The following are well-established causal agents of viral gastroenteritis in humans:

a. Rotavirus  
b. Enteric adenoviruses  
c. Human Caliciviruses  
d. Astrovirus.  
e. Torovirus  
f. HSV, CMV in immunocompromised patients (not discussed here)

Rotavirus was first identified by electron microscopy in 1973 from duodenal biopsies of children with diarrhea and was later detected in stool samples by negative EM.

Human and animal rotaviruses are known.

Family Reoviride includes genus Rotavirus, Reovirus and Colorado Tick Fever virus

- Non-enveloped, icosahedral, 60-80nm in size  
- Electron microscopic appearance of a wheel with radiating spokes (Latin, rota=wheel)  
- Double capsid (outer capsid, inner capsid) and a core.  
- **Major structural proteins**-
  1. **Outer** capsid structural proteins- VP7 (G protein) and VP4 (the viral hemagglutinin or P protein). Both elicit neutralizing antibodies.  
  2. **Inner** capsid structural proteins- Mainly VP6, also VP1, 2, 3.
♦ Inner core contains the genome that has double stranded (ds) RNA in 11 segments. Genome codes for 6 virus proteins (VP1-6) and 6 non-structural proteins (NSP1-6). RNA segments can be separated by gel electrophoresis; segmented genome can reassort with co-infection of cells with different strains.

♦ Groups Seven different groups (A to G) and 2 subgroups based on antigenic specificity of VP6.

Most human pathogens belong to groups A, B, and C; group A viruses with either subgroup I or II, are the most common.

♦ Serotypes 14 human G serotypes (specified by VP7) and 20 P serotypes (specified by VP4)

♦ E-types based on differences in relative migration rates of genome segments in PAGE

Virus is acid-labile but rather stable in the environment.

It is susceptible to disinfection with 95% ethanol, ‘Lysol’ and formalin.

Affected host cells are mature enterocytes lining the middle and upper end of the intestinal villi in the small intestine.

The infectious particle is thought to be an “intermediate subviral particle” (ISVP) that is generated after removal of some of the outer capsid. The viral attachment protein is probably exposed after protease digestion in the GI tract removes some or all of the outer capsid (VP4).

Virions enter the host cell by endocytosis. Virus replicates in the host cell cytoplasm. Large amounts of viral particles are shed in diarrheal stools.

Histopathology of infected intestines shows villous atrophy and blunting, due to death of the mature enterocytes and infiltration of lamina propria with mononuclear cells. Subsequently there is repopulation of the villous tips with immature secretory cells (crypt hyperplasia).

Mechanism of watery diarrhea is cell dysfunction/death, activation of the enteric nervous system, and by NSP4, a non-structural
protein, that may play a role as a viral enterotoxin and secretory agonist. During convalescence, repopulation with immature secretory cells may contribute to the secondary lactose intolerance that is sometimes seen.

♦ **Distribution**

Worldwide: 20% of diarrhea-related deaths under age 5 years and 40% of severe diarrhea cases

♦ **Seasonality**

Winter months -spring.

Seen year round in the tropics.

♦ **Age**

Infests children at a young age. Older infants and young children (4mo-2 years) tend to be more symptomatic with diarrhea. Young infants may be protected due to transplacental transfer of maternal antibody.

♦ **Spread** - mainly person to person via fecal-oral route and through fomites.

Spread by food and water is also possible.

♦ **Contagiousness** -

Contagious period starts before onset of diarrhea to a few days after end of diarrhea.

among susceptible individuals due to the following: -

Small infective dose (only 10 pfu)

High numbers of viral particles being shed in diarrheal stools (1010/gm)

Shedding of virus from asymptomatic hosts

♦ **Nosocomial cases and outbreaks are known to occur.**

♦ **Asymptomatic infections are common, especially in adults.**

♦ **Severe infections are seen in young, elderly, immune compromised hosts.**
♦ Group A infections are most common.

Group B has been associated with outbreaks in adults in China

Group C is responsible for sporadic cases of diarrhea in infants around the world.

Incubation period is < 4 days

Fever- can be high grade

Nausea and vomiting precede diarrhea.

Diarrhea is usually watery (no blood or leukocytes), lasting 3-9 days, but longer in malnourished and immune deficient individuals. Necrotizing enterocolitis and hemorrhagic gastroenteritis is seen in neonates.

Dehydration is the main cause of death.

Secondary malabsorption of lactose and fat, and chronic diarrhea are possible

Antigen-detection in stool-by (uses a monoclonal antibody) and is used for rapid diagnosis.

Electron microscopy

Culture- group A rotaviruses can now be cultured in monkey kidney cells.

Epidemiological studies use patterns of viral RNA migration by polyacrylamide gel electrophoresis. Different genetic strains may circulate in a given community.

RT-PCR

Supportive-rehydration

Hand washing- partly effective
♦ Alcohol-based hand gels
♦ Disinfection of surfaces, toilets, toys etc.

---------------

**Rotashield**, a live tetravalent rhesus-human reassortant vaccine, it was removed from the market (possible relationship between the occurrence of intussusceptions)

**RotaTeq** is a new live pentavalent human-bovine reassortant vaccine (2006/US). Vaccine appears to confer protection that lasts for at least 2 years.

**Rotarix** (Avant Immunotherapeutics) is a live attenuated monovalent vaccine.

---------------

♦ Members of the family Caliciviridae
♦ Now classified into genera **Norovirus** and **Sapovirus**, based on antigenic differences.

♦ Norwalk virus is the prototypic member of the Genus Norovirus. It was first detected in stools of patients with gastroenteritis in Norwalk, Ohio in 1972.

♦ Examples of Sapoviruses include Manchester virus, London/92 virus, etc.

---------------

♦ Non-enveloped, ss RNA viruses with a +ve sense genome.
♦ 27-35 nm in size.
♦ Two *morphologic groups* are based on electron microscopic appearance:

**Atypical**, Small round structured viruses (SRSVs)—smaller, approx. 27 nm, they have a rough, feathery edge, but no internal pattern. (These are the members of **Norovirus** group.)
**Typical**, spiked appearing viruses- are 31-35nm and have 32 cup-shaped depressions on surface (calici= i.e. cup-like).

---

♦ Causal agent referred to for illnesses commonly known as- “stomach flu” or viral gastroenteritis.

♦ Relatively short incubation period (Range 12hrs. to 4 days)

♦ Illness is brief (3-5 days) and usually self-limited

♦ GI symptoms -nausea, vomiting, abdominal cramping and watery diarrhea (fecal leukocytes are absent).

♦ Other symptoms-headache, fever, malaise, myalgia,

♦ Outbreaks in institutions, cruise ships, etc. through contaminated food or water (feco-oral)

---

♦ Worldwide distribution. Higher seroprevalence in developing countries.

♦ Established as the most frequent etiology of infectious GE in some countries.

♦ Infections occur year-round with an apparent predominance in winter season.

♦ Transmission-direct fecal-oral (person-to-person) spread or indirect fecal-oral spread via contamination of food/water, and through fomites contaminated by vomitus or stool.

♦ Possible spread through aerosolization of vomitus and ingestion (rather than inhalation) of infective particles.

♦ Low infective dose (~10 virions).

♦ Viral excretion in stool can continue beyond the cessation of symptoms.

♦ Asymptomatic infections (>30% cases) can result in transmission of infection
Outbreaks can involve infants and school-age children.

Outbreaks related to consumption of contaminated oyster and shellfish have been described.

It is thought that the seafood or water or ice becomes contaminated with fecal material from sewage or food handlers. Estimated to cause >50% of food-borne gastroenteritis outbreaks in the US.

Clinical and microbiologic features as well as epidemiologic criteria suggest viral etiology of gastroenteritis outbreaks.

Analysis of stool or suspected food material; also environmental samples (outbreak investigations).

State public health laboratories mainly use realtime RT-PCR of stool and emesis samples, as well as environmental samples during outbreak investigations.

Serology is used for epidemiological purposes, with paired sera.

ELISA is thought to have poor sensitivity.

CDC recommends environmental disinfection of non-porous surfaces with bleach solution (1 part bleach: 50 parts water).

Genus Astrovirus, family Astroviridae, contains 8 human species (antigenic types) that are known as HuAst 1 to 8.

Small ss RNA, non-enveloped virus 27-32nm in size.

EM appearance of a smooth, round structure with an unbroken surface (unlike indented surface of calicivirus) and a 5 or 6 pointed star within.

Immunologically distinct from Human Caliciviruses.
Incubation period 1-4 days
Diarrhea, headache, nausea, low-grade fever, vomiting
(Similar to other viruses)

♦ Worldwide
♦ Mainly affects children infants and young children <7 years of (clinical illness is less common in adults)
♦ More common in winter season
♦ Transmission by direct person-to-person, via fecal-oral route or ingestion of aerosolized vomitus
♦ Transmission indirectly through fecal contamination of sea-food/water (outbreaks described) and contaminated fomites
♦ Low infective dose
♦ Outbreaks have been seen in child-care centers.

♦ EM especially useful since the virus is often shed in large amounts in stool
♦ Enzyme Immunoassay (EIA) test
♦ RT-PCR in used by research laboratories.

♦ Serotypes implicated are 40 and 41 (enteric serotypes). These are difficult to culture and require special cell lines
♦ Cause diarrheal disease in infants and children<4 years of age
♦ Feco-oral spread
♦ Incubation period is 8-10 days
♦ Diarrhea lasts 5-12 days, longer than other viral gastroenteritis
♦ Diagnosis- Latex agglutination, ELISA, EM
♦ Family Coronaviridae
♦ Genus Torovirus
♦ Human and animal pathogen
♦ Pleomorphic, coated ss (+) RNA virus
♦ Core “doughnut-shaped” (torus)
♦ Watery diarrhea in 2 – 12 months old
♦ Diagnosis: EM