VIRAL AGENTS CAUSING GASTROENTERITIS
Viruses found in the gut (1)

A. Associated with gastroenteritis

- Rotaviruses
- Adenoviruses 40/41/42 (group F)
- Caliciviruses (Norwalk viruses and Norwalk like viruses or SRSV (Small Round Structured Viruses))
- Astroviruses
- SRV (Small Round Viruses)
- Coronaviruses
- Toroviruses
Viruses found in the gut (2)

B. Found in the gut, not normally associated with gastroenteritis

- Polio
- Coxsackie A
- Coxsackie B
- Echo
- Enteroviruses 68-71
- Hepatitis A
- Hepatitis E
- Adenoviruses 1-39
- Reoviruses
Viruses found in the gut (3)

C. Found in the gut as opportunistic infection

- Cytomegalovirus
- Herpes simplex viruses
- Varicella-Zoster virus
- Human immunodeficiency virus
Gastroenteritis

Developed countries

- Unknown
- Rotavirus
- Bacteria
- Astrovirus
- Adenovirus
- Calicivirus

Developing countries

- Unknown
- Rotavirus
- Parasites
- Other bacteria
- Escherichia coli
- Astrovirus
- Adenovirus
- Calicivirus
REOVIRIDAE
REOVIRIDAE

Genus Orthoreovirus - Human reoviruses 1,2,3

Genus Rotavirus - Rotavirus

Genus Coltivirus - Colorado tick fever virus

Genus Orbivirus
Rotavirus - First isolated in 1973 in Australia, EM identification from duodenal biopsies from children with diarrhea.
ROTAVIRUS STRUCTURE

- 60-80nm in size
- Non-enveloped virus
- Icosahedral symmetry
- Double capsid (outer and inner capsid)
Double stranded (ds) RNA in 11 segments
ROTAVIRUS GENOME

VP1
VP2 \[\rightarrow\] inner core proteins, enzymes
VP3

VP4 – structural protein of outer capsid, forms spikes from the surface

VP6 – structural protein of inner capsid (group specific Ag)

VP7 – structural protein of outer capsid (type specific Ag)

NSP1
NSP5
REOVIRIDAE

ROTAVIRUS

VP6

A  B  C  D, E, F, G  VP7  VP4

15 G  23 P
ROTAVIRUS PROPERTIES

- Virus is stable in the environment (months)
- Relatively resistant to handwashing agents
- Susceptible to disinfection with 95% ethanol, ‘Lysol’, formalin
Mature enterocytes lining the tips of intestinal villi are affected

Villous atrophy and blunting

Death of the mature enterocytes

Infiltration of lamina propria with mononuclear cells

Repopulation of the villous tips with immature secretory cells [crypt hyperplasia]
ROTAVIRUS PATHOGENESIS
Rotavirus Epidemiology

- **Age**: children 4 months - 2 years are most affected. *Protection of younger infants through transplacental antibody transfer*

- **Asymptomatic infections** are common, especially in adults

- **Nosocomial infections**

- **Outbreaks**

- **Severe Disease**: young, immunocompromised
WORLDWIDE DISTRIBUTION OF ROTAVIRUS
(Source- Centers for Disease Control and Prevention)
ROTAVIRUS TRANSMISSION

- Mainly person to person via fecal-oral route
- Food and water-borne spread is possible
- Fomites

- Spread via respiratory route is speculated
  - Contagious from before onset of diarrhea to a few days after end of diarrhea
  - Large amounts of viral particles are shed in diarrheal stools
Rotavirus Clinical Syndromes

- Asymptomatic carriers

- Diarrheal illness
  - 2-3 day incubation period
  - diarrhea, vomiting, fever 3-7 days
  - high infectivity

- Complications
  - dehydration
  - chronic diarrhea
  - dissemination
ROTAVIRUS DIAGNOSIS

- **Antigen detection in stool** - ELISA, Latex agglutination, immunochromatographic assay
- **EM** - appearance of a wheel with radiating spikes
- **NA detection** - RT-PCR, Dot blot hybridization
- **Culture** - Group A rotaviruses can be cultured in monkey kidney cells
- **Serology** for epidemiologic studies
ROTAVIRUS – Ag detection

Latex agglutination test ("Rotalex")

negative  positive
ROTAVIRUS - EM STRUCTURE
RV5 (RotaTeq®)
- Live oral vaccine licensed 2006 in US
- Contains 5 reassortants (WC3 bovine strain with viral surface proteins of human serotypes G1-4 and P1A)

RV1 (Rotarix®)
- Live attenuated monovalent vaccine
- Contains the G1P[8] human rotavirus strain
ASTROVIRIDAE
Classification of Astroviruses

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

- Small ss RNA virus, 27-32nm in size
- Non-enveloped
- Round with an unbroken, smooth surface
- EM appearance of a 5 or 6 pointed star *within* smooth edge
ASTROVIRUS- GENOME

- linear, ssRNA(+), 6.8-7kb
- 3’-end poly-A
- Viral RNA = mRNA
ASTROVIRUS - Clinical Features

- Infants and children are most often affected
- Elderly and immune compromised persons also
- Short incubation period 1-4 days
- Nausea, vomiting, abdominal cramping and watery diarrhea
- Constitutional symptoms-fever, malaise, headache
ASTROVIRUS - Epidemiology

- Endemic worldwide
- 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
CALICIVIRIDAE
CALICIVIRIDAE

- **Norovirus**
  - Genogroup I: Norwalk virus
  - Genogroup II: Norwalk-like viruses

- **Sapovirus**
  - Genogroup I: Sapporovirus
  - Genogroup II: Sapporo-like viruses

- **Vesivirus**
  - SVES

- **Lagovirus**
  - RHDV
CALICIVIRIDAE, Genus Norovirus

(Source: ICTV database)
Genus Norovirus

Non-enveloped, 27–35nm, icosahedral symmetry
Capsid – 180 VP1 protein units
Small, empty virions 23nm, 60 VP1 protein units
Genome: ss (+) RNA
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
Norwalk virus: Clinical Features

- 24 hour (range 12-96) incubation
- Vomiting prominent
- Headache, myalgia, fever
- Diarrhea 1-3 days, less severe than rotavirus
- Affects all ages
- Treatment symptomatic
  - rehydration, antidiarrheals
- Complications rare
  - immunocompromised
SPREAD

- Person-to-person fecal-oral spread (stool/vomitus)
- Fecal contamination of food or water
- Fomites (stool/vomitus)
- Ingestion of aerosolized particles
SPREAD- Viability of Caliciviruses

- Survive on surfaces for several days
- Survive in water chlorinated at routine levels (up to 10 ppm)
- Survive freezing, heating up to 60 °C
- 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
ADENOVIRIDAE

(Courtesy of Linda Stannard, University of Cape Town, S.A.)
Adenoviridae – Structure

• Non-enveloped, 70–90 nm
• Capside: icosahedral symmetry
Adenoviridae – genome

- linear ds DNA with inverted terminal repeat sequences (ITR)
- On 5’ end of both chains covalently linked TP (terminal protein)
Adenovirus pathogenesis

From Medical Microbiology, 5th ed., Murray, Rosenthal & Pfaller, Mosby Inc., 2005., Fig. 50-4.
Adenovirus Gastroenteritis

- Types 40, 41, 42 (serogroup F)
- Associated with cases of endemic gastroenteritis, usually in young children and neonates. Can cause occasional outbreaks.
- Possibly the second most common viral cause of gastroenteritis (7-15% of all endemic cases).
- Incubation period 3 -10 days
- Diarrhea lasts for 10 -14 days
- ELISA for rapid detection is available, DIF, PCR
Other Possible Diarrhoeal Viruses

**Coronaviruses**
- RNA viruses with a crown-like appearance
- Not convincing associated with gastroenteritis at present

**Small Round Viruses**
- Small virus-like particles with a smooth surface, 22-28nm in diameter
- Occasionally seen in the faeces of endemic or epidemic cases of gastroenteritis