GIT Module
2021-2022
(Rotaviruses, Caliciviruses, Adenoviruses)

Dr. Mohammad Odaibat
Department of Microbiology and Pathology
Faculty of Medicine, Mutah University

GIT infections

Bacterial
H. pylori
Campylobacter
Salmonella
E.coli
Vibrios
S. aureus *Bacillus cereus* *Clostridium botulinum and perfringens* *Shigella*

Viral
rotaviruses and others
hepatitis viruses

protozoa and parasites

Gastrointestinal Tract

Pathology:

- Host - pathogen factors
- Viruses: destroy villous epithelial leading to decreased water and electrolytes absorption
- Bacteria: epithelial damage and/or toxin production

General principles in GIT infections

Diagnosis:

- History:
- Travel, recently eaten food, contacts, underlying illnesses, antibiotic exposure
- Examination:
- Vital signs and systemic examination
- Assessing dehydration level
- Laboratory diagnosis
- Treatment: Supportive ± antibiotics

Manifestations:

- Asymptomatic
- Symptomatic: mild to severe
- Gastroenteritis ± systemic manifestations

- Diarrhoea:

having three or more loose or liquid stools per day, or as having more stools than is normal for that person

General principles in GIT infections

- Small bowel diarrhoea: large volume, watery, less frequent, painless stools. Blood and WBCs are rare. Pain is mid-abdominal.

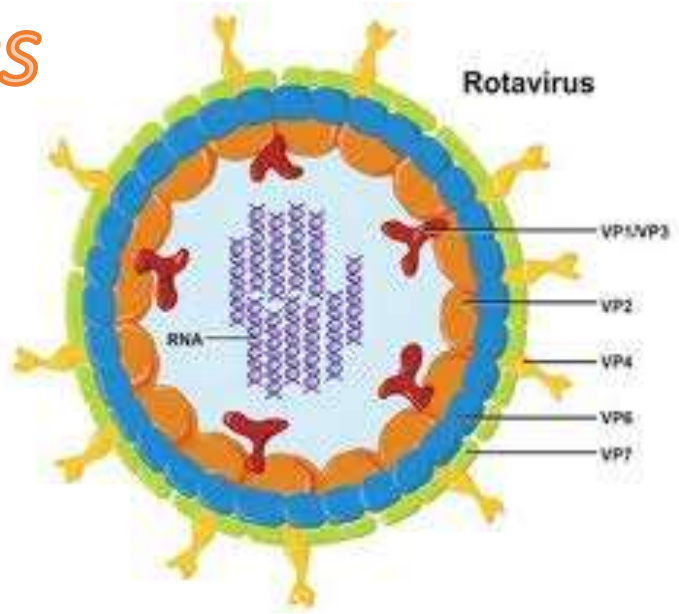
- Large bowel diarrhoea: small volume, often mucoid, more frequent, painful stools. Blood and WBCs are common. Pain is lower-abdominal (left lower quadrant)

Rotaviruses

- The cardinal disease syndrome is acute gastro-enteritis, which is usually mild to moderately severe among children in developed countries but can be very severe and associated with high mortality rates in developing countries.

- Rotaviruses also cause diarrhoea in the young of a wide variety of birds and mammals including cattle, sheep, goat, horses, pigs, dogs, cats and mice, and also rabbits, monkeys and many others.

Rotaviruses



Characteristics:

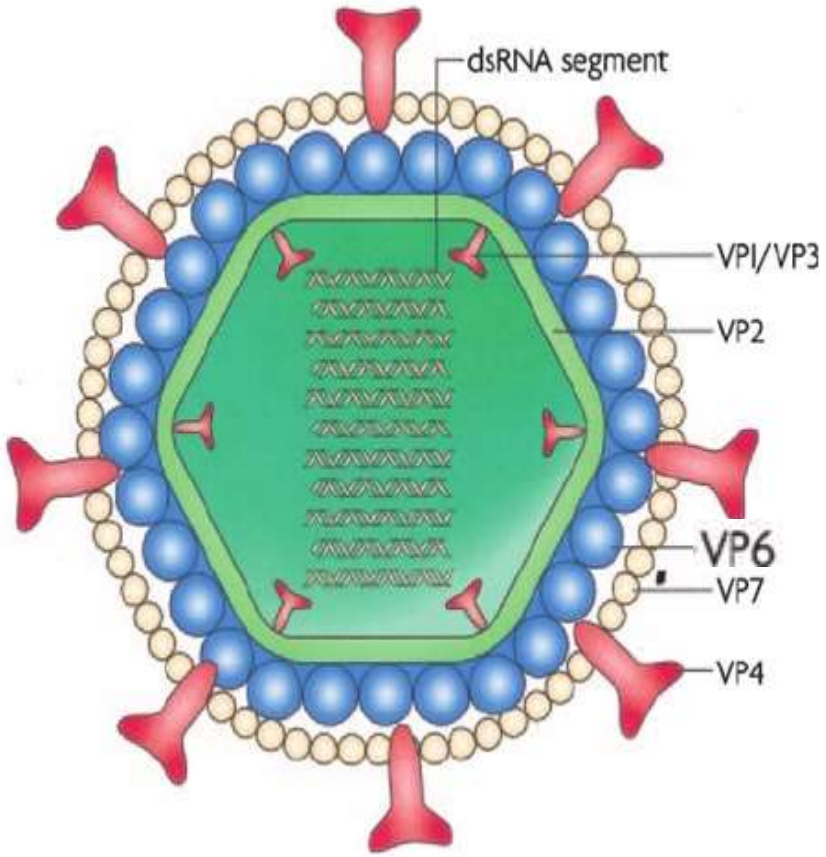
- Belongs to Reoviruses
- Has characteristic double-shelled capsid (inner and outer layer), which in electron micrographs look like spokes grouped around the hub of a wheel (the Latin word, *rota*, means wheel)
- Non-enveloped

➢Genome

- Double stranded RNA genome, 11 segments, RNA polymerase, non-enveloped

Rotaviruses

- Generally, each genome segment codes for only one virus-specific protein (VP).
- RNA segment 6 codes for the inner capsid proteins.
- VP6 carries epitopes specifying groups and subgroups.
- To date, seven different groups (A-G) have been identified.
- Only groups A, B and C have been associated with human illness.
- Group A rotavirus, or *Rotavirus A*, is responsible for the vast majority of human rotavirus infections (mostly children).



Rotaviruses /epidemiology

- Worldwide infections, but the vast majority of deaths occur in children in developing countries.
- About 2 million children under 5 years die from diarrhoeal disease in developing countries each year, and rotavirus accounts for about 40% of these deaths
- By the age of 5 years, virtually all children have been infected with rotavirus.
- The most severe disease occurs among children 3-24 months of age
- Only a few virus particles (~100 particles) are sufficient to cause disease in the susceptible host.

Rotaviruses /epidemiology

- Multiple rotavirus infections commonly occur during infancy and early childhood; the first rotavirus infection typically results in the most severe disease outcome, with subsequent infections generally associated with milder disease or even asymptomatic infection.

- Extra-intestinal spread of rotaviruses in man has been documented, with occasional reports of infection in the liver and central nervous system

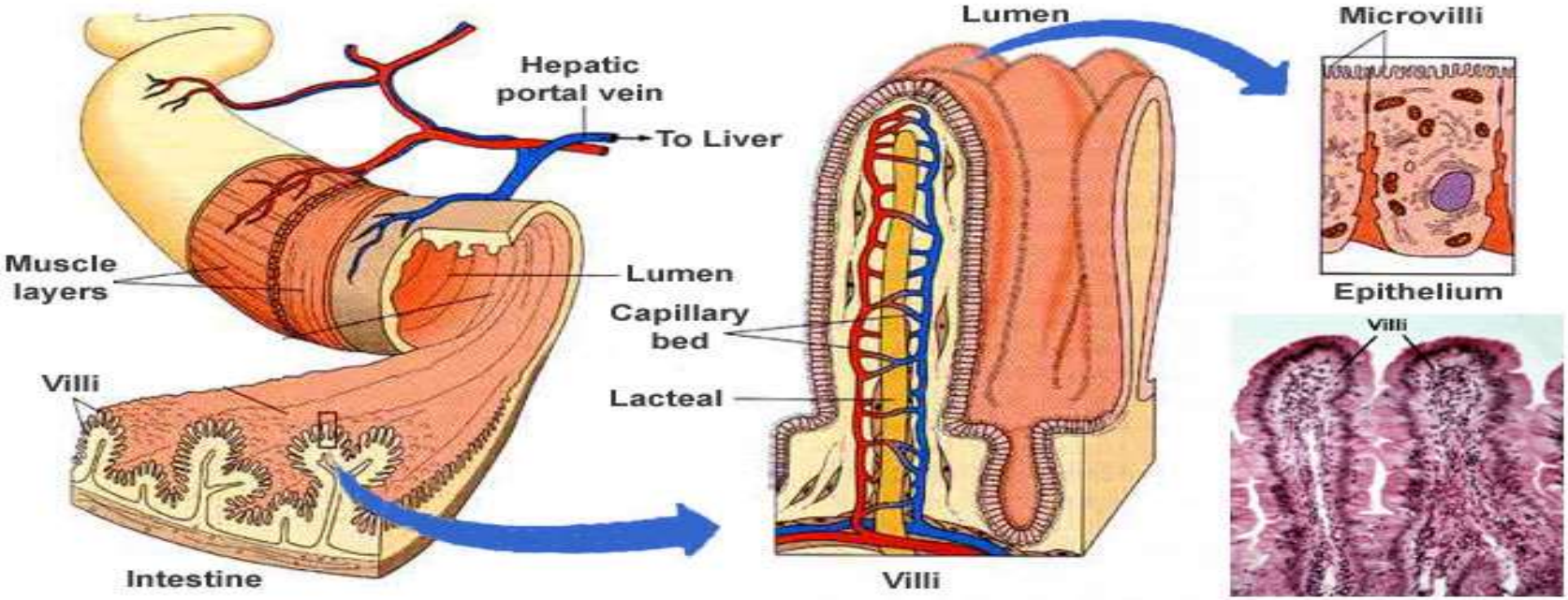
Rotaviruses/Pathogenesis and immunity

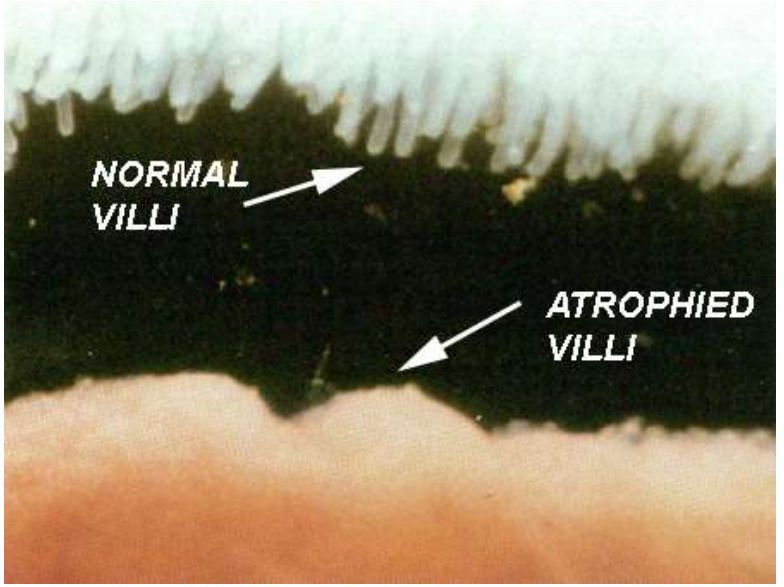
- Rotaviruses replicate exclusively in the differentiated epithelial cells at the tips of the small intestinal villi.

- Progeny virus is produced after 10-12 h, and released in large numbers into the intestinal lumen ready to infect other cells.

- Biopsies show atrophy of the villi and mononuclear cell infiltrates in the lamina propria.

- The cellular damage leads to malabsorption of nutrients, electrolytes and water, resulting in diarrhoea with vomiting followed by dehydration.


Hepatic portal vein
To Liver
Muscle layers
Lumen
Capillary bed
Lacteal
Villi
Intestine
Lumen
Villi
Microvilli
Epithelium
Villi


NORMAL VILLI
ATROPHIED VILLI

Rotaviruses/Pathogenesis and immunity

- Additional mechanism that may contribute to the pathogenesis of rotavirus diarrhoea include:

  - stimulation of the enteric nervous system leading to increased paracellular permeability e.g via rotavirus **NSP4**, which functions as a viral enterotoxin.

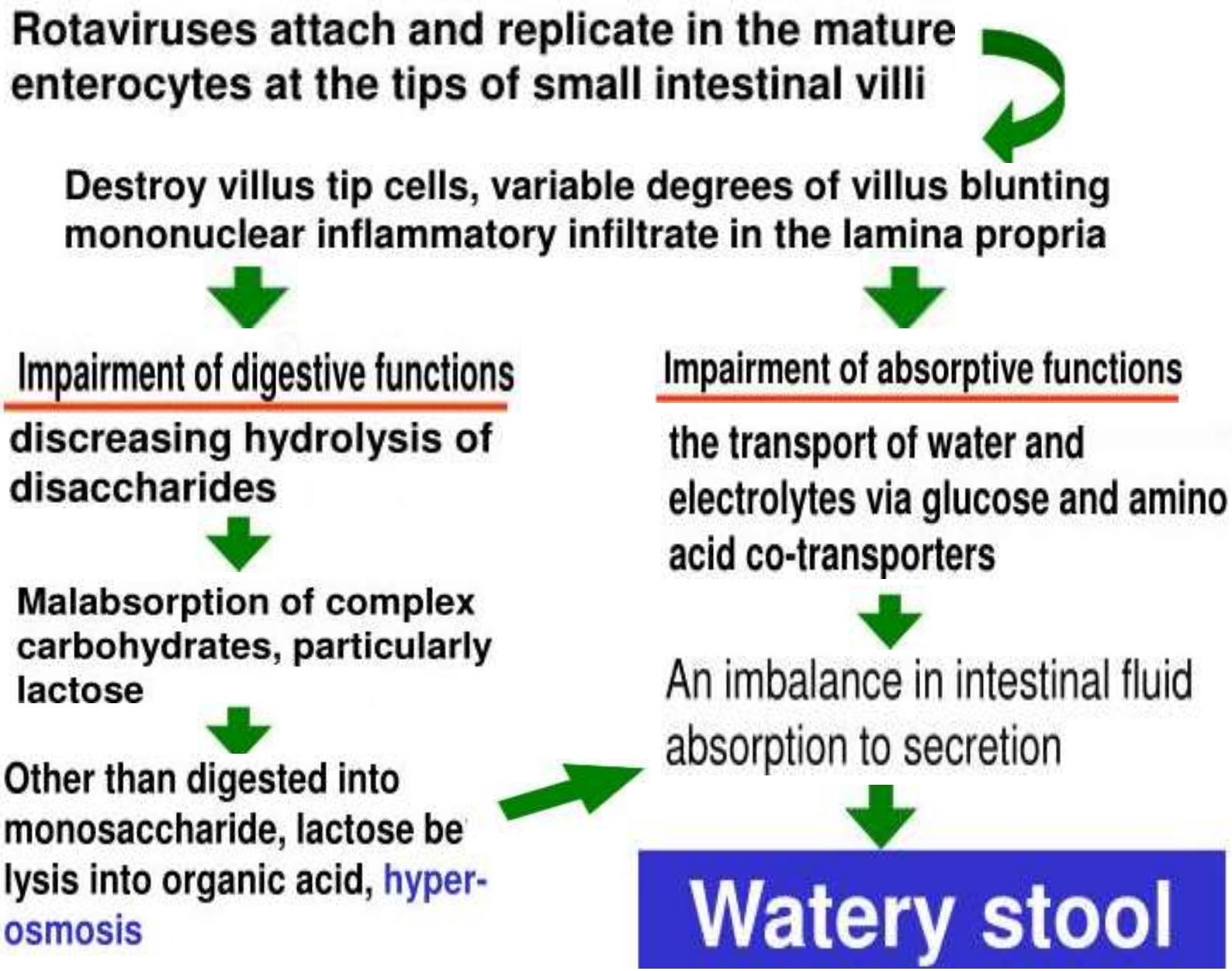
- Infection is followed by a mucosal humoral and cell-mediated immune response, and the virus is normally cleared within 1 week.

Rotaviruses/Pathogenesis and immunity

- Rotavirus-specific immunoglobulin (Ig) A antibodies on the enteric mucosal surface are thought to mediate protective immunity.

- Infection with one serotype provides serotype-specific (homotypic) protection, and repeated infections lead to partial cross-serotype (heterotypic) protection.

Rotaviruses/Pathogenesis and immunity



Rotaviruses / clinically

- The onset of symptoms is abrupt after a short incubation period of 1-2 days
- Transmitted by faecal oral route/fomites.
- Communicability: 2 days before onset and 10 days after
- Fever, vomiting and watery diarrhoea are seen in the majority of infected children, lasting for 2-6 days.
- If body fluids are not replaced, dehydration / metabolic acidosis follows that may range in severity from mild to life threatening.

Rotaviruses / lab. diagnosis

- At the peak of infection, as many as 10^{11} virus particles per millilitre of faeces are present, and can be detected by a variety of methods.

1. Antigen detection tests, targeted on VP6, include latex agglutination assays, and ELISA assays.

2. Electron microscopy will easily detect the characteristic virus particles.

3. Rotaviruses can be propagated in cultures of monkey kidney cells (Not commonly used in diagnosis).

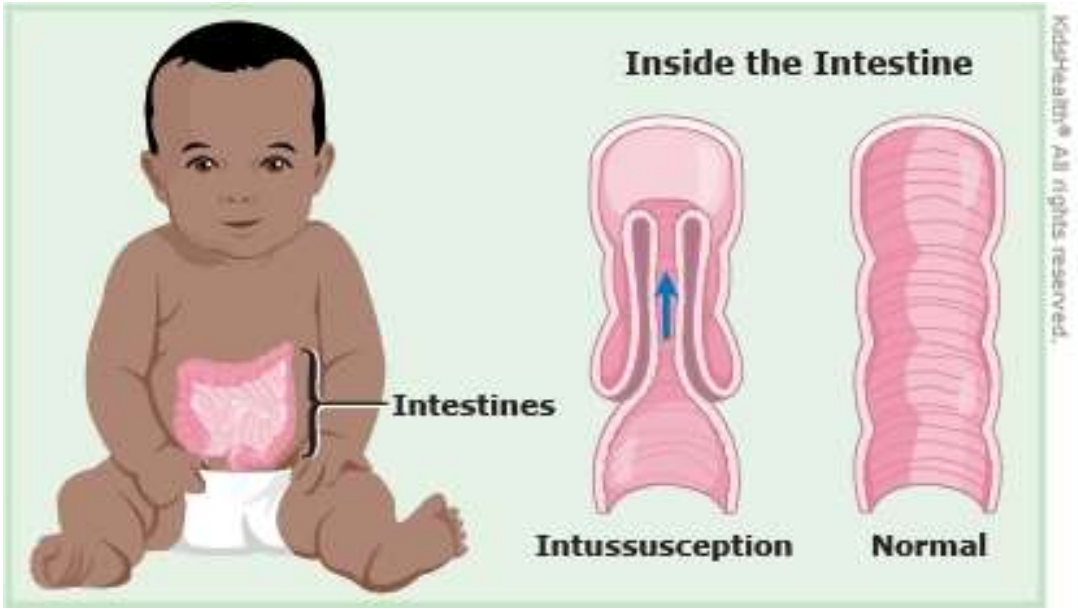
4. RT-PCR

Rotaviruses / treatment

- No specific anti-rotavirus treatment is available routinely
- Probiotic therapy (e.g. with *Lactobacillus*) has been shown in clinical trials to shorten the duration of symptoms of gastro-enteritis.
- The mainstay of therapy consists of oral rehydration with fluids of specified electrolyte and glucose composition
- Intravenous rehydration therapy is reserved for patients with severe dehydration, shock or reduced level of consciousness.

Rotaviruses / control

- hygienic measures such as handwashing, safe disposal of faeces and disinfection of contaminated surfaces.
- Oral live-attenuated vaccine:
- The first licensed rotavirus vaccine, RotaShield, was withdrawn after this live oral vaccine was associated with the development of intestinal intussusception



Rotaviruses / control

- Two further live-attenuated/Live oral rotavirus vaccines (Rotarix and RotaTeq)
- both appear to be safe with respect to intussusception.
- vaccines are licensed for global use by FDA
- Given at age of 6 weeks-32 weeks

Adenoviruses

Adenoviruses serotypes 40 & 41:

- Adenoviruses are second to rotaviruses in causing diarrhoea
- Incubation period 8-10 days
- Diarrhoea last longer than Rotaviruses but tends to be milder

Caliciviruses / noroviruses & sapoviruses

General background:

- Caliciviruses are nonenveloped with an icosahedral capsid
- +ss RNA without a polymerase
- sapo and norovirus Replicate in the cytoplasm
- Sapo and noroviruses have approximately 5 and 12 antigenic strains respectively
- Sapovirus transmitted by faecal oral route, while norovirus routes can be faecal oral and airborne (inhalation of vomit, faecal material bed-linen or nappies) Both have similar host range > human

Caliciviruses / noroviruses & sapoviruses

Pathogenesis:

- Infects the proximal part of small intestine, mainly jejunum
- Broadening and blunting of villi in the proximal part of the small Intestine

Clinically:

- The incubation period is between 12 and 72 h.
- Abdominal pain and vomiting which can be projectile (winter vomiting disease)
- Some times: 'gastric flu' (i.e. diarrhoea, headache, fever, aching limbs and malaise)

Caliciviruses / noroviruses & sapoviruses

- The norovirus is highly infectious and can lead to serious outbreaks in hospitals and community (infectious dose is < 100 virions)
- Clinical symptoms usually resolve in 1-4 days.

Diagnosis:

- Stool / blood sample
- Electron microscope
- ELISA
- RT-PCR

Caliciviruses / noroviruses & sapoviruses

Control:

- Staff who develop or have had symptoms such as diarrhoea and/or vomiting should be excluded from work until 48 h after recovery
- If kitchen or adjacent areas have been fouled (e.g. by vomitus) then: 1. the area should be thoroughly cleaned and disinfected with a 10 000 ppm hypochlorite solution, and 2: all food to be eaten uncooked should be destroyed
- The importance of hygienic practices, particularly hand-washing, should be reinforced.
- High-risk foods such as shellfish / food to be eaten raw should be excluded from the kitchen
- Unnecessary kitchen traffic should be stopped: the kitchen should not be used as a short cut for other staff, particularly during an outbreak.

Caliciviruses / noroviruses & sapoviruses

Additional measures in a hospital outbreak:

- Ensure that both bacteriological and virological investigations are initiated at the same time.

- Whenever possible, affected patients should be isolated and infected nursing, medical and support staff excluded from work.

- Some outbreaks it may be necessary to close wards to new Admissions until all patients have stopped excreting virus and no new cases have occurred for a period of 72 h.

- Staff movement from affected to unaffected wards should be restricted, group activities stopped and visits by children discouraged.

Bacterial vs. viral gastroenteritis

Bacterial	Viral
Tend to affect children >2 years of age	Viral Tend to affect children <2 years
Blood often present	Blood absent
Fecal leukocytes often present	Fecal leukocytes absent
May be associated with travel, exposure to animals, consumption of meat	Not often associated with travel, animals, or meat
accounts for 10-20% of cases	accounts for 70-90% of cases