and young children.
- Symptoms:** fever, nausea, vomiting preceding watery diarrhea lasting 3-9 days.
- Transmission:** fecal-oral route via contaminated food, water, or surfaces; environmentally stable.
- Pathophysiology:** malabsorption, NSP4 enterotoxin-mediated secretion, ENS activation.
- Immunity:** partial protection after infection; repeated exposures increase immunity.
- Vaccination:** RotaTaq (3 doses) and Rotarix (2 doses) are safe and highly effective.

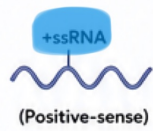
NOROVIRUS GASTROENTERITIS

- 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

smaller than Rota



Size: 37–41 nm



(Positive-sense)

CALICIVIRIDAE FAMILY

- Noroviruses
- 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. *Because it's naked*
- It cause about 18% of gastroenteritis cases worldwide and is the leading cause of foodborne illness in the United States.



~18% of gastroenteritis cases worldwide



Leading cause of foodborne illness in the United States



Affects people of all ages

Like S. typhi & V. cholera (when people are taking PPI)

NOROVIRUS GASTROENTERITIS – EPIDEMIOLOGY



According to the CDC, Norovirus causes annually 19–21 million illnesses, 56,000–71,000 hospitalizations, 570–800 deaths.

ANNUAL IMPACT IN THE U.S.



19–21 million illnesses



56,000–71,000 hospitalizations



570–800 deaths



(G2 strain)

GII strain is the **most common norovirus genotype**. Common **outbreak** settings include **cruise ships**, **nursing homes**, **schools**, **workplaces**.

The virus is commonly in outbreaks



Cruise ships



Nursing homes



Schools



Workplaces



Outbreaks occur most commonly in **winter** ("**winter vomiting disease**"), but **infection can occur year-round**

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. *↑ infectious → outbreaks*



Prolonged diarrhea may occur in **children** and **chronically immunosuppressed patients**.



Vomiting results from **delayed gastric emptying** and **abnormal gastric motor function**.

COMMON SYMPTOMS



Nausea



Vomiting



Watery diarrhea



Abdominal cramps



Low-grade fever

HIGH-RISK GROUPS



Infants and young children



Elderly



Immunocompromised patients



Travelers

NOROVIRUS GASTROENTERITIS – OUTBREAKS & INFECTION CONTROL

OUTBREAK CONTROL IS DIFFICULT



Aggressive environmental cleaning



Bleach-based disinfectants (1,000–5,000 ppm sodium hypochlorite)



Strict soap-and-water hand hygiene



Norovirus is not effectively inactivated by alcohol-based hand sanitizers.

FACTORS CONTRIBUTING TO EXPLOSIVE OUTBREAKS



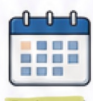
Close-contact environments



High infectivity



Environmental persistence



Prolonged viral shedding

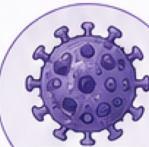


Lack of long-lasting immunity

MOST WORLDWIDE OUTBREAKS IN THE PAST DECADE HAVE BEEN ASSOCIATED WITH THE **GII.4 STRAIN**



Most common global strain



GII.4 strain



Causes the majority of recent outbreaks



Evolves frequently (new variants emerge)



Highly transmissible and adaptable

TRANSMISSION ROUTES



Fecal-oral route



Contaminated food



Contaminated water



Contaminated surfaces



Person-to-person contact

VIRAL CHARACTERISTICS



Very low infectious dose (as few as 18 viral particles)



Stable in the environment

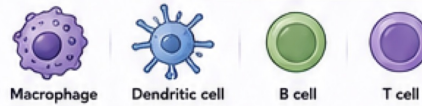


Resistant to heat and many disinfectants

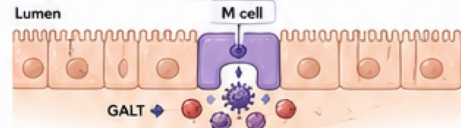


NOROVIRUS GASTROENTERITIS - PATHOPHYSIOLOGY (PART 1)

1 ^{imp!!} Norovirus primarily **targets immune cells** including **macrophages, dendritic cells, B cells, and T cells**



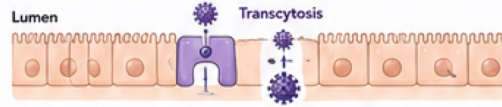
2 Microfold (M) cells are specialized epithelial cells in gut-associated lymphoid tissue (GALT).



3 Norovirus exploits M cells to cross intestinal epithelium and reach immune target cells



4 It **avoids enterocyte damage** since the **virus crosses epithelium by transcytosis**



5 Productive epithelial infection is not required



6 Norovirus **VP1** binds to **HBGAs**, influencing susceptibility to infection



NOROVIRUS INFECTION PATHWAY

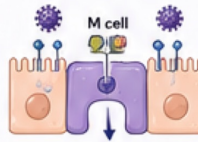
1 Ingestion of norovirus



2 Norovirus reaches small intestine



3 Virus binds to HBGA receptors on M cells



4 Transcytosis across M cell



5 Norovirus reaches immune cells in GALT and other sites



6 Replication occurs in immune cells



No significant destruction of enterocytes
Minimal intestinal inflammation

NOROVIRUS GASTROENTERITIS - PATHOPHYSIOLOGY (PART 2)

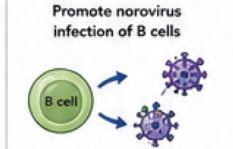
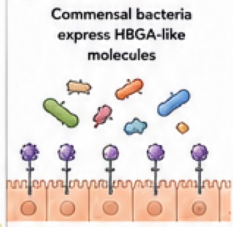
• Gut microbiota strongly influence norovirus infection.

• Commensal bacteria express **HBGA-like** molecules and promote norovirus infection of B cells

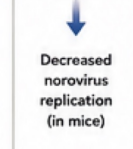
• Antibiotic treatment in mice decreased norovirus replication

• 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

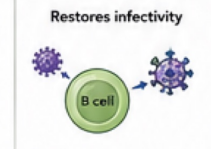
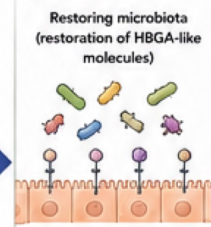
1 HEALTHY GUT MICROBIOTA



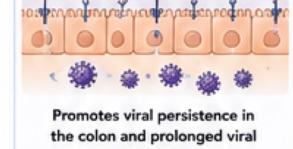
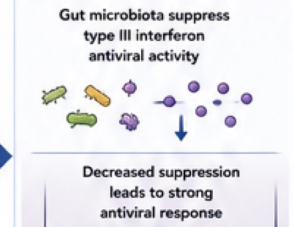
2 ANTIBIOTIC TREATMENT



3 RESTORE MICROBIOTA



4 EFFECT ON ANTIVIRAL RESPONSE



NOROVIRUS GASTROENTERITIS - DIAGNOSIS & INFECTION CONTROL



STOOL SAMPLE

• Specific stool antigen tests are available for identification of Norovirus.

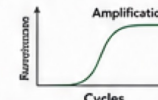
+ PCR

Immunoassay (ELISA)



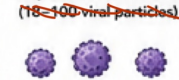
OR

PCR (molecular testing)

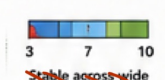


• Noroviruses are among the **most contagious enteric viruses** because of the very low infectious dose and high environmental stability

Very low infectious dose (18-100 viral particles)



Highly stable in environment



CONTACT ISOLATION

• 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.

Contact isolation



- Gown
- Gloves
- Dedicated equipment

Environmental disinfection



Chlorine bleach 1000-5000 ppm (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

Handwashing steps (at least 20 seconds)

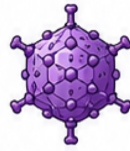




ASTROVIRUS GASTROENTERITIS

- 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** **PCR**

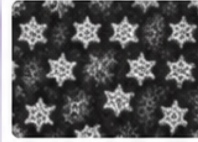
VIRUS STRUCTURE



25–30 nm

- Family: **Astroviridae**
- Genome: **Single-stranded RNA (+ sense)**
- Structure: **Non-enveloped**
- Shape: **Five- or six-pointed star appearance**

ELECTRON MICROSCOPY APPEARANCE



Five- or six-pointed star

EPIDEMIOLOGY



Affects children



2–10% of viral gastroenteritis



Type 1 is the most common

Adeno
↓
DNA



ADENOVIRUS GASTROENTERITIS

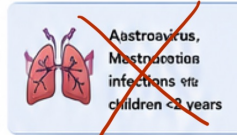
- Human adenovirus is a non-enveloped double-stranded DNA virus, **70–90 nm** in size
- Adenoviruses commonly cause **respiratory and ocular infections**
- **Gastroenteritis is mainly associated with adenovirus species F serotypes 40 and 41**
- Adenoviruses cause **1.5–5%** of viral gastroenteritis in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

VIRUS STRUCTURE



70–90 nm

- Family: **Adenoviridae**
- Genome: **Double-stranded DNA**
- Structure: **Non-enveloped**
- Shape: **Icosahedral with fiber proteins**



COMMON INFECTIONS CAUSED



Respiratory infections



Ocular infections

EPIDEMIOLOGY



1.5–5% of viral gastroenteritis in children <2 years



No clear seasonality

GASTROENTERITIS ASSOCIATED WITH

Adenovirus species F, serotypes 40 and 41



ADENOVIRUS GASTROENTERITIS (CLINICAL & LABORATORY FEATURES)



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**

INCUBATION & DURATION



Incubation period: **8–10 days**



Illness duration: **5–12 days**

DIAGNOSIS



Multiplex PCR testing of stool samples

POPULATIONS MOST AFFECTED



Children



Immunocompromised patients

ENVIRONMENTAL STABILITY



Resistant to common disinfectants
May remain infectious for **prolonged periods on medical instruments and surfaces**

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**

VIRUS STRUCTURE



25–30 nm

- Family: **Caliciviridae**
- Genus: **Sapovirus**
- Genome: **Single-stranded RNA (+ sense)**
- Structure: **Non-enveloped**

CLINICAL FEATURES



Diarrhea



Vomiting



Nausea



Abdominal cramps



Chills



Headache



Myalgia



Malaise

INCUBATION PERIOD



< 1 day to 4 days

FEVER



Rare clinical symptom

ILLNESS DURATION



Diarrhea usually resolves within 1 week

PROLONGED SYMPTOMS (REPORTED)



From over a week to up to 20 days

SEVERITY



Generally milder than rotavirus and norovirus