# VIRAL GASTROENTERITIS

**Gastroenteritis : Diarrhea is one of the leading causes of death in developing countries, responsible for 25-30% of deaths among children younger than five years of age.**

- **Diarrhea and vomiting syndromes lasting less than two weeks are classified as acute gastroenteritis.**
- **This disease is characterized by watery diarrhea, dysentery, or/and accompanied by bloody diarrhea, fever, dehydration, vomiting, nausea and abdominal pain.**
- **Acute gastroenteritis is a major cause of childhood morbidity and mortality, especially in developing countries.**
- **More than 1 billion cases of acute diarrhea are estimated to occur annually in children and adults worldwide, and are responsible for an annual mortality rate of about 6 million children under 5 years of age.**

## The causes of ACUTE DIARRHEA

- **Staphylococcus aureus**
- **Viral gastroenteritis**
- **Clostridium perfringens**
- **Salmonella**
- **Shigella**
- **Cryptosporidiosis**
- **Drug-induced diarrhea**
- **Clostridium difficile**

## Viral Gastroenteritis

- **The etiological agents of diarrhea are numerous, including multiple viral, bacterial, and parasitic pathogens.**
- **Viral infection which accounts for 51-88% incidence is the most important, whereas bacterial infection (9-13%).**
- **Several different groups of viruses have been shown to be responsible for the high incidence of acute viral diarrhea among children during their first few years of life.**
- **Usually five types of viruses are the main causes of this infection in all over the world: Rotaviruses, Norovirus, Sapovirus, Astroviruses and Adenoviruses.**

**Among viruses, Rotavirus group A is the major causative pathogen, but the roles of Norovirus, Sapovirus, Astrovirus and Adenovirus are increasingly being recognized**

# Rotavirus

- **First described in 1973 by electron microscopy from duodenal biopsy specimens**
- **Causes 40-60% of cases of diarrhoea in cooler months in infants and children < 2 years**
- **Rotavirus is a member of the Reoviridae family. Its genome consists of eleven double-stranded RNA segments.**
- **Rotavirus is classified into seven distinct groups (A-G). However, only groups A, B and C have been identified in humans, and the most common group leading to outbreaks is group A Rotavirus.**
- **Rotavirus diarrhea is an acute infection primarily of children less than 2 years of age, characterized by watery diarrhea and vomiting.**

**The viruses have a worldwide distribution and are recognized as the most important viral cause of acute gastroenteritis in children**

## Morphology-Rotaviruses

- **Reoviridae Family**
- **Non-enveloped icosahedral structure, 70nm**
- **EM: Wheel shape**
- **Capsid: Outer(VP7 and 4) and Inner(VP6) proteins**
- **Core encloses 11 segments of DS RNA**
- **~spherical; icosahedral ,~75-80 nm diameter, double-layered capsid**

### Nucleic acid:

- **double-stranded RNA,11 segments (rota) ;10 segments (reo)**
- **electropherotypes : 7 Groups (A-G) by VP6, Subgroups, serotypes**
- **Group A most important in humans (children)**
- **Group C causes sporadic illness**
- **Group B has caused large outbreaks (adults), rare,**

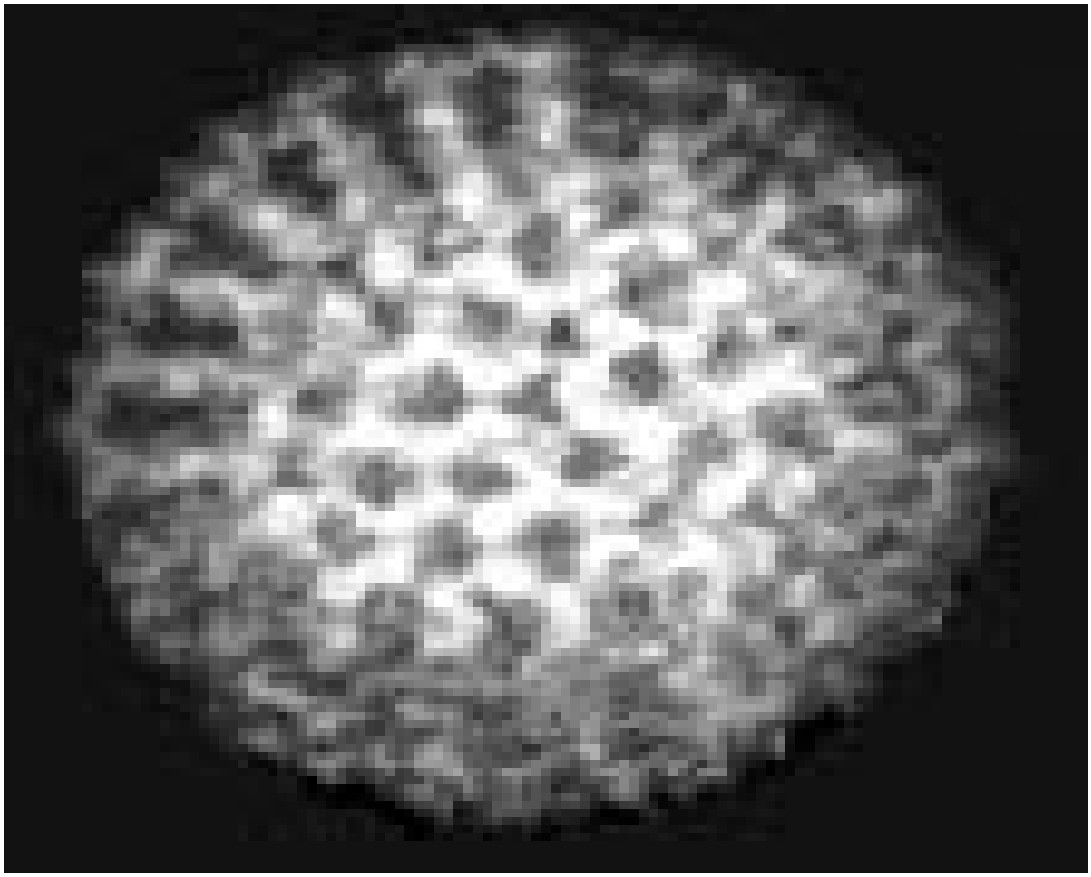
**Genome encoded Structural proteins VP1-7 and NSP 1-5, NSP4 has enterotoxinlike activity**

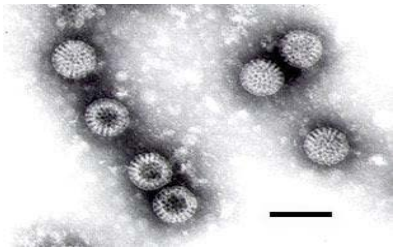
**Outer structural proteins - VP7 and VP4, Viral surface glycoprotein activated by stomach trypsin**

**VP7=glycoprotein, VP4=protease-cleaved, P protein, viral hemagglutinin, and forms spikes from the surface,**

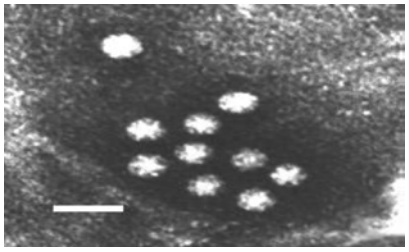
- **Inner core structural proteins VP 1, 2, 3, 6;**
- **VP6 is an important antigenic determinant**

- **Targeted host cells- <u>mature enterocytes</u> lining the tips of intestinal villi**
- **Intermediate/infective sub-viral particle (<u>ISVP</u>) produced through proteolysis(Trypsin treatment)**
- **Enter host cell by <u>endocytosis</u>**
- **Virus replicates in the host cell cytoplasm**

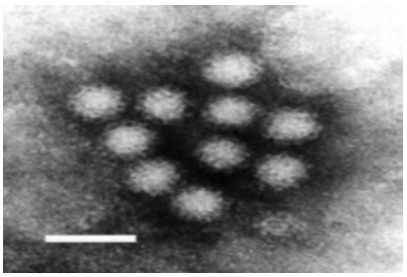


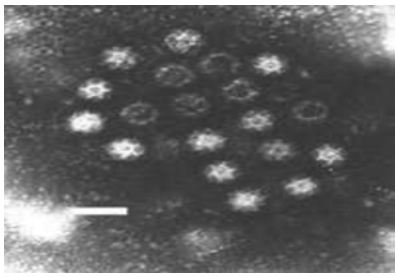


Rotavirus

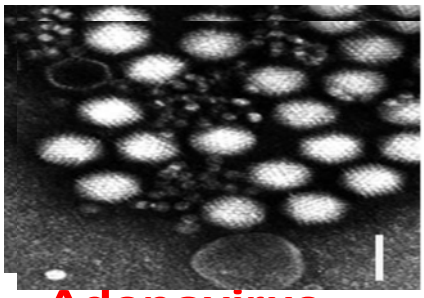


Astrovirus

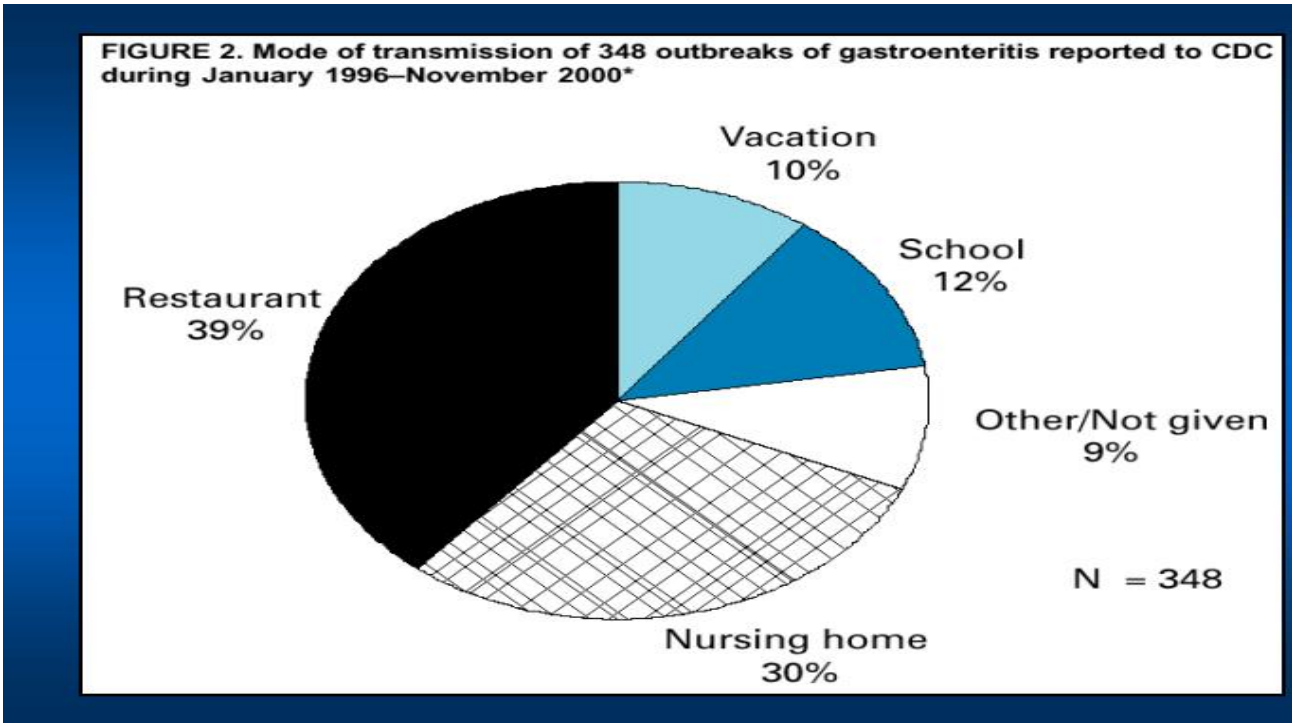




Sapovirus



Adenovirus



## Epidemiology of Rotavirus

- **Incubation period : 2-4 days**
- **Those affected :4-24 month old infants, infection before and reinfection after this usually asymptomatic (Breastfeeding results in milder disease)**
- **Spread within families and institutions**
- **Most common cause of noscomial diarrhoea**
- **Human to human, faecal-oral route**
- **Found on fomites in childcare**
- **Main cause of severe diarrhoea in children < 5 years**
- **130 million episodes per year in the world**
- **Between 600,000-870,000 *deaths*, mostly in the developing world**
- **Rate of hospitalisation in developed world 2.5%**
- **Seasonal pattern**
- **Most persons infected by 3 years of age**
- **Group A predominates**
- **Mainly person to person via fecal-oral route**
- **Fomites**
- **Food and water-borne spread is possible**
- **Spread via respiratory route is speculated**
- **Virus is stable in the environment**
- **Relatively resistant to handwashing agents**
- **Susceptible to disinfection with 95% ethanol, 'Lysol', formalin**

## Immune Response to Rotavirus

- **Localised Immune response protects against severe subsequent infections**
- **NSP4 protein results in cell mediated immunity**
- **Immunity: infection induces specific Ig G/A/M even if there is previous exposure**
- **2 weeks post infection there is ⇧ in jejunal Ig A , resistance to reinfection lasts 4-6 months,**
- **NO LONG TERM PROTECTION**

# Pathogenesis

- **Accounts for >85% of non-bacterial outbreaks of gastroenteritis**
  - **DIARRHOEA**
  - **VOMITING**
  - **Commonly accompanied by fever, malaise, myalgia and abdominal cramps**
  - **Symptoms last 1 day to 2 weeks**
  - **Virus excreted 5 to 7 days after the onset of symptoms in half of people although may last 13 days**

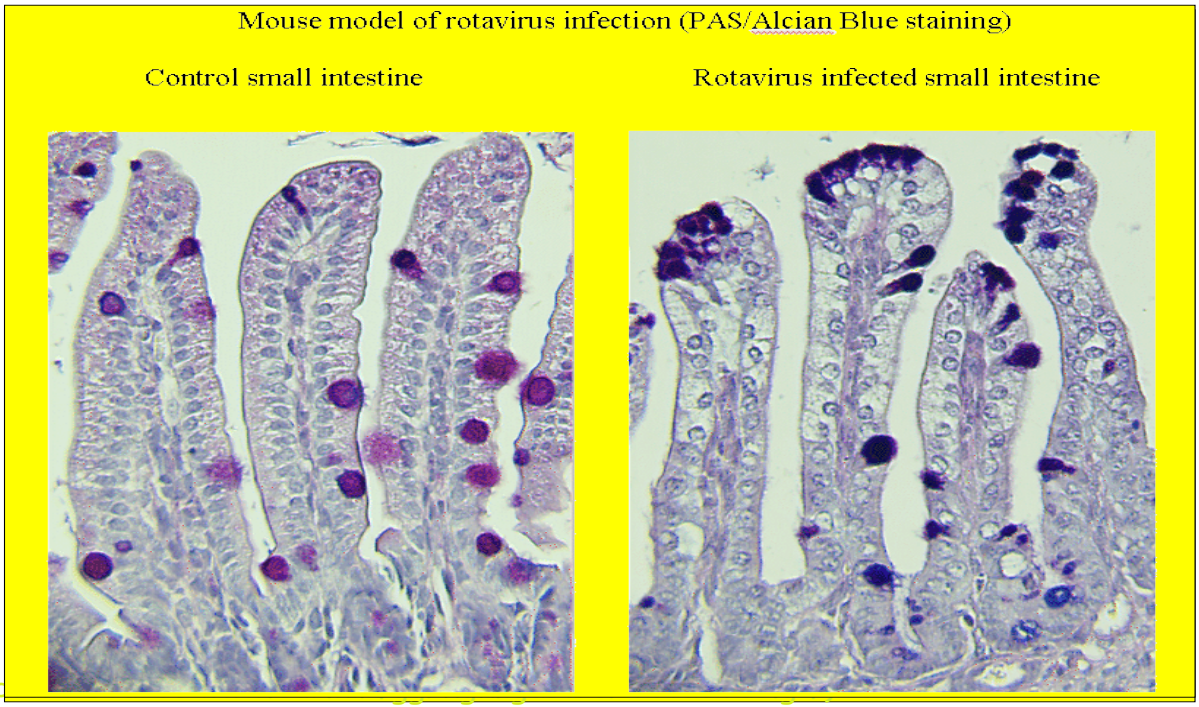
## Rotavirus replication:

- **Targeted host cells- mature enterocytes lining the tips of intestinal villi**
- **Intermediate/infective sub-viral particle (ISVP) produced through proteolysis (Trypsin cleavage)**

**Enter host cell by endocytosis Virus replicates in the host cell cytoplasm**

- **mRNA transcription with viral RNA polymerase**

- **Capsid proteins formed**
- **mRNA segments formed, assembled into immature capsid**
- **mRNA replicated to form double stranded RNA genome**
- **Mature enterocytes lining the tips of intestinal villi are affected**
- **Villous atrophy and blunting**
- **Death of the mature enterocytes**

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## Vaccine

- **Live tetravalent rhesus-human reassortant vaccine (*Rotashield*)**

  **Licensed for use in August 1998**

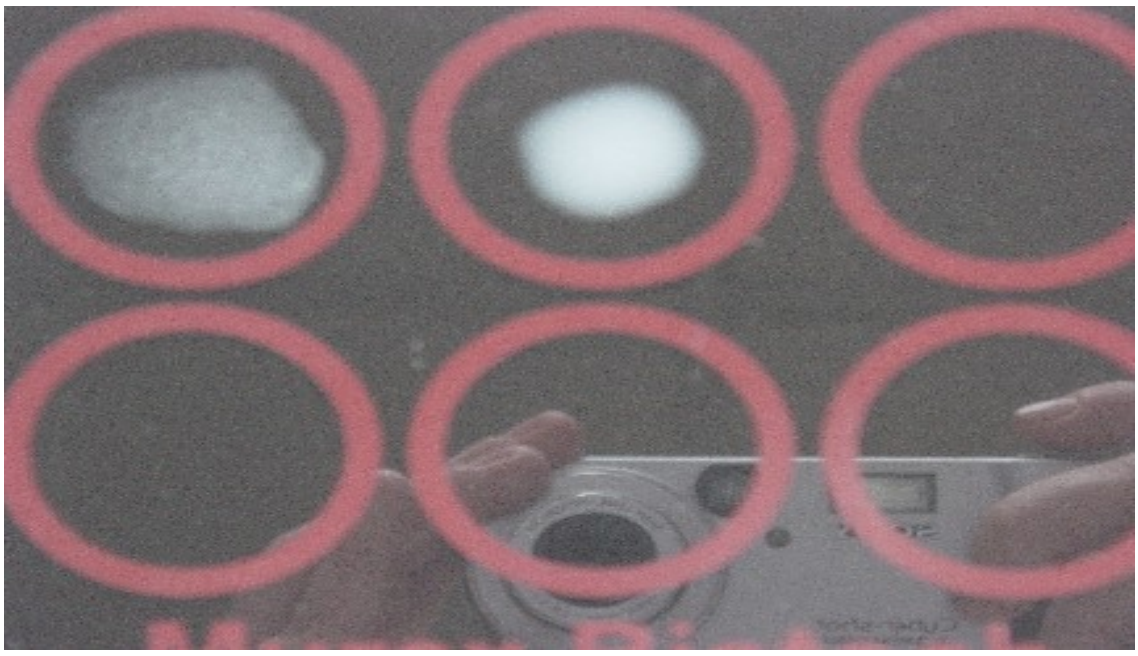
- **Removed from the market in October 1999 due to risk of intussusception**

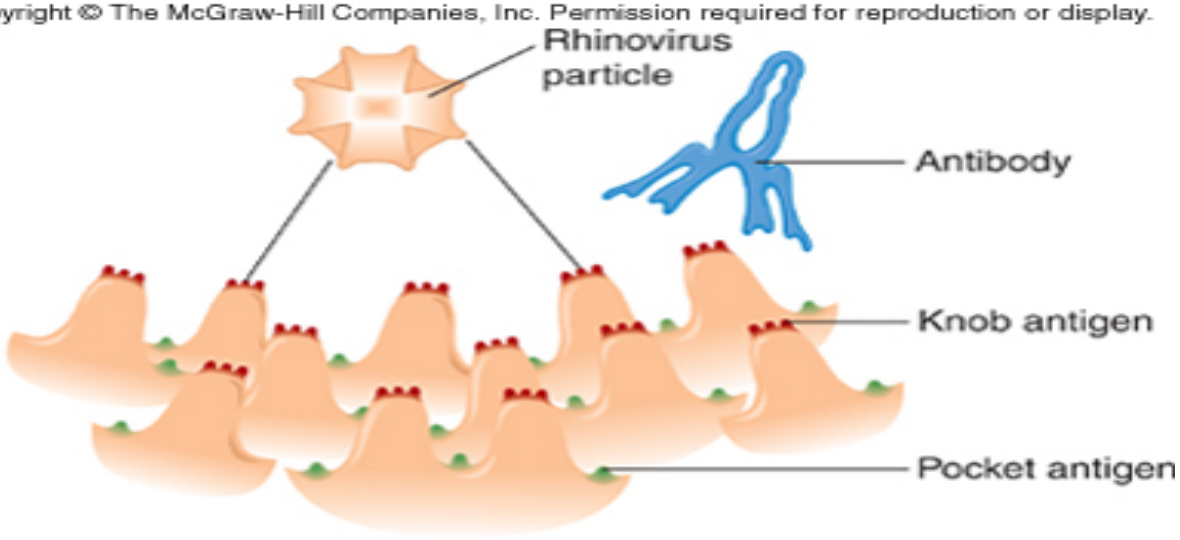
  **Cases were seen 3-20 days after vaccination**

## Diagnosis

- **Antigen detection in stool by ELISA, LA (for Group A rotavirus)**
- **EM- non-Group A viruses also**
- **Culture- Group A rotaviruses can be cultured in monkey kidney cells**
- **Serology for epidemiologic studies :**

***Latex agglutination*** **Kit testing for Group A , Rv *antigen in stool* Group A Enzyme Immunoassay, Less common EM and molecular methods**



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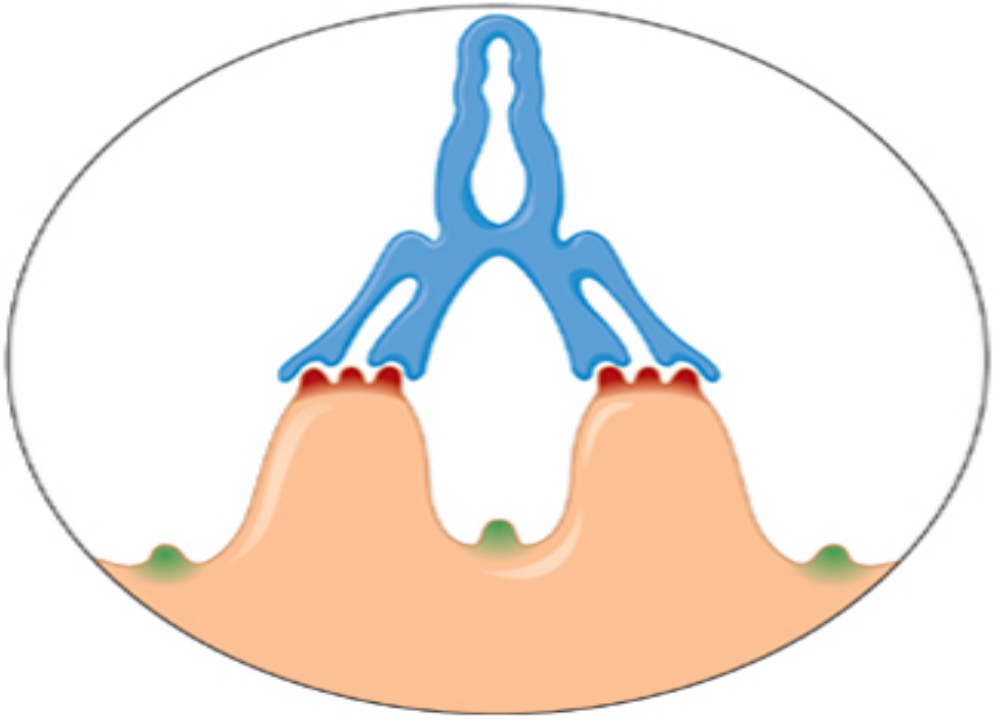

(b)

# Adenovirus

- **Adenoviruses are viral particles with double-stranded DNA. There are six groups of adenoviruses (A-F).**
- **There are two serotypes 40 and 41 belonging to group F which result gastroenteritis therefor referred as enteric Adenoviruses.**
- **Enteric Adenoviruses are the second commonest cause, after Rotaviruses, of viral diarrhea requiring hospitalization of young children.**
- **Disease develops after an 8- to10-day incubation and is characterized by watery diarrhea that lasts for 10 days. Vomiting and fever may occur. Secondary lactose malabsorption has been associated.**

**Most cases in developing countries are in children under 2 years of age**

# Norovirus

- **Norovirus and Sapovirus are two genera belonging to the Caliciviridae family, which infect humans.**
- **They are small non-enveloped viruses with icosahedral symmetry that contain a single-strand-positive sense RNA.**
- **Norovirus (previously called "Norwalk-like viruses") together with Sapoviruses are caliciviruses causing acute viral gastroenteritis in humans.**
- **The clinical symptoms include diarrhea, vomiting and fever. The Caliciviruses cause diarrhea and vomiting of abrupt onset and short duration.**
- **Diarrhoea may occur without vomiting and vomiting without diarrhea.**
- **Noroviruses are divided into five genogroups. The genogroups are further divided into genotypes, currently there are eight types in genogroup I (GI), at least 17 in GII and two in GIII. GI, GII and GIV infect humans.**

- **GII has been described as the predominant strain around the world. Numbers of recent studies have investigated the prevalence of Norovirus infection in hospitalized children.**

**A wide range of prevalence (6–48%) were reported with a median of 14% and in some studies Norovirus associated gastroenteritis was almost as common as Rotavirus infections indicating that Noroviruses may be clinically more relevant than previously thought**

## Sapovirus

- **Sapoviruses are divided into seven genogroups (GI-GVII), among which GI, GII, GIV and GV are known to infect humans.**

**Sapoviruses have been described in association with both outbreaks and sporadic cases of acute gastroenteritis in both young children and adults**

# Astrovirus

- **Astrovirus belongs to the Astroviridae family and is a small non-enveloped virion. It contains a single-stranded positive-sense RNA and its characteristic five- or six-pointed star morphology has been detected by electron microscopy.**
- **Eight human Astroviruses genotypes (1-8) have been described, and human Astroviruses -1 has been reported as the most prevalent type in both developing and developed countries.**

**Epidemiologic studies have revealed that Astrovirus is one of the significant causes of gastroenteritis in children**