Digestive System

University of Jordan

Faculty of Medicine

Batch of 2013-2019

Medical Committee
The University of Jordan

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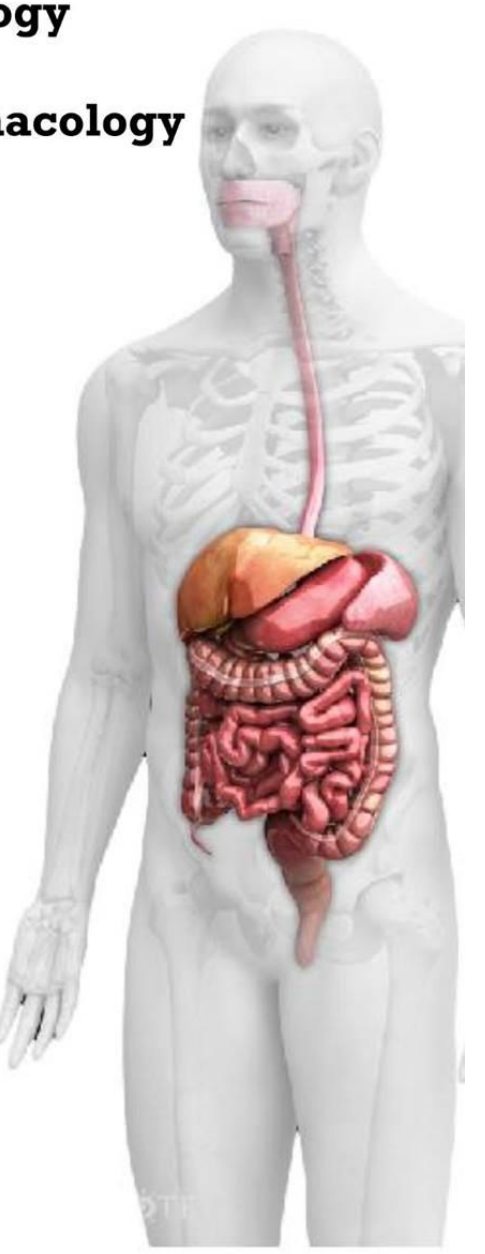

Number # : 1-Viral Infections of the GIT

Doctor's name: Dr. Mazen

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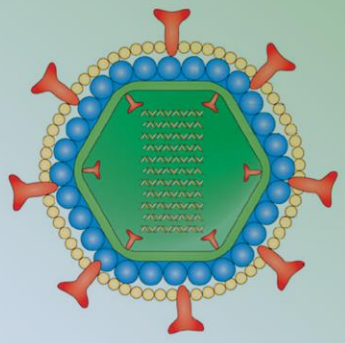
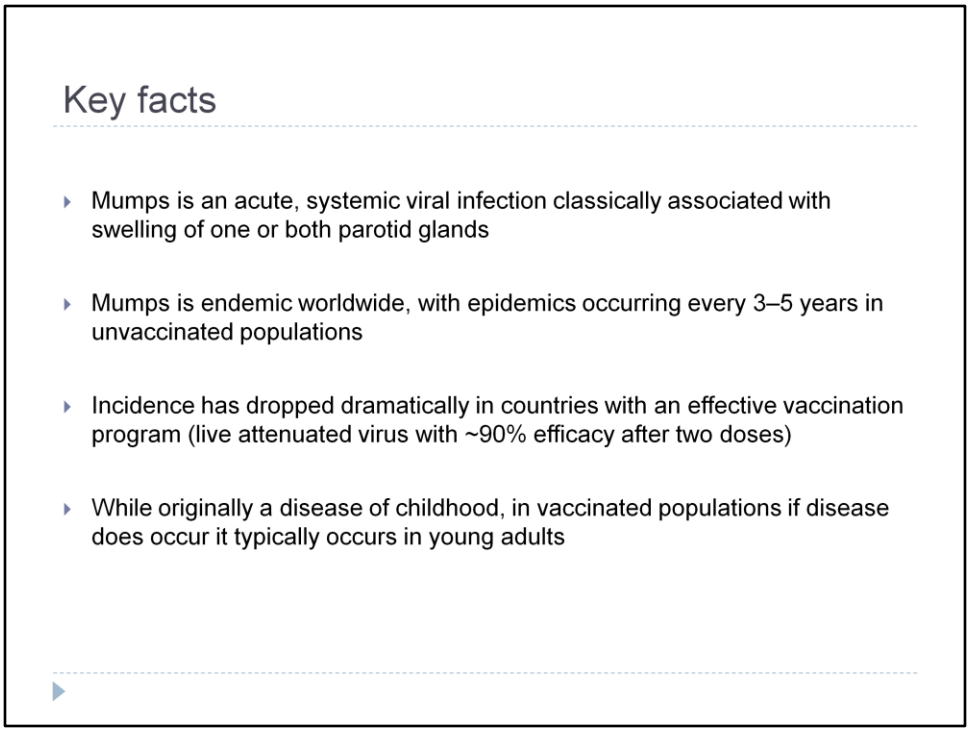


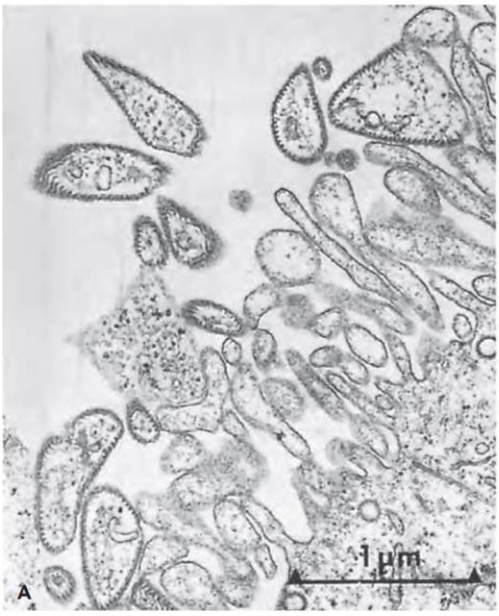
Viral infections of the GIT

Dr. Mazin Al-Salihi

Salivary Glands
Mumps



Whereas in the pre- and early postvaccine era mumps was historically a disease of childhood, the majority of U.S. cases now occur in previously vaccinated young adults. The majority of cases occurred in college students 18–23 years of age, most of whom had been vaccinated in early childhood. These outbreaks are probably the result of several coincident circumstances, including (1) situations promoting the spread of respiratory viruses among young adults (e.g., residence in college dormitories), (2) waning of vaccine immunity with time, (3) lack of endemically circulating wild-type virus to periodically boost vaccine-induced immune responses, and (4) continuing global epidemics of mumps (due either to lack of mumps vaccination programs or to low rates of mumps vaccination where such programs do exist).



Molecular Biology

Paramyxoviridae family

Pleomorphic particles

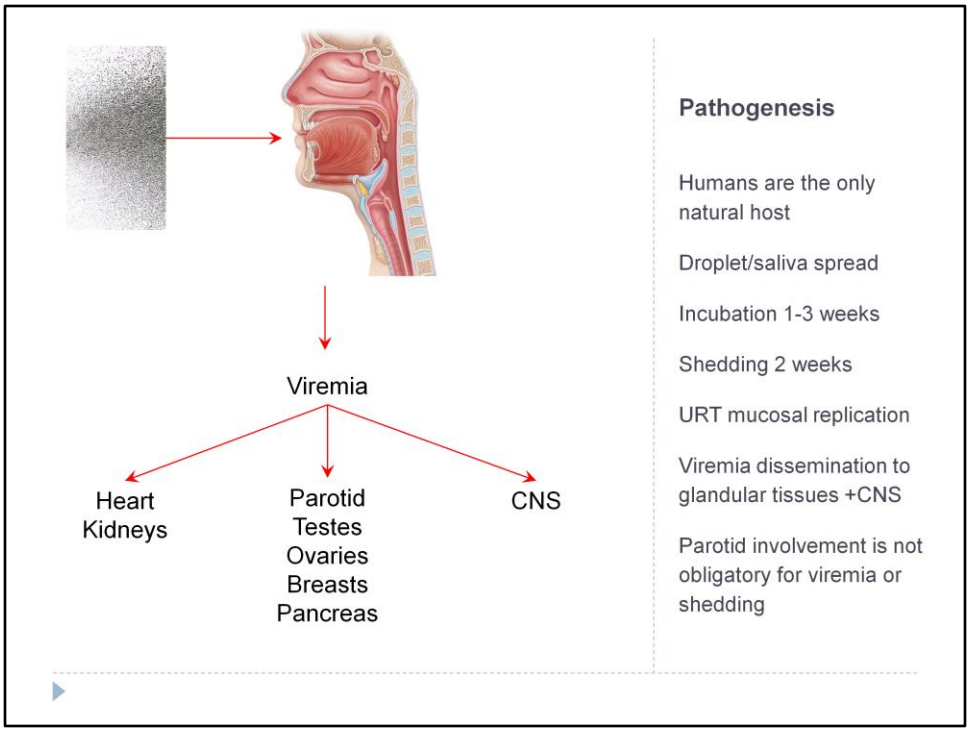
Ribonucleoprotein core surrounded by a host cell-derived lipid envelope

Core (replicative):
- Negative ssRNA
- Nucleoprotein
- Phosphoprotein
- Polymerase

Envelope contains viral proteins (binding/entry)

Mumps virions are pleomorphic particles ranging from 100 to 600 nm in size, consisting of a helical ribonucleoprotein (RNP) core surrounded by a host cell–derived lipid envelope

Envelope contains the viral hemagglutinin-neuraminidase (HN) and fusion (F) proteins, which are responsible for cell binding by and entry of the virus and are major targets of virus-neutralizing antibodies

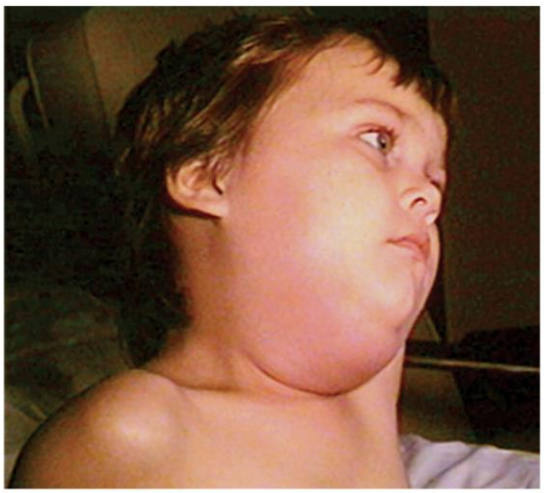


Transmissibility after nasal or buccal mucosal inoculation of virus suggests that natural infection is initiated by droplet spread. Mumps virus is typically shed from 1 week before to 1 week after symptom onset. The incubation period is 1-3 weeks, during which the virus multiplies in the upper respiratory mucosa before spreading to draining lymph nodes.

Termination of viral shedding correlates with the local appearance of virus-specific secretory IgA and IgM, as early as a few days after disease onset

The virus disseminates via a transient plasma viremia, potentially infecting multiple tissues and organ systems. The most common sites of virus dissemination are glandular tissues (parotid glands, testes, ovaries, breasts, and pancreas), kidneys, and the CNS. In rare cases, MuV can be transmitted transplacentally.

Plasma viremia disappears coincident with the development of MuV–specific antibody, which can be detected in serum as early as 11 days after infection of humans



Clinical Features

~1/2 of infections are asymptomatic/ non-specific respiratory symptoms

Prodrome

Mild fever

Characteristic parotid swelling in most symptomatic infections

Epididymo-orchitis (esp. postpubertal)

Aseptic meningitis <10%

The prodrome of mumps consists of low-grade fever, malaise, myalgia, headache, and anorexia.

The submaxillary and sublingual glands are involved less often than the parotid gland and are almost never involved alone. Parotid tenderness and pain on salivation precede swelling. Glandular swelling increases for a few days and then gradually subsides, disappearing within 1 week.

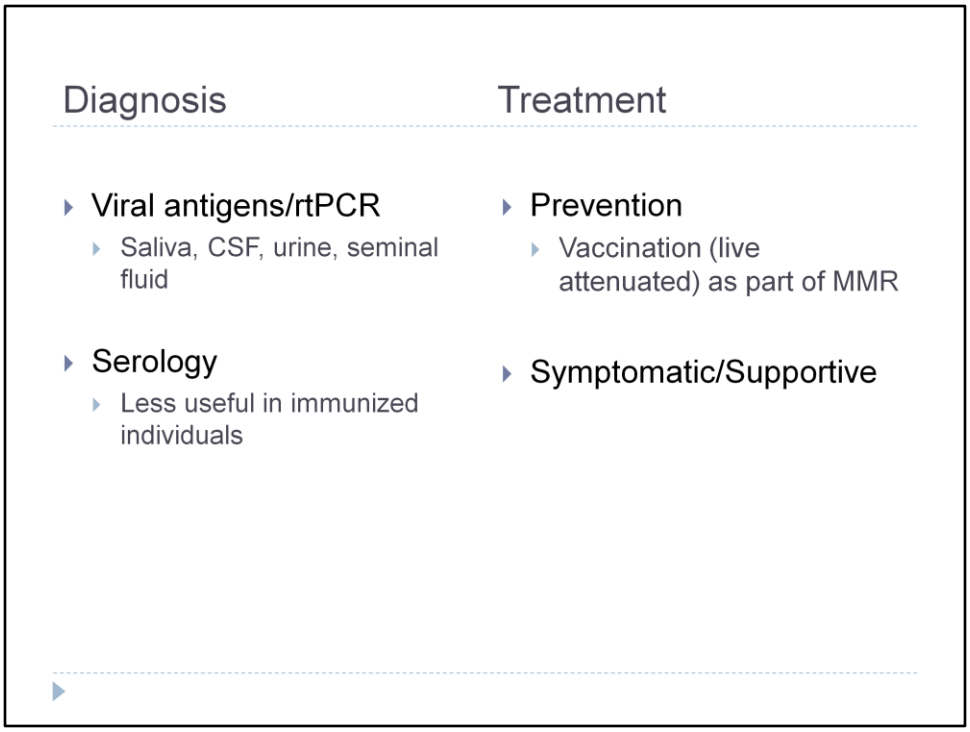
Epididymo-orchitis is the next most common manifestation of mumps, accompanied by fever. The testis is painful and tender and can be
enlarged to several times its normal size; this condition usually resolves within 1 week. Testicular atrophy develops in one-half of affected men. Sterility after mumps is rare, although subfertility can occur especially with bilateral involvement.

Oophoritis occurs in ~5% of women with mumps and only rarely associated with sterility or premature menopause. Mumps infection in postpubertal women may also present with mastitis.

Mumps virus invades the CNS in ~50% of cases; however, symptomatic CNS disease, typically in the form of aseptic meningitis, occurs in <10% of cases, with a male predominance. CNS symptoms of aseptic meningitis (stiff neck, headache, and drowsiness) appear ~5 days after parotitis and also occur often in the absence of

parotid involvement. Adult infections more commonly have poor outcomes than do pediatric infections.

Pancreatic involvement may be mild or severe and hemorrhagic



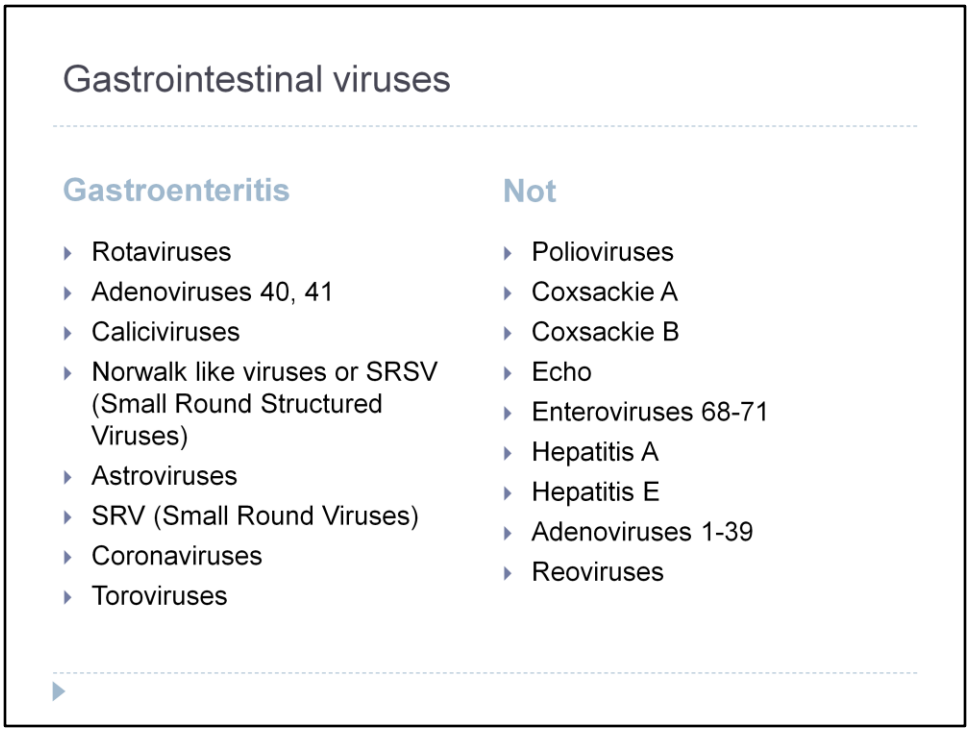
When parotitis is present, the clinical diagnosis of mumps is straightforward, even if the disease is not epidemic. Virus is typically assayed in material obtained by throat swab, although it has been detected in CSF, urine, and seminal fluid. Despite the apparent frequency of viremia, mumps virus has only rarely been isolated from blood, possibly because of the presence of specific antibodies

Mumps is generally a benign, self-resolving illness. Therapy for parotitis and other clinical manifestations is symptom based and supportive. The administration of analgesics and the application of warm or cold compresses to the parotid area may be helpful.

Viral Gastroenteritis

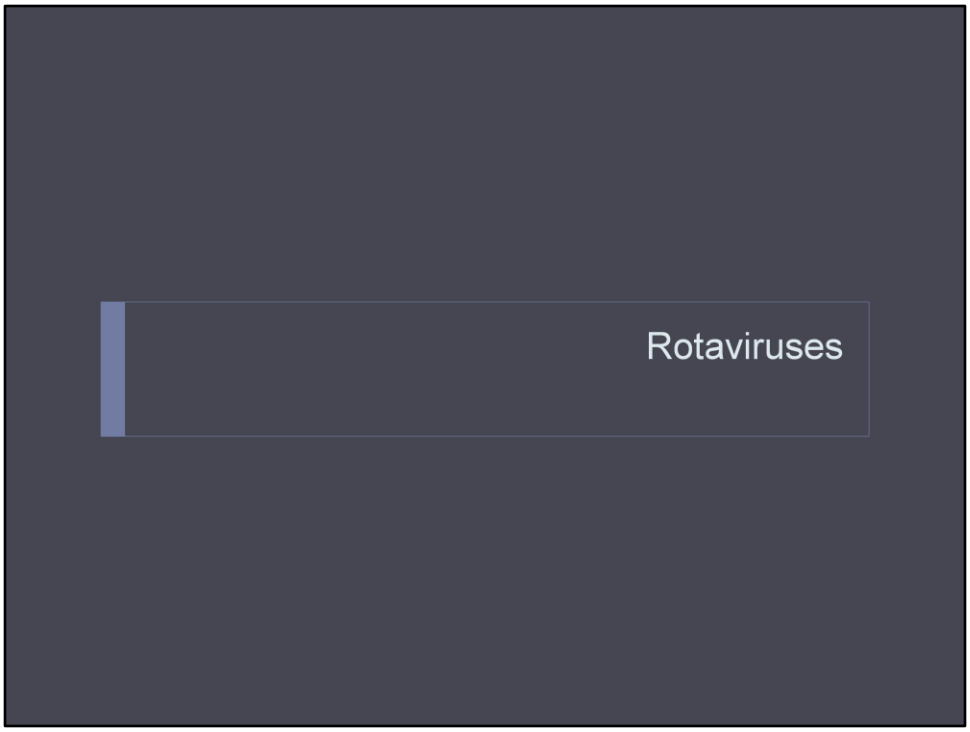
Key facts

- Viral diarrheal diseases are one of the most common illnesses in children and infants worldwide (developed & developing)
- In developing countries, viral gastroenteritis is a major killer of infants who are undernourished
- Elderly persons, especially those with debilitating health conditions, are also at risk of severe complications and death from acute gastroenteritis
- Many different types of viruses are found in the gut but only some are associated with gastroenteritis

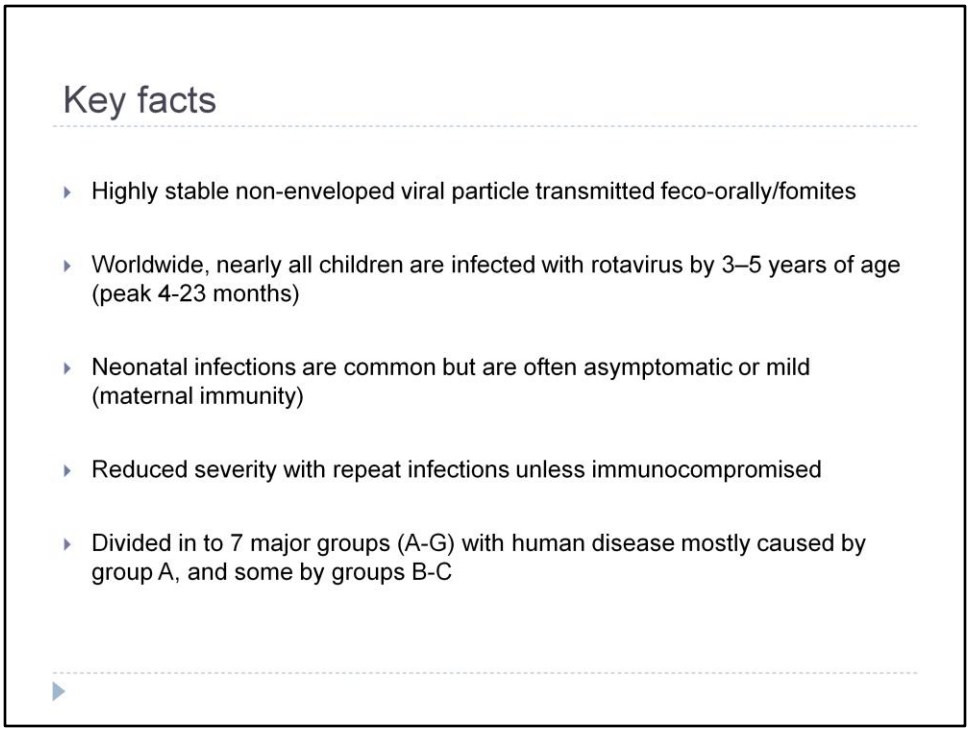


Illness caused by these viruses is characterized by the acute onset of vomiting and/or diarrhea, which may be accompanied by fever, nausea, abdominal cramps, anorexia, and malaise

Opportunistic infections by CMV, HSV, VZV, HIV in the immunocompromised



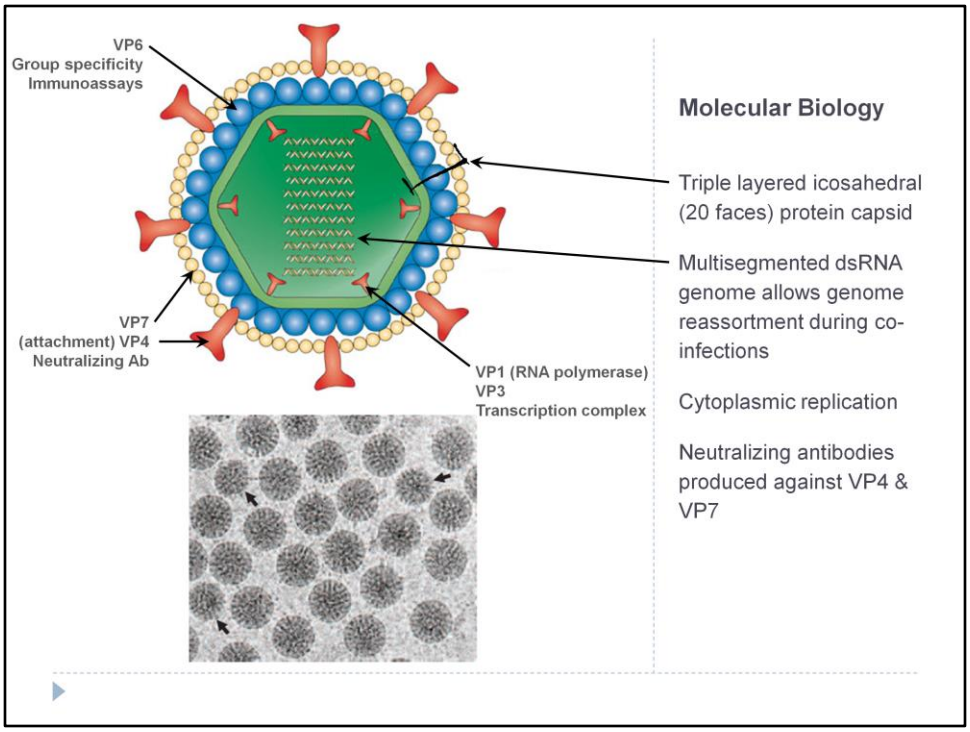
Rotaviruses are members of the family Reoviridae



In tropical settings, rotavirus disease occurs year-round, with less pronounced seasonal peaks than in temperate settings, where rotavirus disease occurs predominantly during the cooler fall and winter months.

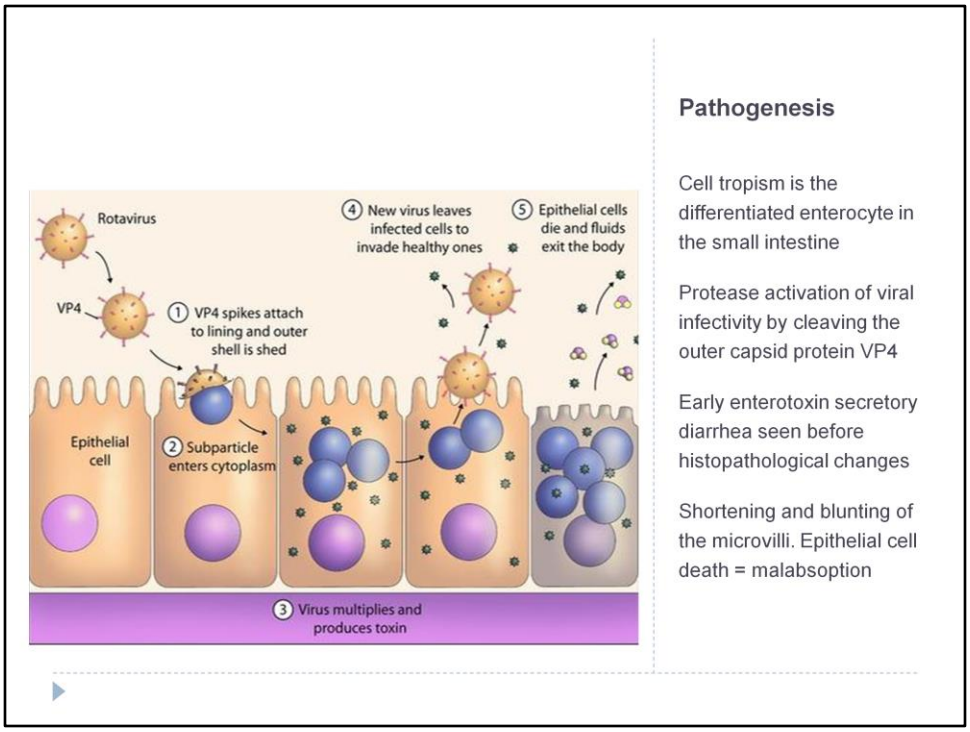
Rotaviruses are composed of seven distinct groups (A to G, now designated RVA, RVB, RVC, etc.). RVA, RVB, and RVC strains are found in both humans and animals, whereas rotaviruses of groups D, E, F, and G have been found only in animals to date.

RVAs cause significant diarrheal disease in infants and in the young of various mammalian and avian species. RVBs have been associated with epidemics of severe diarrhea primarily in adults in Asia. RVCs have been sporadically reported in fecal specimens from children with diarrhea and in several family outbreaks



The particle is composed of three concentric protein shells (VP7, VP6, and VP2, shown in different colors) and the spike protein VP4 that spans the VP6 and VP7 layers and extends out from the particle. A transcription complex of VP1 and VP3 is inside the VP2 layer. The viral double-stranded RNA (dsRNA) genome is segmented. **EM image** Rotavirus triple-layered particles (TLPs) and a few double-layered particles (DLPs) (arrows) are easily visualized (these are missing VP7 & VP4)

Viruses within each group are capable of genetic reassortment, but reassortment does not occur among viruses in different groups

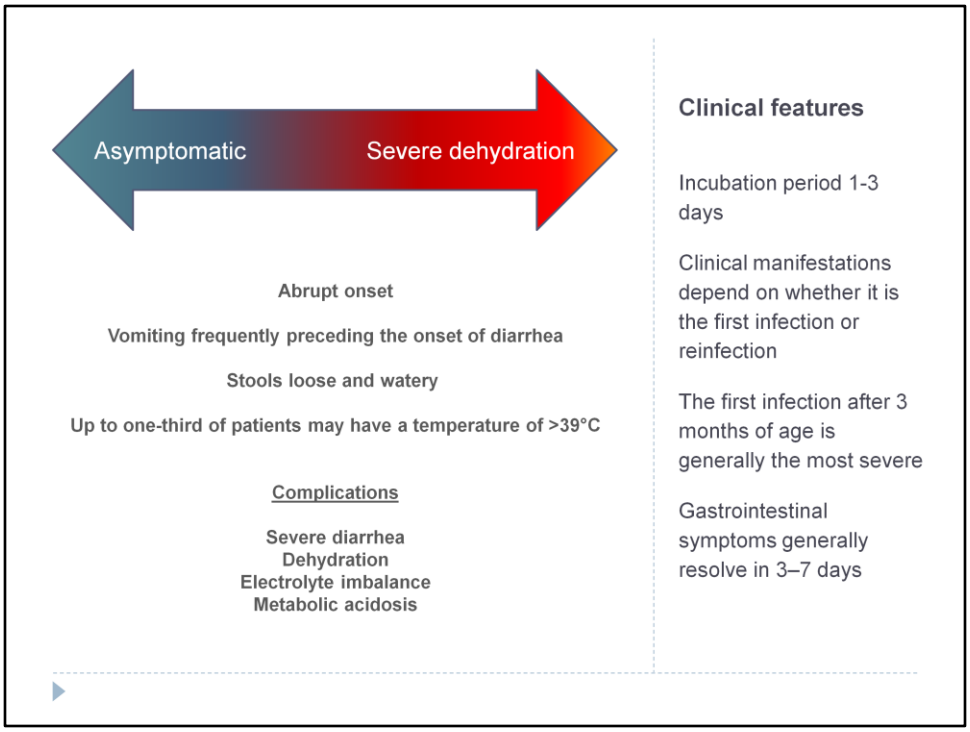


Extraintestinal spread of rotavirus also occurs in humans and all animal models studied, demonstrating a wider range of host cells than previously thought and possible additional receptors

Rotaviruses infect and ultimately destroy mature enterocytes in the villous epithelium of the proximal small intestine. The loss of absorptive
villous epithelium, coupled with the proliferation of secretory crypt cells, results in secretory diarrhea. Brush-border enzymes characteristic of differentiated cells are reduced, and this change leads to the accumulation of unmetabolized disaccharides and consequent osmotic diarrhea.

Some studies also show that one of the viral proteins (NSP4) may function as an enterotoxin and contributes to secretory diarrhea by altering epithelial cell function and permeability. In addition, rotavirus may evoke fluid secretion through activation of the enteric nervous system in the intestinal wall.

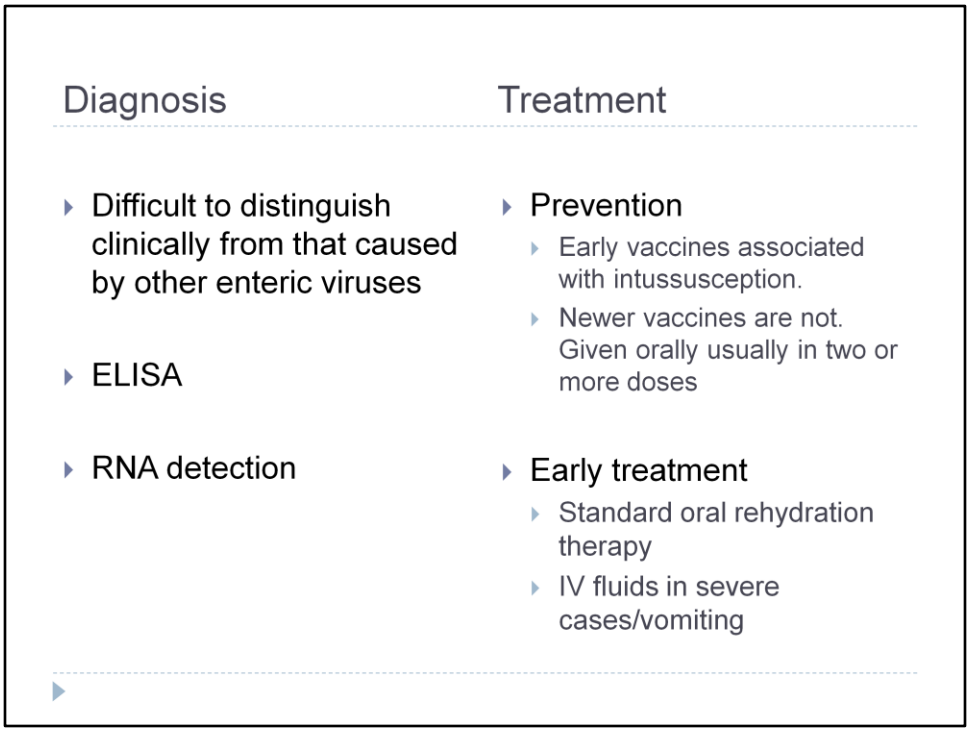
Whatever the underlying mechanism loss of fluids and electrolytes can lead to severe dehydration and even death



Transmission can occur 2 days before to 10 days after onset of diarrhea

Protection against rotavirus disease is correlated with the presence of virus-specific secretory IgA antibodies in the intestine and, to some extent, the serum. Because virus-specific IgA production at the intestinal surface is short lived, complete protection against disease is only temporary. However, each infection and subsequent reinfection confers progressively greater immunity; thus severe disease is most common among young children with first or second infections.

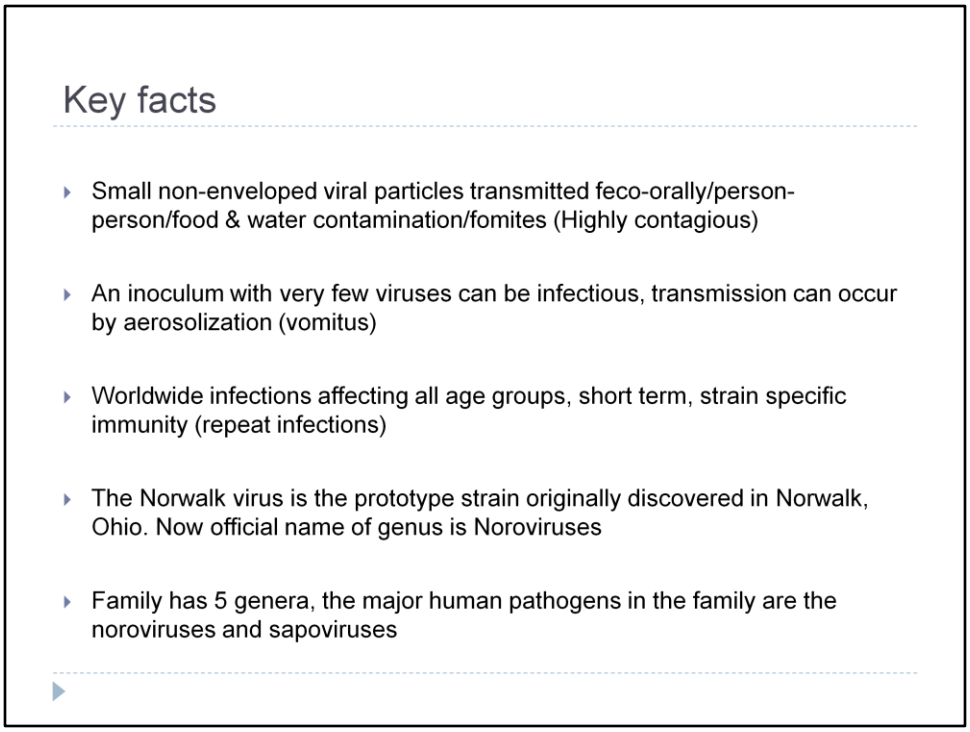
Rotavirus does not appear to be a major opportunistic pathogen in children with HIV infection. In severely immunodeficient children, rotavirus
can cause protracted diarrhea with prolonged viral excretion and, in rare instances, can disseminate systemically. Persons who are
immunosuppressed for bone marrow transplantation are also at risk for severe or even fatal rotavirus disease



Rotavirus gastroenteritis can lead to severe dehydration. Thus appropriate treatment should be instituted early

Antibiotics and antimotility agents should be avoided

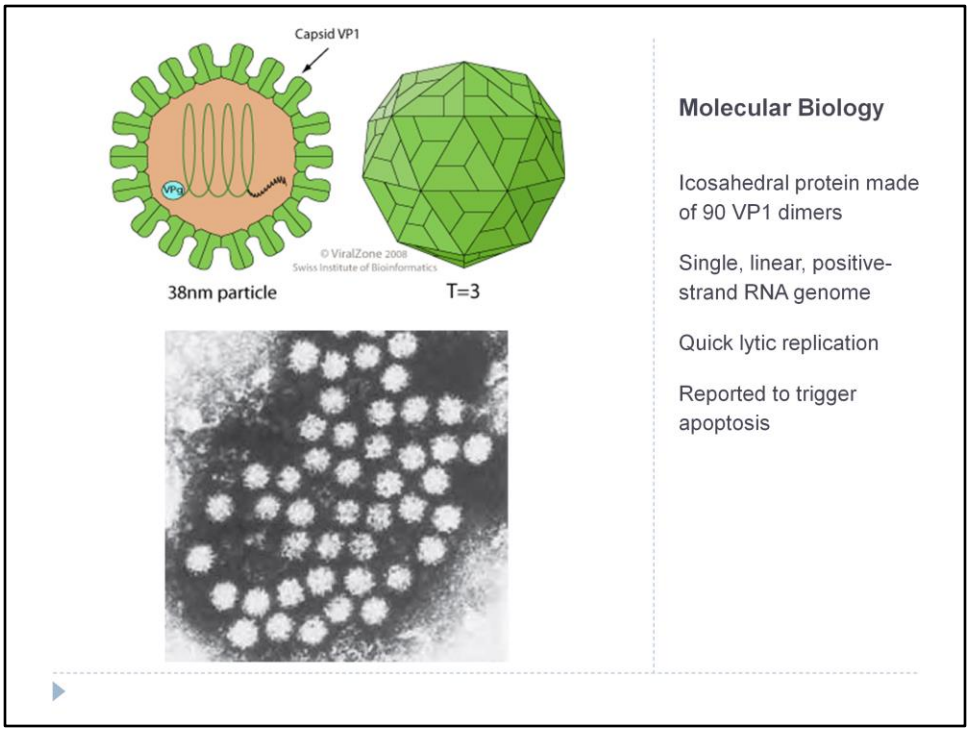
Caliciviruses



Infections with the Norwalk and related human caliciviruses are common worldwide, and most adults have antibodies to these viruses. Antibody is acquired at an earlier age in developing countries—a pattern consistent with the presumed fecal-oral mode of transmission. Infections occur year-round, although, in temperate climates, a distinct increase has been noted in cold-weather months. Noroviruses affect all age groups, whereas sapoviruses primarily cause gastroenteritis in children.

Noroviruses also cause traveler's diarrhea, and outbreaks have occurred among military personnel deployed to various parts of the world. The limited data available indicate that norovirus may be the second most common viral agent (after rotavirus) among young children and the most common agent among older children and adults.

Approximately 50% of persons challenged with Norwalk virus become ill and acquire short-term immunity against the infecting strain. Since there are many different types of noroviruses, people can get infected many times during their lifetime

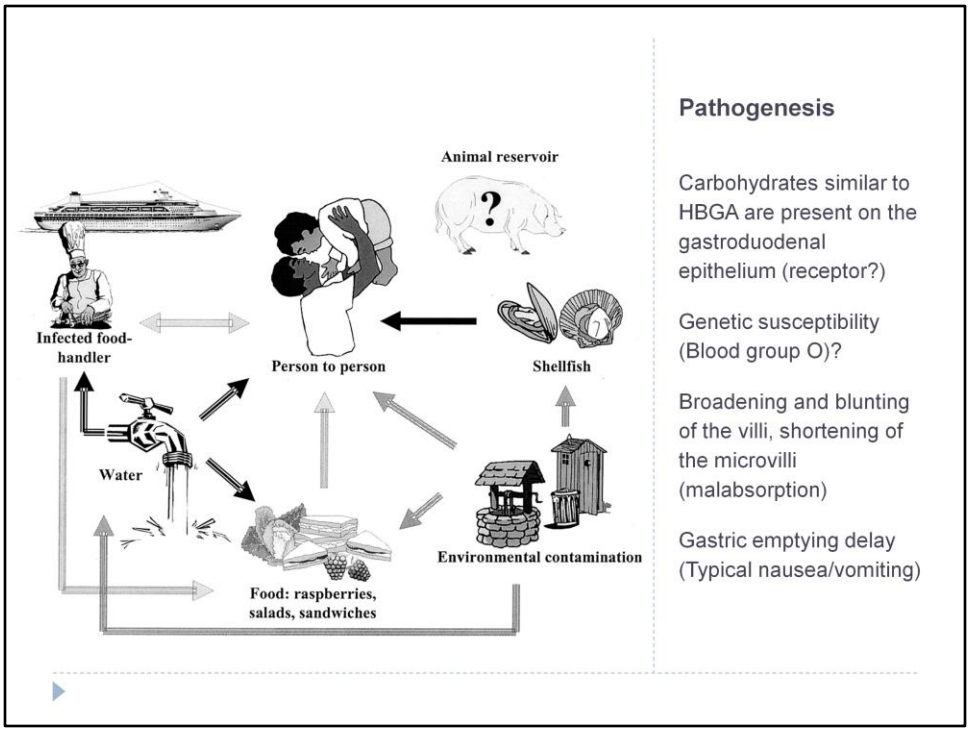


Large hollows are seen as cuplike structures on the surface of caliciviruses (*calici* is derived from the Latin word *calyx,* or "cup").

The VP2 is considered a minor structural protein because it is present in only one to two copies per virion, and its function is unknown

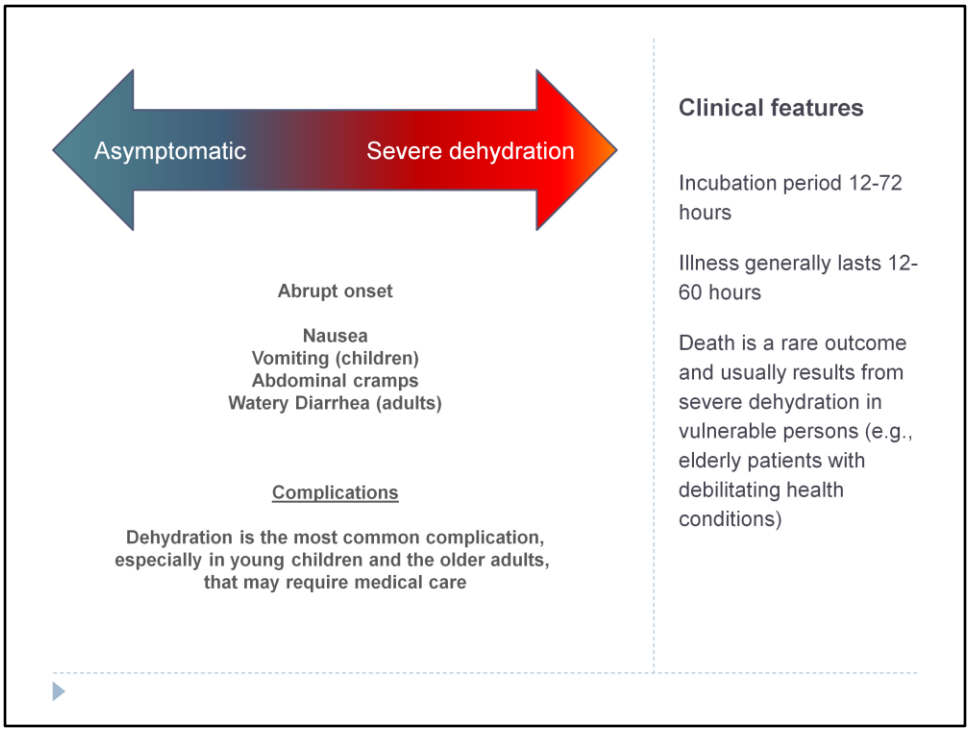
Although the VPg is present in virions, it likely functions primarily as a nonstructural protein during RNA replication. Newly synthesized positive-strand RNA genomes are covalently linked to VPg and packaged into virions that are released from lysed cells

The replication cycle of a calicivirus is rapid: new viral progeny can be detected within hours after infection. Calicivirus-infected cells undergo lysis and it is presumed that the majority of progeny viruses are released during this process. The triggering of apoptosis has been associated with calicivirus infection, and apoptotic changes in cellular membranes may be one of the mechanisms by which cells lyse and release viral particles.



Structural studies have verified that the norovirus VP1 interacts with histo-blood group antigens (HBGA) carbohydrates. Some individuals may have a genetic predisposition to illness. Specific ABO, Lewis, and secretor blood group phenotypes may influence susceptibility to norovirus infection

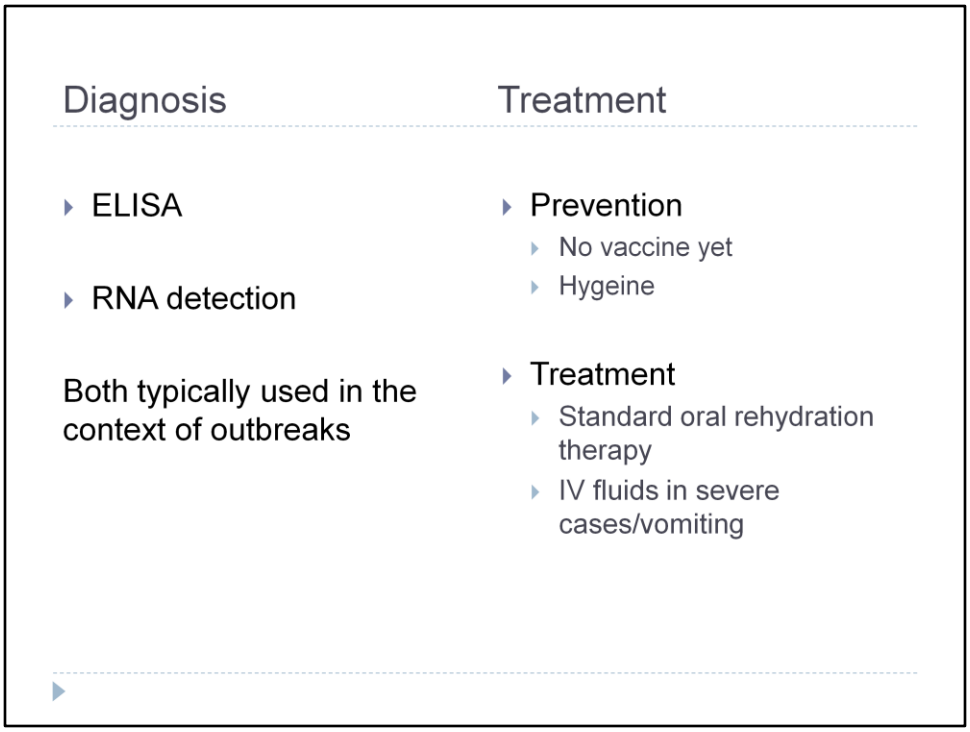
After the infection of volunteers, reversible lesions are noted in the upper jejunum, with broadening and blunting of the villi, shortening of the microvilli, vacuolization of the lining epithelium, crypt hyperplasia, and infiltration of the lamina propria by polymorphonuclear neutrophils and lymphocytes. The lesions persist for at least 4 days after the resolution of symptoms and are associated with malabsorption of carbohydrates and fats and a decreased level of brush-border enzymes. No histopathologic changes are seen in the stomach or colon, but gastric motor function is delayed, and this alteration is believed to contribute to the nausea and vomiting that are typical of this illness



Viral shedding and infectivity are greatest during the acute illness, but challenge studies with Norwalk virus in volunteers indicate that viral antigen may be shed by asymptomatically infected persons and also by symptomatic persons before the onset of symptoms and for several
weeks after the resolution of illness

Vomiting is more prevalent among children, whereas a greater proportion of adults develop diarrhea.

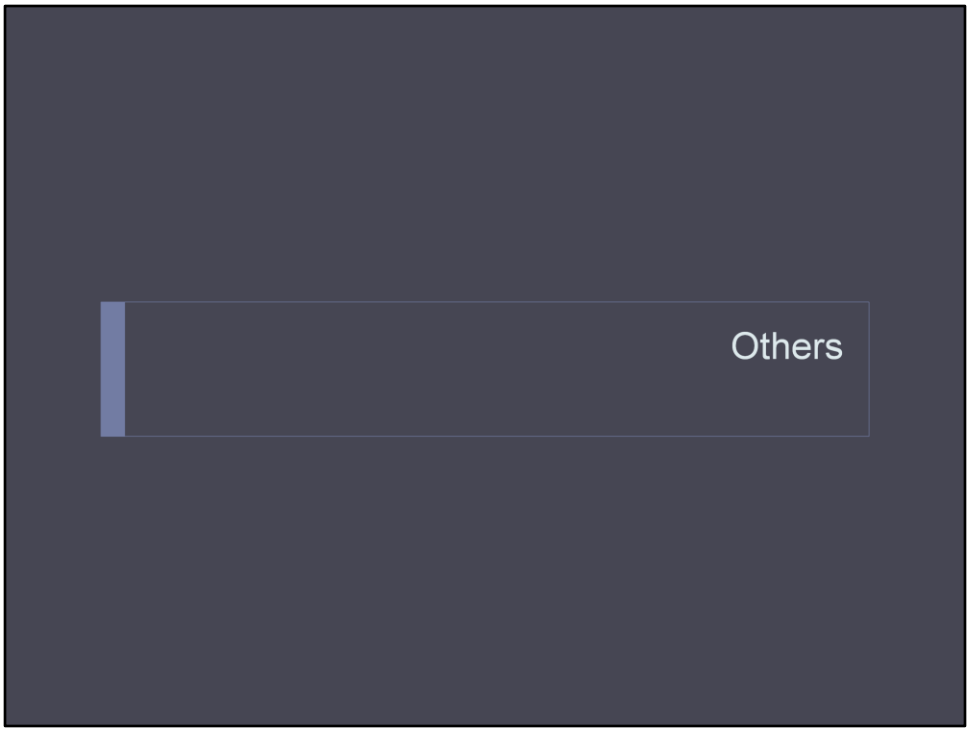
Constitutional symptoms are common, including headache, fever, chills, and myalgias.

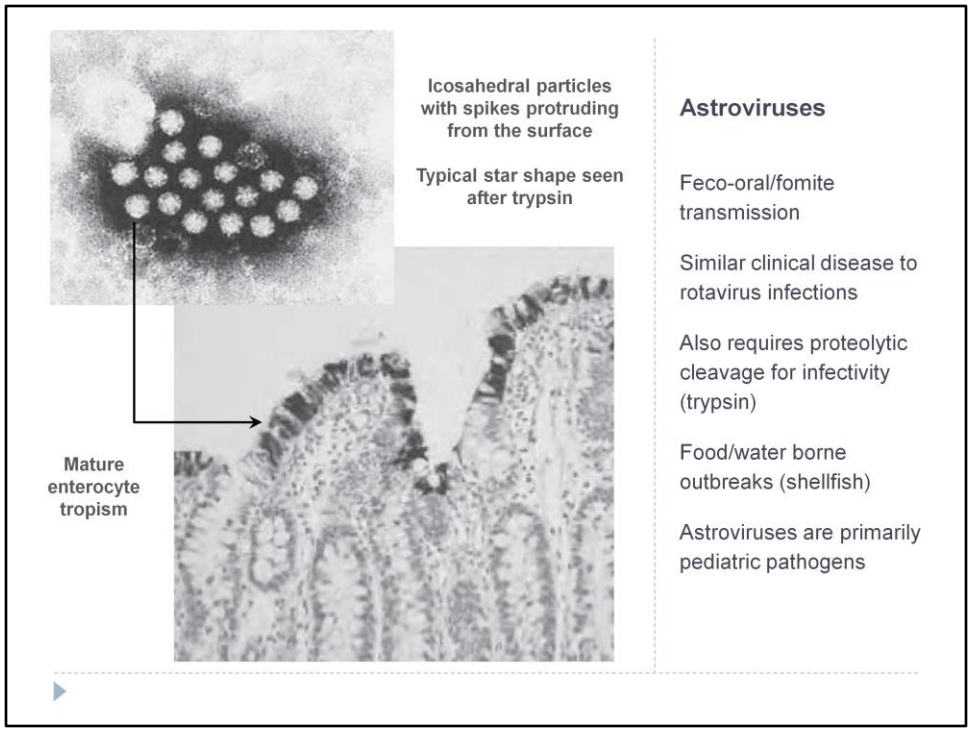


No currently available single assay can detect all human caliciviruses because of their great genetic and antigenic diversity.

The assays are still cumbersome and are available primarily in research laboratories, although they are increasingly being adopted by public
health laboratories for routine screening of fecal specimens from patients affected by outbreaks of gastroenteritis. Commercial EIA kits have limited sensitivity and usefulness in clinical practice and are of greatest utility in outbreaks, in which many specimens are tested and only a few need be positive to identify norovirus as the cause

An analysis of the common features of 38 NV outbreaks indicates that a provisional diagnosis of illness by the noroviruses can be made during an outbreak if the following criteria are met: (a) bacterial or parasitic pathogens are not detected, (b) vomiting occurs in more than 50% of cases, (c) the mean or median duration of illness ranges from 12 to 60 hours, and (d) the incubation period is 24 to 48 hours. These so-called Kaplan criteria were found to be 99% specific and 68% specific for the provisional diagnosis of a norovirus outbreak when reevaluated with samples confirmed as norovirus positive.

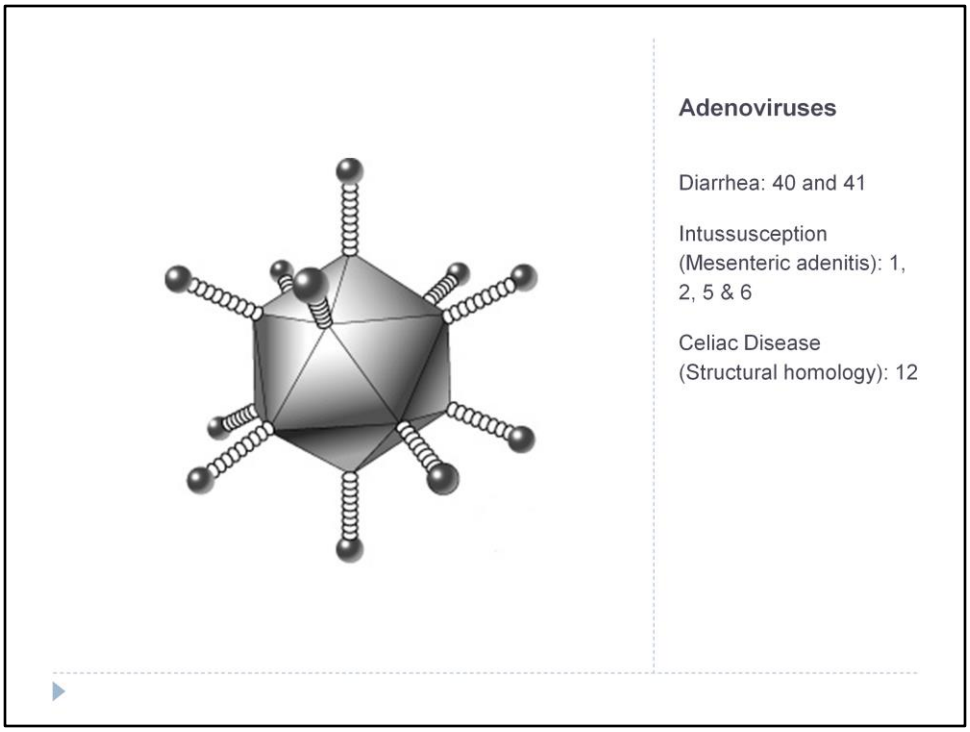

Others



Most astrovirus infections in humans are detected in the winter months in temperate regions and in the rainy season in more tropical climates. However, outbreaks occur year around in schools, resorts, hospitals, nursing homes, restaurants and cruise ships

Gastroenteritis caused by astroviruses is usually a mild, self-limiting illness that does not require hospitalization, more severe gastroenterologic disease that may result in death has also been reported

Epidemiologic data indicate that contaminated food is the main source for HAstV infection. HAstV has been found in bivalve mollusks, indicating that seafood may contribute to gastroenteritis caused by HAstV. HAstV has also been detected in water from different origins, including drinking water, rivers, dams, wastewater, and efluents from water treatment plants



In general, adenovirus (Ad 40,41)gastroenteritis it is not as prevalent as rotavirus, occurs most often in children younger than 4 years of age, &
is not easily distinguished on clinical grounds from rotavirus

The telescoping bowel characteristic of intussusception may be caused by mesenteric adenitis acting as a lead point to the mechanical obstruction

E1B-55K protein from Ad12 found in the intestine may play a role in the pathogenesis of celiac disease, perhaps by inducing crossreacting antibodies to A-gliadin