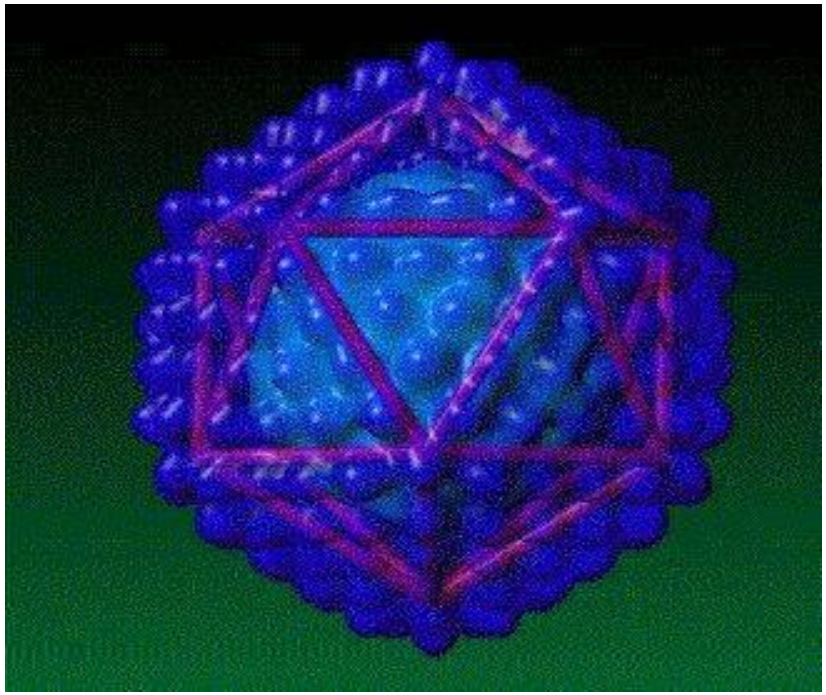
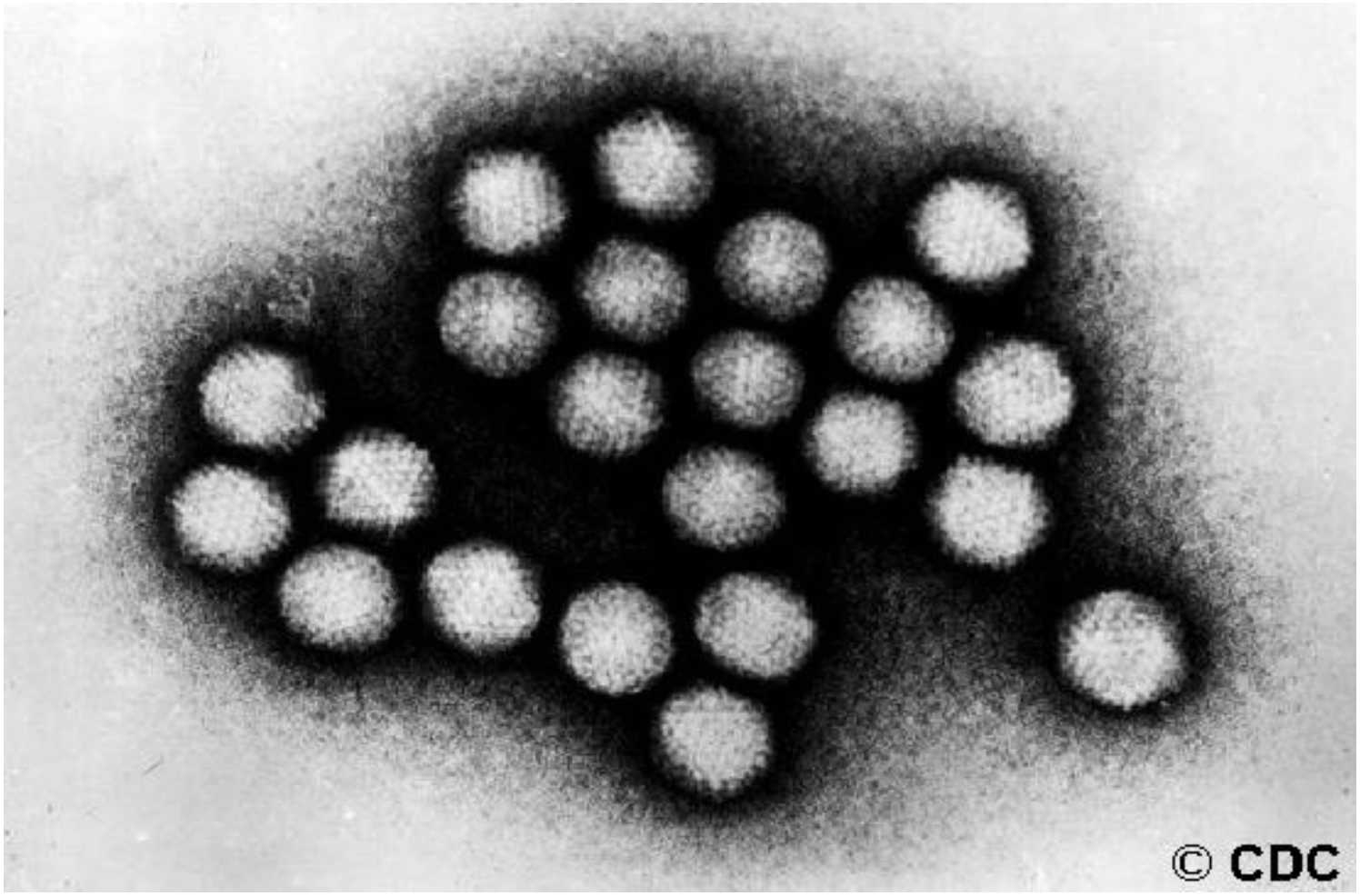
# GASTROENTERITIS DUE TO ENTERIC ADENOVIRUS



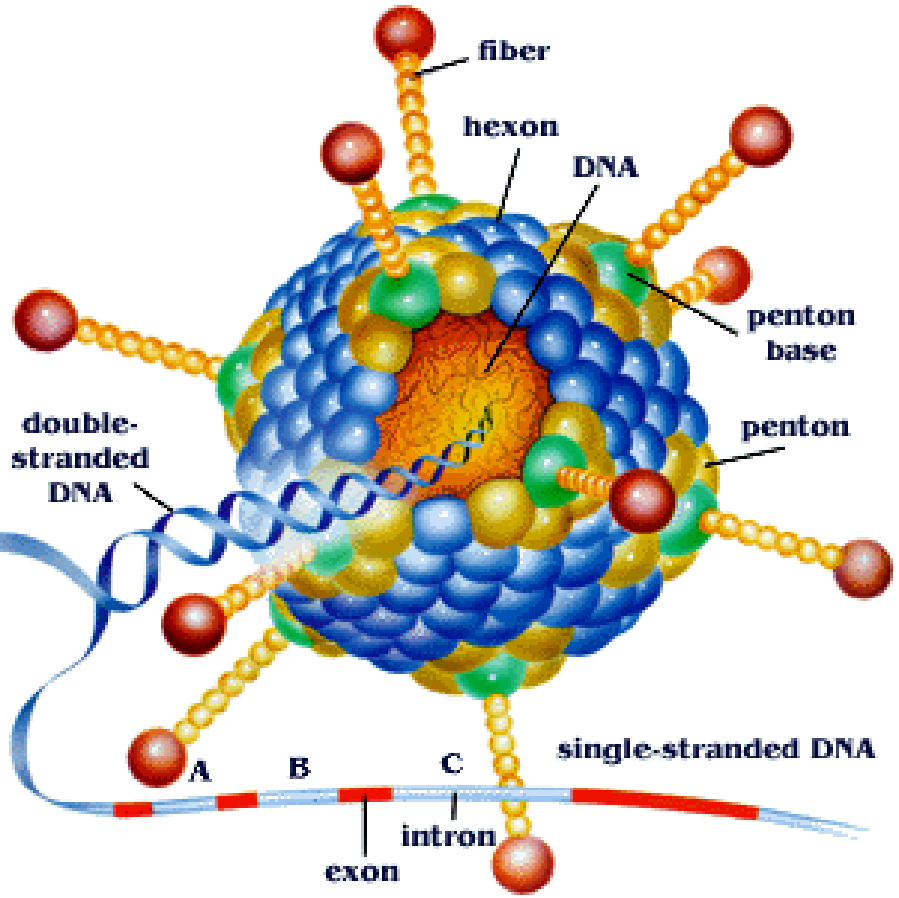
# Adenovirus Gastroenteritis

- Isolated in 1953 by Rowe from adenoidal tissue
- Virion:
  - Icosahedral, non-enveloped,70-90 nm in diameter, 252 capsomeres; fibers project from each other
  - Composition: DNA (13%), protein (87%)
  - Genome: Double-stranded DNA, linear, 26-45 kbp, protein-bound to termini, infectious
  - Proteins: Important antigens (hexon, penton base, fiber) are associated with the major outer capsid proteins
  - Replication: Nucleus
  - Virus classification: Group I: ds DNA; Family: Adenoviridae; Genus: Mastadenovirus; Species: Human adenovirus (H Ad)
- At least 51 serotypes are known
- classified into 6 subgenera: A to F




- Known oncogenic potential of some serotypes
- Commonly used as vectors in gene therapy and vaccine delivery

# Adenoviral structure




- Outstanding characteristics
  - Excellent models for molecular & biochemical studies of eukaryotic cell processes; a few models serve as models for cancer induction in animals
    - Largest viruses (maximum size able to be transported through the endosome)
    - virion has unique "spike" or fiber associated with each penton base of the capsid that aids in attachment to the host cell via the coxsackie-adenovirus receptor on the surface of the host cell
  - Adenovirus has tropism for cells of epithelial origin
  - Replicative cycle is sharply divided into EARLY & LATE events

# Adenovirus pathogenesis

- Virus replicate in epithelial cells producing cell necrosis and inflammation
- After acute infection; the virus may remain in tissues (tonsils, adenoids, peyer's patches) and become reactivated and shed asymptomatically 6-18 months.
- Reactivation enhanced by stressful events
- Integration of adenoviral DNA into host cell genome may occur leading to latency in tonsils and peripheral lymphocytes
- Some times smudgy intranuclear inclusions may be seen

Adenovirus infection leads to the following:

- Pentons have toxic effects on host cells
- Encode a protein in the E3 genomic region that binds class I MHC antigens in the ER which restricts their expression on the surface of infected cells and interfere with recognition and targeting by cytotoxic T cells. (Helps in latency)
- E1A protein has been associated with increased susceptibility of infected cells to destruction by TNF and other cytokines.
- Adenovirus death protein; important for efficient lysis of infected cells and release of progeny virions.

# Diarrhea due to Enteric Adenovirus

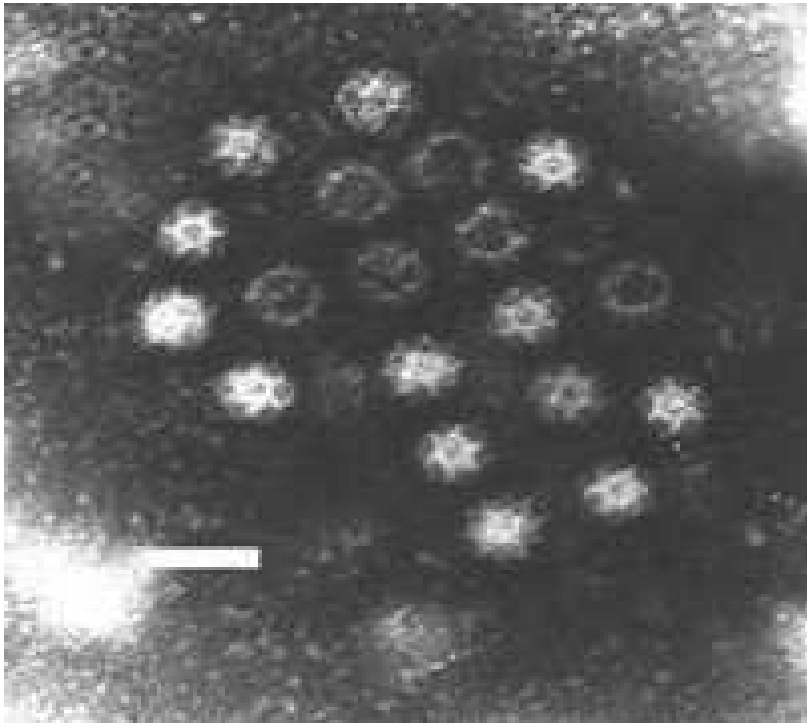
- Cause 5-15% of all viral gastroenteritis
- Belong to serogroup F (Types 40, 41) 38??
- Age <4 years
- Year round
- Spread via fecal-oral route
- Isolation requires special media-Graham 29
- ELISA for rapid detection is available

# CLINICAL FEATURES

## Adenovirus gastroenteritis

- Incubation period 3 -10 days
- Diarrhea lasts for 10 -14 days
- Can also cause intussusception, mesenteric adenitis, appendicitis
- Treatment with cidofovir promising for severe disease in immunocompromised

# HUMAN CALICIVIRUSES



# HUMAN CALICIVIRUSES (HuCV)

- Family *Caliciviridae*
- Non-enveloped RNA viruses with ss [+] sense RNA
- 27-35 nm in size
- Icosahedral capsid
- Contains single capsid protein
- Resistant to acid, ether and heat
- Have not been effectively propagated in cell culture

# Calicivirus

- Norwalk virus and “Norwalk-like”
- “Sapporo-like” viruses
- Vesivirus
- Lagovirus

**NLV (Norovirus) round shaped**

Norwalk virus

Hawaii virus

Snow Mountain virus

Montgomery county virus

Taunton (England)

**SLV (Sapovirus) star shaped**

Sapporo virus

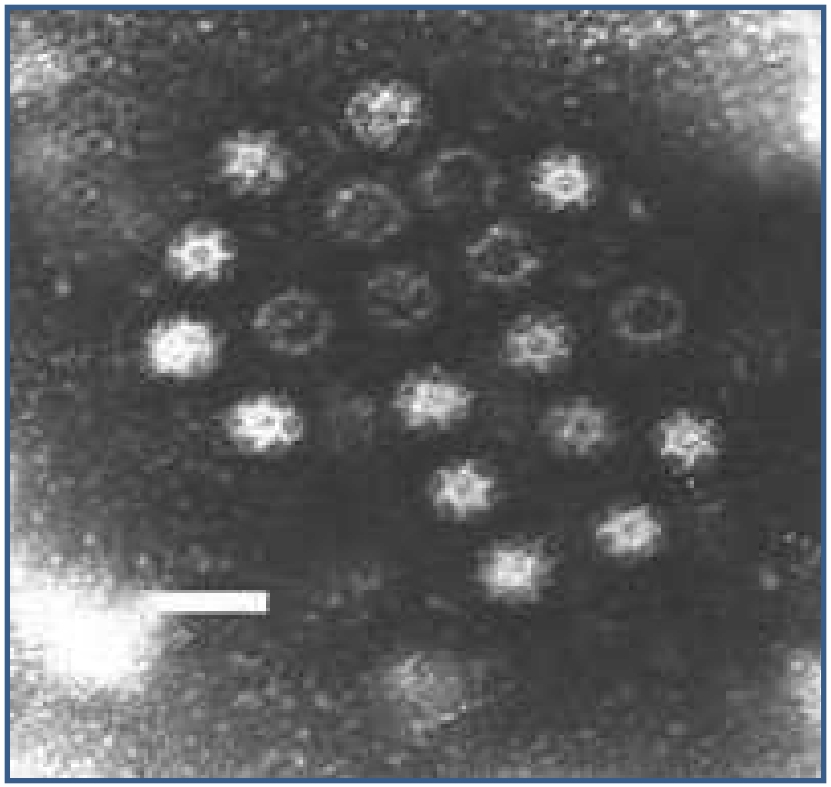
Manchester virus

Houston/86

London/92

# MORPHOLOGY- typical

- 32 cup-like depressions
- EM appearance of “Star”
- 31-35 nm size
- E.g.- Sapporo-like viruses



# Morphology of HuCV- atypical

- Smaller size- approx. 27 nm
- Rough, feathery surface but no internal pattern
- Small Round Structured viruses, e.g.- Norwalk-like viruses

# Norwalk virus

- “winter vomiting disease” 1968, Norwalk OH
- Cause 40% of nonbacterial epidemics
  - 45% foodborne, 52% shell fish associated outbreaks
- Explosive epidemics
  - camps, cruise ships, nursing homes
- Food borne illness
  - raw shellfish

# EPIDEMIOLOGY - Noroviruses

- Worldwide distribution
- Affects all ages
- >23 million cases/year in the U.S.
- Major cause of food-borne outbreaks of GE (>50%)
- Prevalence of antibodies reach ~50% by the fifth decade.
- Asymptomatic infections- seroconversion but asymptomatic shedding of virus
- Low infective dose (~10 pfu)
- Viral shedding 3-4 days
- Mucosal changes revert in ~2 weeks.
- Protective immunity short-lived
- NLV cross protection?

# Norwalk virus: Clinical Features

- 24 hour (range 10-50hr) incubation period
- Vomiting prominent
- Headache, myalgia, fever
- Diarrhea 1-3 days, less severe than rotavirus
- Treatment symptomatic
  - rehydration, antidiarrheals
- Complications rare
  - immunocompromised

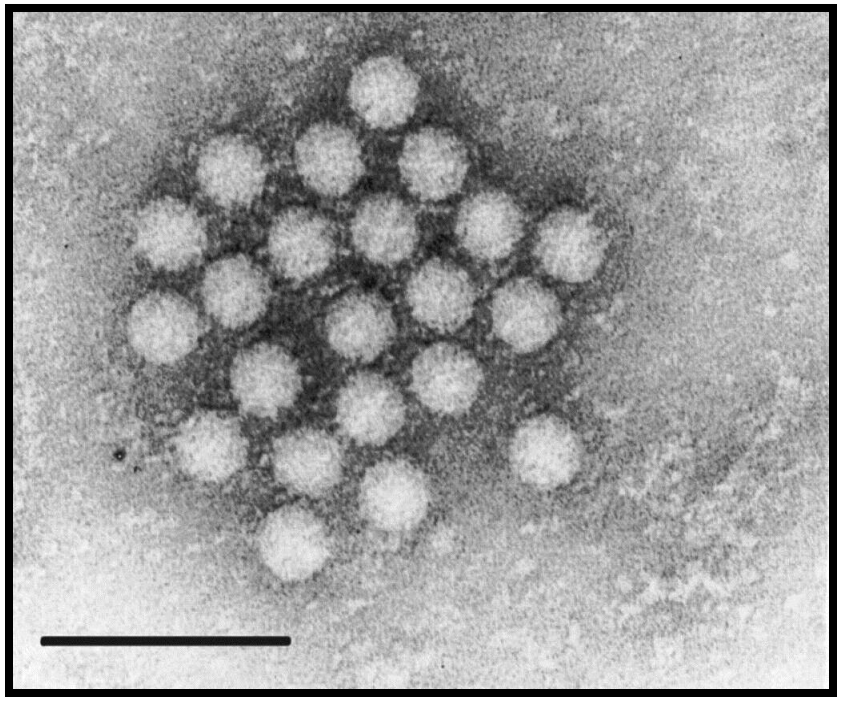
# SPREAD

- Person-to-person fecal-oral spread (stool/vomitus)
- Fecal contamination of food or water (uncooked shellfish)
- Fomites (stool/vomitus)
- Ingestion of aerosolized particles
- Survive on surfaces for several days
- Survive in water chlorinated at routine levels (up to 10 ppm)
- Survive freezing, heating up to 60°C (30min)
- Evidently survive in steamed shellfish

# DIAGNOSIS

- Specimen- stool, vomitus, food, environmental swabs (during outbreak investigations)
- RT-PCR in state public health labs.
- Serology for epidemiologic purposes
- Immune EM is less used

# HUMAN ASTROVIRUS



# ASTROVIRUS

- Described in relation to an outbreak of gastroenteritis in 1975
- Detected by EM
- Immunologically distinct from Hu CV
- Animal strains are known

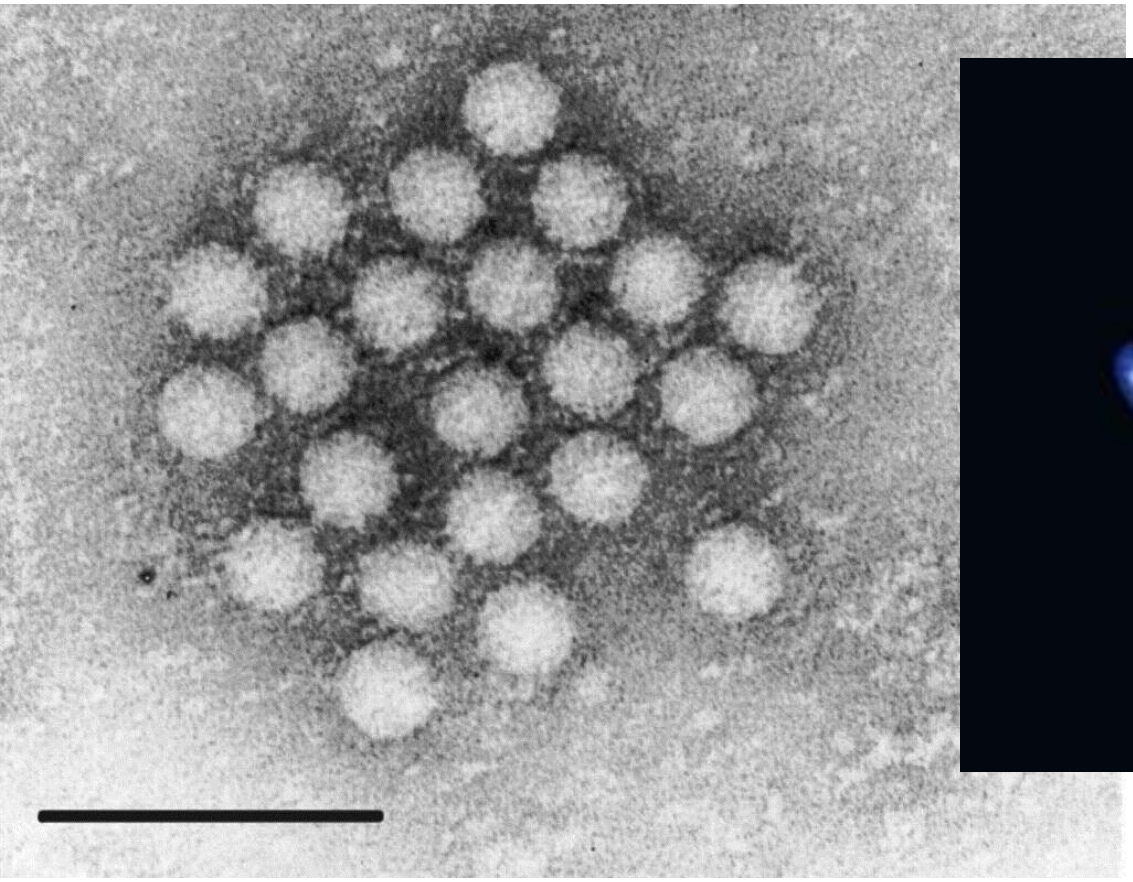
# Classification of Astrovirus

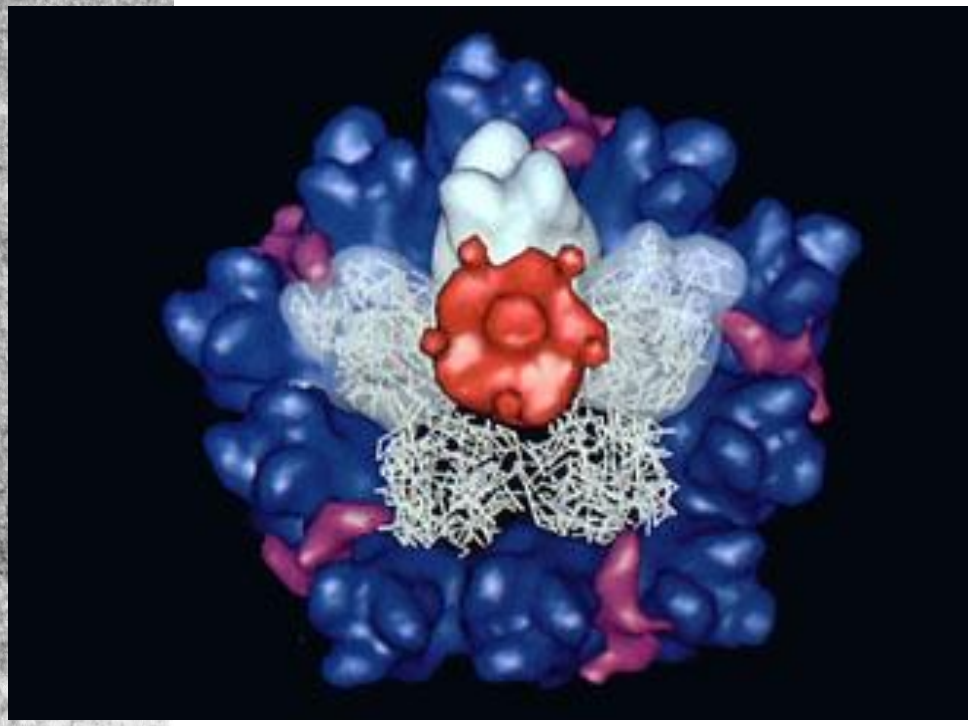
- Family *Astroviridae*
- Genus *Astrovirus*
- Human serotypes: HuAstV 1-8

# ASTROVIRUS- structure

- Small ss RNA virus
- Non-enveloped
- 27-32nm in size
- Round with an unbroken, smooth surface
- EM appearance of a 5 or 6 pointed star *within* smooth edge
- Contain 3 structural proteins
- Genome has been sequenced

# ASTROVIRUS- STRUCTURE





- heat stable
- acid resistant
- Replication cycle not characterized

# ASTROVIRUS - Clinical Features

- Infants and children are most often affected
- Elderly and immune compromised persons as well
- Short incubation period 1-4 days
- Nausea, vomiting, abdominal cramping and watery diarrhea
- Constitutional symptoms-fever, malaise, headache
- Symptoms last 3-4 days

# ASTROVIRUS - Epidemiology

- Endemic worldwide
- Astroviruses are associated with 5%–9% of cases of gastroenteritis in young children
- Mainly in children <7 years of age
- Transmission- person-to-person [fecal-oral]
- Outbreaks due to fecal contamination of sea-food or water

# ASTROVIRUS - Diagnosis

- EM (virus shed in stool in great numbers)
- EIA
- RT-PCR

# Toroviruses

- Family Coronaviridae
- Genus Torovirus
- They cause gastroenteritis in mammals, but rarely in humans
- Enveloped, ss (+) RNA virus
- Core “doughnut-shaped” (torus)
- Watery diarrhea in 2 – 12 months old
- Diagnosis: EM, ELISA, HI