9- Enteroviruses, rotaviruses and caliciviruses

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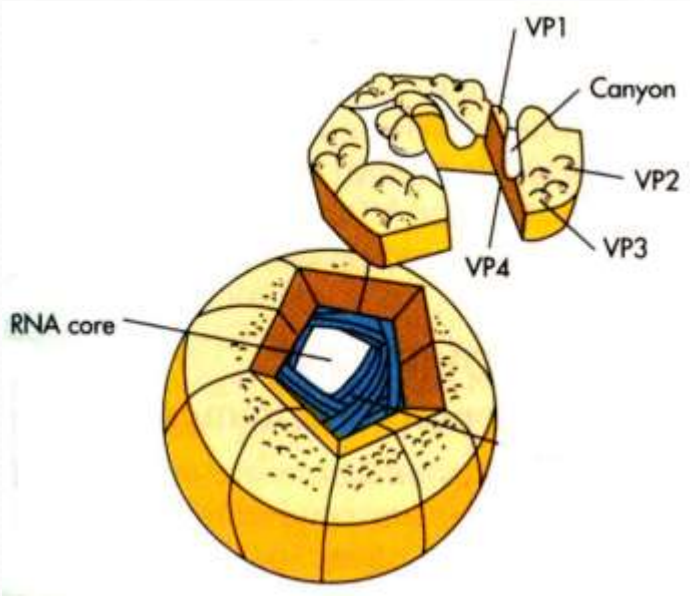
Objectives

- Understand the structure, properties, classification, pathogenesis epidemiology, clinical presentation, laboratory diagnosis and treatment of:
- Enteroviruses
- Polioviruses
- Coxsackie viruses
- Echoviruses

Enteroviruses

- Enteroviruses are a genus of the picornavirus family which replicate mainly in the gut.
- Single-stranded naked RNA virus with icosahedral symmetry
- Capsid has 60 copies each of 4 proteins, VP1, VP2, VP3 and VP4 arranged with icosahedral symmetry around a positive sense genome.
- Divided into 5 groups:
  1. Polioviruses
  2. Coxsackie A viruses
  3. Coxsackie B viruses
  4. Echoviruses
  5. Enteroviruses



Poliovirus

- 3 serotypes of poliovirus (1, 2, and3) but no common antigen.
- Have identical physical properties but only share 36-52% nucleotide homology.
- Humans are the only susceptible hosts.
- Polioviruses are distributed globally before the availability of immunization
- The availability of immunization and the poliovirus eradication campaign has eradicated poliovirus in most regions of the world except in the Indian Subcontinent and Africa.
- Poliovirus is on course of being eradicated worldwide

Pathogenesis

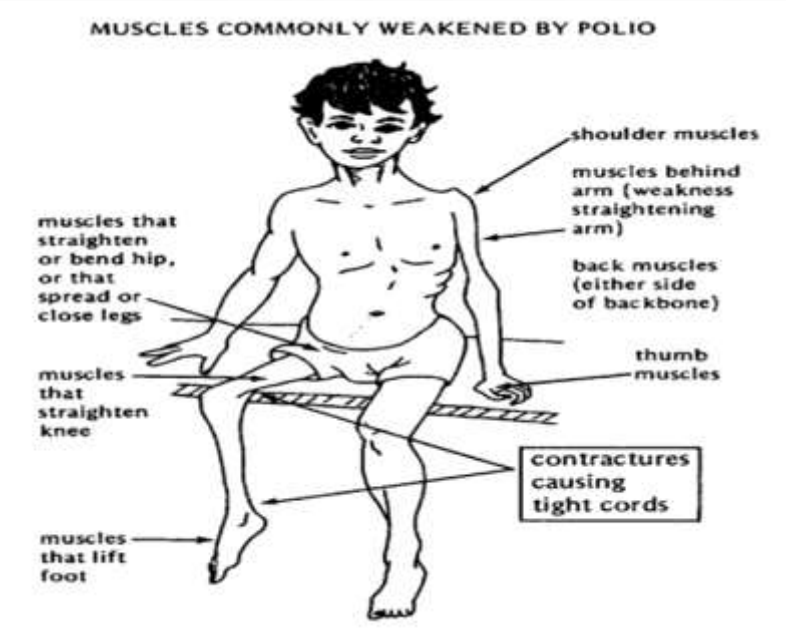
- The incubation period is usually 7 - 14 days.
- Following ingestion, the virus multiplies in the oropharyngeal and intestinal mucosa.
- The lymphatic system, in particular the tonsils and the Peyer's patches of the ileum are invaded and the virus enters the blood resulting in a transient viraemia.
- In a minority of cases, the virus may involve the CNS following dissemination.

Clinical Manifestations

- There are 3 possible outcomes of infection:
- Subclinical infection (90 - 95%) - inapparent subclinical infection account for the vast majority of poliovirus infections.
- Abortive infection (4 - 8%) - a minor influenza-like illness occurs, recovery occurs within a few days and the diagnosis can only be made by the laboratory.
- Major illness (1 - 2%) - the major illness may present 2 - 3 days following the minor illness or without any preceding minor illness. Signs of aseptic meningitis are common.
  - Involvement of the anterior horn cells lead to flaccid paralysis.
  - Involvement of the medulla may lead to respiratory paralysis and death.

Paralytic poliomyelitis

- Prodrome: Headache, malaise, meningeal sign
- Sever myalgia, Meningismus, Weakness, Flaccid paralysis
- Asymmetric distribution
- Proximal muscles involve more than distal muscles
- Sensory function remains intact
- Diagnosis: PCR, isolation, and serology
- Prevention:
  1. Intramuscular Poliovirus Vaccine (IPV)
  2. Oral Poliovirus Vaccine (OPV)



Coxsackieviruses

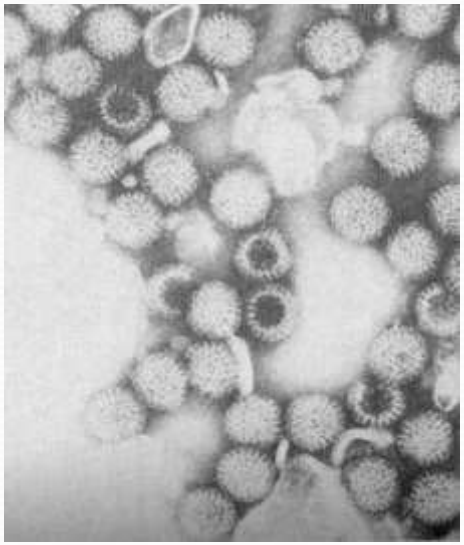
- They are divided into 2 groups on the basis of the lesions observed in suckling mice.
- Group A viruses produce a diffuse myositis with acute inflammation and necrosis of fibers of voluntary muscles.
- Group B viruses produce focal areas of degeneration in the brain, necrosis in the skeletal muscles, and inflammatory changes in the dorsal fat pads, the pancreas and occasionally the myocardium.
- Each of the 23 group A and 6 group B coxsackieviruses have a type specific antigen.

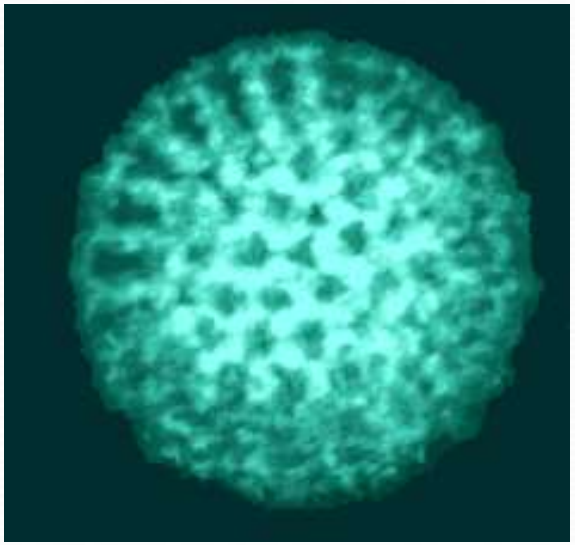
Echoviruses

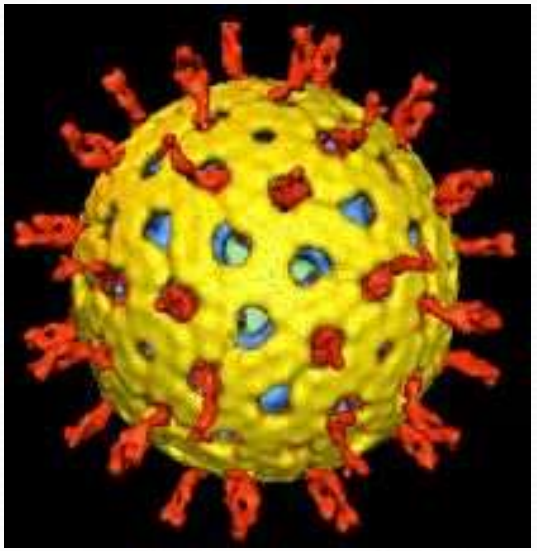
- The first echoviruses were accidentally discovered in human faeces, unassociated with human disease during epidemiological studies of polioviruses.
- These viruses were produced CPE in cell cultures, but did not induce detectable pathological lesions in mice.
- Altogether, There are 32 echoviruses (types 1-34; echovirus 10 and 28 were found to be other viruses and thus the numbers are unused)

Rotavirus

- 70 nm round, double-shelled, enclosing a genome of 11 segments of double-stranded RNA.
- Non-enveloped virus
- Icosahedral symmetry
- Double capsid (outer and inner capsid)
- EM appearance of a wheel with radiating spokes







Classification

- Group A subtypes 1, 2, 3, 4 (main human pathogens) (Further 7 subtypes) also infect animals (monkey, calf, mouse)
- Group B Infects pigs and rats
  Found to cause extensive outbreaks in China in past decade
- Group C Infects Pigs (Occasionally Man)
- Group D Infects birds
- Group E Infects pigs

Epidemiology

- Millions are affected, with 600,000-850,000 deaths/year
- Outbreaks of rotavirus infection are common, particularly during the cooler months, among infants and children 1 to 24 months of age.
- Older children and adults can also be affected, but attack rates are usually much lower.
- Outbreaks among elderly, institutionalized patients have also been recognized.
- By the age of 4 years, more than 90% of individuals have humoral antibodies, suggesting a high rate of virus infection early in life.
- Transmission is mainly by faecal oral rout

Clinical Manifestations

- Incubation period of 1 to 3 days
- Abrupt onset of vomiting, followed within hours by frequent, copious, watery, brown stools.
- In severe cases, the stools may become clear; the Japanese refer to the disease as **hakuri, the "white stool diarrhea"**
- Fever, usually low grade, is often present.
- Vomiting may persist for 1 to 3 days, and diarrhea for 4 to 8 days.
- The major complications result from severe dehydration, occasionally associated with hypernatremia.

Diagnosis

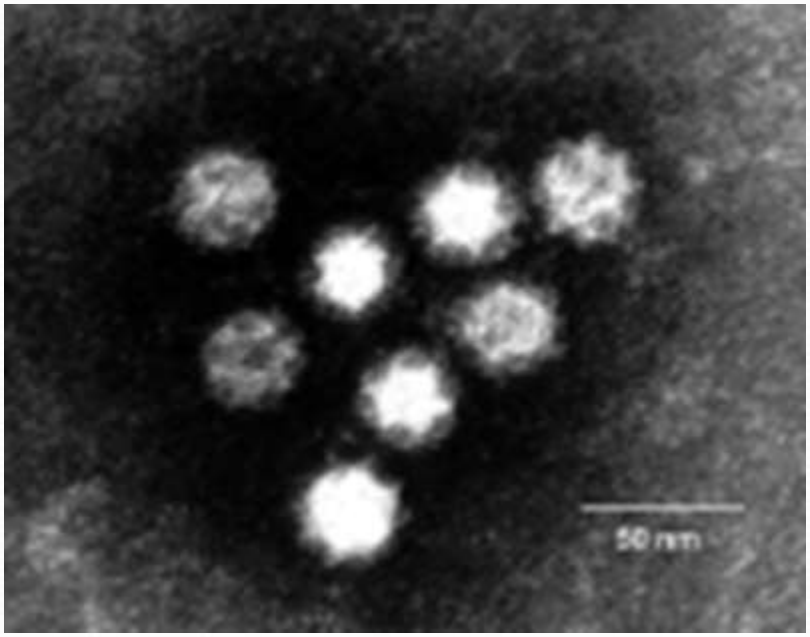
- Diagnosis of acute rotavirus infection is usually by detection of virus particles or antigen in the stools during the acute phase of illness.
- This can be accomplished by direct examination of the specimen by electron microscopy or, more conveniently, by immunologic detection of antigen with EIA methods.
- PCR can be used to confirm the diagnosis
- No RBC or WBC in stool

Treatment and Prevention

- There is no specific treatment. Vigorous replacement of fluids and electrolytes is required in severe cases and can be life-saving.
- The rotaviruses are highly infectious and can spread quickly in family and institutional settings.
- Control consists of rigorous hygienic measures, including careful hand washing and adequate disposal of enteric excretions.
- Recently rota virus vaccine has been developed and licensed for infants used. Vaccine developed in 1998 an effectiveness of 80% with good safety. Vaccine has been adopted by many developed countries.

Caliciviruses

- Small ssRNA viruses
- Naked icosahedral capsid
- Characteristic surface morphology consisting of hollows.
- particles 35 nm in diameter.



Epidemiology

- Sharp family and community outbreaks are common and can occur in any season. Unlike rotaviruses, caliciviruses are much more common causes of gastrointestinal illness in older children and adults.
- The prevalence of antibodies rises slowly, reaching approximately 50% by the fifth decade of life, a striking contrast to the frequent acquisition of antibodies to rotaviruses early in life.
- Transmission is primarily fecal–oral; outbreaks have also been associated with consumption of contaminated water, uncooked shellfish, and other foods.

Clinical Manifestations

- The incubation period is 10 to 51 hrs
- Followed by abrupt onset of vomiting and diarrhea, a syndrome clinically indistinguishable from that caused by rotaviruses.
- Respiratory symptoms rarely coexist, and the duration of illness is relatively brief (usually 1–2 days).

Diagnosis and Treatment

- These viruses can be detected by electron microscopy or immunoelectron microscopy in stools during the acute phase of illness.
- In addition, EIA and PCR methods have been developed.
- As with rotavirus infection, there is no specific treatment other than fluid and electrolyte replacement.
- Prevention requires good hygienic measures.