Gastroenteritis and viral infections

A large number of viruses are found in the human gut; these include some that are associated with gastroenteritis:

- Rotaviruses
- Adenoviruses 40/41
- Caliciviruses
- Norwalk-like viruses or small round structured viruses (SRSV)
- Astroviruses
- Coronaviruses
- Toroviruses

**Table 1: Types of acute viral gastroenteritis**

<table>
<thead>
<tr>
<th>Virus</th>
<th>Incubation Period</th>
<th>Duration</th>
<th>Seasonality</th>
<th>Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus</td>
<td>1-3 days</td>
<td>5-7 days</td>
<td>Predominantly in winter and fall</td>
<td>Fecal-oral route and respiratory transmission</td>
</tr>
<tr>
<td>Norovirus</td>
<td>12-48 hours</td>
<td>1-4 days</td>
<td>Year-round, but especially in winter</td>
<td>Fecal-oral route, aerosolization, respiratory transmission, food, fomites, and water</td>
</tr>
<tr>
<td>Sapovirus</td>
<td>1-2 days</td>
<td>3-4 days</td>
<td>Year-round</td>
<td>Fecal-oral route</td>
</tr>
<tr>
<td>Astrovirus</td>
<td>4-5 days</td>
<td>5-6 days</td>
<td>Predominantly in winter</td>
<td>Fecal-oral route and water</td>
</tr>
<tr>
<td>Enteric adenovirus (40 and 41)</td>
<td>3-10 days</td>
<td>6-9 days</td>
<td>Predominantly in summer</td>
<td>Fecal-oral route</td>
</tr>
</tbody>
</table>

*This is not a comprehensive list.*
ROTAVIRUSES
- Rotaviruses are a major cause of diarrheal illness in human, infants and young. Adults are rarely affected
- It is a double-stranded RNA viruses in the family Reoviridae.
- Nearly every child in the world is infected with rotavirus at least once by the age of five.
- Immunity develops with each infection, so subsequent infections are less severe.
- Among the rotaviruses are the agents of human infantile diarrhea, Nebraska calf diarrhea, epizootic diarrhea of infant mice.

Classification and Antigenic Properties
- Rotaviruses have been classified into five species (A–E) plus two tentative species (F and G) based on antigenic epitopes on the internal structural protein VP6.
- Group A rotaviruses are the most frequent human pathogens.
- Outer capsid proteins VP4 and VP7 carry epitopes important in neutralizing activity, with VP7 glycoprotein being the predominant antigen.

Pathogenesis
- Rotaviruses infect cells in the villi of the small intestine. They multiply in the cytoplasm of enterocytes and damage their transport mechanisms.
- One of the rotavirus-encoded proteins, NSP4, which is a viral enterotoxin.
- Damaged cells may slough into the lumen of the intestine and release large quantities of virus, which appear in the stool (up to $10^{12}$ particles per gram of feces).
- Diarrhea caused by rotaviruses may be due to **impaired sodium and glucose absorption** as damaged cells on villi are replaced by nonabsorbing immature crypt cells. It may take from 3 to 8 weeks for normal function to be restored.

![Rotavirus Diagram](image)

**Clinical Findings and Laboratory Diagnosis**
- **Rotaviruses cause the major portion of diarrheal illness in infants and children worldwide but not in adults.**
- Typical symptoms include:
  - Watery diarrhea
  - Fever
  - Abdominal pain
  - Vomiting, leading to dehydration.
- In infants and children, severe loss of electrolytes and fluids may be fatal unless treated.
Viral excretion in the stool may persist up to 50 days after onset of diarrhea. Adult contacts may be infected, but they rarely exhibit symptoms. Laboratory diagnosis rests on demonstration of virus in stool collected early in the illness and on a rise in antibody titer detected by ELISA. Genotyping of rotavirus nucleic acid from stool specimens by the polymerase chain reaction (PCR) is the most sensitive detection method.

**Epidemiology and Immunity**
- Rotaviruses are the single most important worldwide cause of gastroenteritis in young children. Estimates range from 3 to 5 billion for annual diarrheal episodes in children younger than 5 years.
- Symptomatic infections are most common in children between ages 6 months and 2 years, and transmission appears to be by the fecal–oral route.
- Local immune factors, such as secretory immunoglobulin A (IgA) or interferon, may be important in protection against rotavirus infection.

**Adenoviruses**
- Adenoviruses can replicate and produce disease in the respiratory, gastrointestinal, and urinary tracts and in the eye.
- Many adenovirus infections are subclinical, and the virus may persist in the host for months.
- Adenoviruses display icosahedral symmetry, no envelope. Adenoviruses are unique among icosahedral viruses in that they have a structure called a “fiber” projecting.

**HOW ROTAVIRUS ATTACKS**

The rotavirus attacks the villus tip cells of the small intestine, and obstructs digestion and absorption.

1. Once rotavirus enters the small intestine, it sticks to glycolipids on villus cells (see figure) lining small intestine.
2. It invades the villus tip cells, causing atrophy, loss of digestive enzymes, and a dip in absorption.
3. Once the villi become blunted, the resulting malabsorption of carbohydrates results in diarrhea.

Adenovirus infections

Pathogenesis

- Adenoviruses infect and replicate in epithelial cells of the gastrointestinal tract.
- They usually do not spread beyond the regional lymph nodes.
- Viruses may persist as latent infections for years in adenoids and tonsils and are shed in the feces for many months after the initial infection.
- In fact, the name “adenovirus” reflects the recovery of the initial isolates from human adenoids (belong to lymphoid tissue).
- Most human adenoviruses replicate in intestinal epithelium after ingestion but usually produce subclinical infections rather than overt symptoms.

Gastrointestinal Disease

- Many adenoviruses replicate in intestinal cells and are present in stools. However, two serotypes (types 40 and 41) have been etiologically associated with infantile gastroenteritis and may account for 5–15% of cases of viral gastroenteritis in young children.
- Adenovirus types 40 and 41 are abundantly present in diarrheal stools. The enteric adenoviruses are very difficult to cultivate.
• Symptoms may include fever, diarrhea, vomiting, and abdominal pain, and last for approximately 10 days

**Norwalk Virus and Norwalk-Like Viral Agents**

- Norwalk virus was first detected in stools of patients with gastroenteritis (Winter Vomiting Disease) in Norwalk, Ohio in 1968.
- 45% are food-borne and 52% are raw shellfish associated.
- They tend to cause rapid (explosive) epidemics in places of close contact such as cruise ships, nursing homes, hospitals and camps.

**Epidemiology**

- Noroviruses are found world-wide and cause more than 23 million cases of gastroenteritis every year in the US.
- There are asymptomatic infections in which the patient is infectious, and sheds virus. The infective dose may be very low and virus may continue to be secreted during the convalescent period.

**Clinical Features**

- Adults and children are affected. The infection has a relatively short incubation period of about 24 hours. The resulting illness is short (less than 3 days).
- The most prominent symptoms are is vomiting, nausea, abdominal cramping and watery diarrhea accompanied by headache, fever and malaise.

**Coronaviruses**
Genome: Single-stranded RNA, linear
Proteins: Two glycoproteins and one phosphoprotein. Some viruses contain a third glycoprotein (hemagglutinin esterase)
Envelope: Contains large, widely spaced, club-shaped spikes
Replication: Cytoplasm; particles mature by budding into EPR and Golgi

Listing of human Coronaviruses

- Human coronavirus 229E
- Human coronavirus OC43
- SARS-Corona V
- Human Coronavirus NL63 (HCoV-NL63, New Haven coronavirus)
- Human coronavirus HKU1
- Middle East respiratory syndrome coronavirus (MERS-CoV)

Pathogenesis

- Coronaviruses tend to be highly species-specific.
- Coronavirus infections may be disseminated, or localized.
- Coronaviruses are suspected of causing of some gastroenteritis in humans. Disease is marked by epithelial cell destruction and loss of absorptive capacity.
Laboratory Diagnosis

A. ANTIGEN AND NUCLEIC ACID DETECTION
- Enteric coronaviruses can be detected by examination of stool samples
- Polymerase chain reaction (PCR) assays are useful to detect coronavirus nucleic acid in stool samples.

B. SEROLOGY
- Because of the difficulty of virus isolation, serodiagnosis is the practical means of confirming coronavirus infections.
- **ELISA** and **hemagglutination tests** may be used. Serologic diagnosis of infections is possible using a **passive hemagglutination test** in which red cells coated with coronavirus antigen are agglutinated by antibody-containing sera.

ASTROVIRUSES

- Astroviruses exhibit a distinctive **star-like morphology**, nonenvelop, single stranded RNA.
- At least eight serotypes of human viruses are recognized.
- Astroviruses cause diarrheal illness and may be shed in extraordinarily large quantities in feces.
Astroviruses are transmitted by the **fecal-oral route** through contaminated food or water, person-to-person contact, or contaminated surfaces.

They are recognized as **pathogens for infants and children, elderly institutionalized patients**, and **immunocompromised persons**.

They may be shed for prolonged periods by immunocompromised hosts.

**Pathogenicity**

- Astroviruses cause gastroenteritis by causing **destruction of the intestinal epithelium**, **inhibition of usual absorption mechanism**, **loss of secretory functions**, and **decrease in epithelial permeability in the intestines**.

**Signs and symptoms**

The main symptoms are

- diarrhea
- Nausea
- vomiting
- fever
- malaise and abdominal pain.

- Incubation period of the disease is approximately 3-4 days.
- Infection is not usually a severe situation and only in some rare cases leads to dehydration.

**Viral and bacterial gastroenteritis**
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Viral</th>
<th>Bacterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involved site</td>
<td>Small intestine</td>
<td>Colon</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Watery</td>
<td>Bloody, mucoid</td>
</tr>
<tr>
<td>Vomiting</td>
<td>+++ or +</td>
<td>+ or –</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>+ or –</td>
<td>+++ or ++</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>–</td>
<td>++ or +</td>
</tr>
<tr>
<td>Anorexia</td>
<td>+ or –</td>
<td>+++ or ++</td>
</tr>
<tr>
<td>Systemic illness symptom</td>
<td>+ or –</td>
<td>+++ or ++</td>
</tr>
</tbody>
</table>