PICORNAVIRUSES
ENTEROVIRUSES

DR.N.M.SHAIKH
ASST. PROFESSOR

- Comprises large number of very small, single stranded RNA viruses.
- Medical important Picornaviruses includes two genera:
- Enteroviruses of enteric tract
- Rhinoviruses of respiratory tract.

Characteristics

- Size -20 – 30nm in diameter
- Capsid- 60 capsomere arranged in cubic symmetry
- Lack of envelope
- Positive sense RNA genome

Biological Properties

1. Found in feces & spread by fecal-oral route
2. Grow in tissue culture with or without CPE
3. Cause silent infections but also cause a number of important illnesses
4. Several genera of Enteroviruses can cause similar symptoms, e.g. aseptic meningitis or exanthems, but some diseases have a more specific association with a single genus, e.g., *pleurodynia* and *herpangina*

Cont.

5. Distinguished by their pathogenicity for experimental animals: polioviruses are pathogenic only for primates; coxsackie A viruses are pathogenic for newborn mice; Coxsackei B viruses are pathogenic for newborn mice in which they cause necrosis of brown fat pads, encephalitis, pancreatitis, myocarditis, and hepatitis (cause similar lesions in human newborns). Human echovirus types are not pathogenic for animals.

VIRAL PATHOGENESIS

The basic pathogenesis of most human enteroviral infections is the same. They enter the body through the mucosa of the oropharynx and upper respiratory tract, then begin to multiply in the tissues around the oropharynx. The exact cells in which the virus multiplies are not known, although there is some reason to suspect the reticuloendothelial system. The virus is shed back into the oral secretions, whence it is swallowed.

Cont.

Because the enteroviruses are stable in acid they are able to pass through the stomach into the intestines, where they undergo further rounds of replication. Roughly at the same time as it reaches the intestine, the virus begins to spill into the systemic circulation. This early (primary) viremic phase is usually asymptomatic and involves fairly low titers of virus in the blood.

Cont.

During the primary viremia tissues are seeded according to the tropism of the virus (those tissues for which it does or does not have an affinity). In the case of the polioviruses, the tissues infected include neurons, especially the anterior horn cells of the spinal cord. However, not all people infected with poliovirus have seeding of their central nervous system, for reasons that are not clear. After the primary viremia, the virus replicates in susceptible tissues and symptomatic manifestations of the disease begin to occur. There is often fever, malaise, and the peripheral symptoms of the disease such as aseptic meningitis and myocarditis.

Enterovirus

Group	Serotype
Poliovirus	1-3
Coxsackei virus A	1-22, 24
Coxsackei virus B	1-6
Echovirus	1-9,11-27,29-31
Numbered Enterovirus	68-71

Poliovirus-Morphology

- A spherical particle, about 27nm in diameter with four viral proteins, VP1 to VP 4 arranged in icosahedral symmetry.
- Genome is a single strand of positive strand RNA.

Resistance

- Resistant to ether, chloroform, bile.
- Stable at pH 3.
- In feces, it can survive for months at 4^{o}C and years at -20^{o}C.
- Readily inactivated by heat(55oC for 30 minutes).
- Chlorination destroys the virus in water but organic matter delays inactivation.

Antigenic properties

- By neutralization test, poliovirus have been classified in to three types: 1,2,3
- By CFT,ELISA or precipitation tests, two antigens C and D (coreless or capsid, D=dense) can be recognised.
- Anti D antibody is protective.

Cultivation

- Natural infection occur only in humans, Chimpanzees and cynomolgus monkeys may also be infected.
- Primary monkey kidney cultures are used for diagnostic cultures and vaccine production.
- CPE: infected cells round up and become pyknotic and retractile. Eosinophilic intranuclear inclusion bodies may be seen.

Pathogenesis

- Route of transmission : fecal-oral
- Primary viremia
- Secondary viremia
- Carried to the spinal cord
- Destruction of anterior horn cells with flaccid paralysis

Clinical features

- Incubation period : 10 days

Inapparent infection (90-95%)

clinical illness (5-10%)

Abortive Poliomyelitis

Nonparalytic Poliomyelitis

paralytic Poliomyelitis

Laboratory diagnosis

- Virus isolation from feces, throat, blood or CSF. Most commonly from feces.
- Serological diagnosis by neutralization or CFT tests.
- In the Cf test, C antigen appear first but soon disappear while anti D antibodies take some weeks to appear but last for five years.
- The CF test is useful to identify exposure to poliovirus but not for type specific diagnosis.

Immunity

- Type specific immunity
- IgM appears early and persists for 6 months
- IgG antibody persists for life.

Prophylaxis

- Active immunization :Two vaccines

1) Salk`s killed polio vaccine is formalin inactivated preparation of the three types of poliovirus.

   killed vaccine is given by injection. It is therefore called Injectable poliovaccine (IPV).

2) Sabin`s live attenuated poliovaccine developed by plaque selection in monkey kidney tissue culture.(OPV)

Prophylaxis cont…

- Markers to differentiate wild from attenuated strains :

1) d marker: bicarbonate
2) rct 40 :
3) MS :
4) McBride's intratypic antigenic marker
5) Molecular methods : monoclonal antibodies, oligonucleotide finger printing and nucleic acid sequencing.

Prophylaxis cont…

- OPV used in India is stated to contain Type 1 virus 10 lakh, Type 2 virus 2 lakh and Type 1 virus 3 lakh TC ID50 per dose (0.5 ml).
- Vaccine is stabilized by $MgCL_2$ at below 7 pH.
- Improper storage conditions and `cold chain` failure may be partly responsible for the failure of OPV to control poliomyelitis.

Merits and Demerits of OPV and IPV

- Safety: IPV > OPV
- Efficiency: IPV > OPV (because of interference with Coxsackei B virus and practice of Breast feeding after vaccination)
- Ease of administration : OPV > IPV
- Economy : OPV > IPV
- Nature of immunity : OPV > IPV (because of local immunity).

Merits and Demerits of OPV and IPV cont..

- Duration of immunity : OPV > IPV
- Use in epidemics : only OPV
- Spread of vaccine virus in the community: pulse immunization with OPV
- Eradication of poliomyelitis : setback

Coxsackievirus

- Ist isolated in 1949 in Cosackie of New York state.
- Two group : A 23 types & B 6 types
- Can be isolated from throat secretions or feaces in suckling mouse brains.
- Cosackie B & A grow in monkey kidney tissue culture.
- Morphology & susceptibility is similar to enteroviruses.
- Serodiagnosis is difficult due to several types.

Diseases Associated with Coxsackie Viruses

1. **Summer Minor Illness** –

   This is an acute febrile illness of short duration and without distinctive features, usually occurring in summer and fall, and may be accompanied by a rubelliform rash on the face, neck and chest.

2. ## Herpangina

mostly in children; caused by Coxsackie A (types 1-10), B (types 1-5) and some echoviruses;virus is isolated from stool in 86% of cases; epidemic in the summer months; symptoms are mild and patients recover; characterized by abrupt onset of fever, sore throat, anorexia, abdominal pain and tiny, discrete vesicles with red aureola on the anterior pillars of the fauces, the tonsils, pharynx and edges of the soft palate; need to rule out Herpes gingivostomatitis in differential diagnosis--herpangina involvement is posterior vs anterior part of the oropharynx and in contrast to herpes does not involve the tongue, lip or eye.

3. Pleurodynia

Caused by Coxsackie group B (all6 types can be involved); characterized by acute sudden chest pain, fever, malaise (can act like coronary occlusion); may also be accompanied by abdominal and testicular pain; viremia is followed by seeding of the virus to striated intercostal muscles; recovery is complete but relapses are common.

4. Aseptic Meningitis

No bacteria cultivated from CNS; caused by Coxsackie B1, B6, A7, A9; fever, malaise headache, anorexia, abdominal pain and sometimes mild muscle weakness and severe stiff neck.

5. Neonatal Disease

Group B coxsackie and some group A; ranges from inapparent infection to fatal disease, lethargy, feeding difficulty, vomiting and in severe cases myocarditis and/or pericarditis.

6. **Respiratory Infections**

   Coxsackie A10, A24, B3; common cold-like symptoms.

7. **Hand, Foot & Mouth Diseases**

   Coxsackie A16, A4, A5, A9, A10; vesicular lesions.

8. **Myocardiopathy**

   Involves several Coxsackie B types.

9. **Sudden Onset Diabetes**

   Associated in some rare cases Coxsackie B4

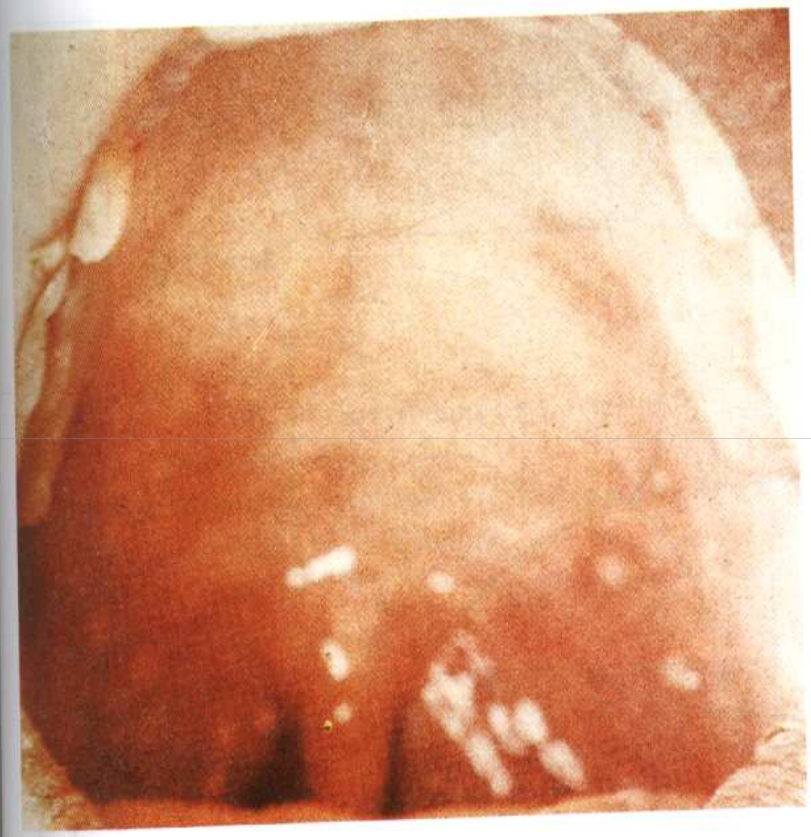

FIGURE 59-8 Herpangina. Characteristic discrete vesicles are seen on the anterior tonsillar pillars. (Courtesy Dr. GDW McKendrick; From Lambert HP et al.: *Infectious diseases illustrated*, London, 1982, Gower Medical Publishing.)

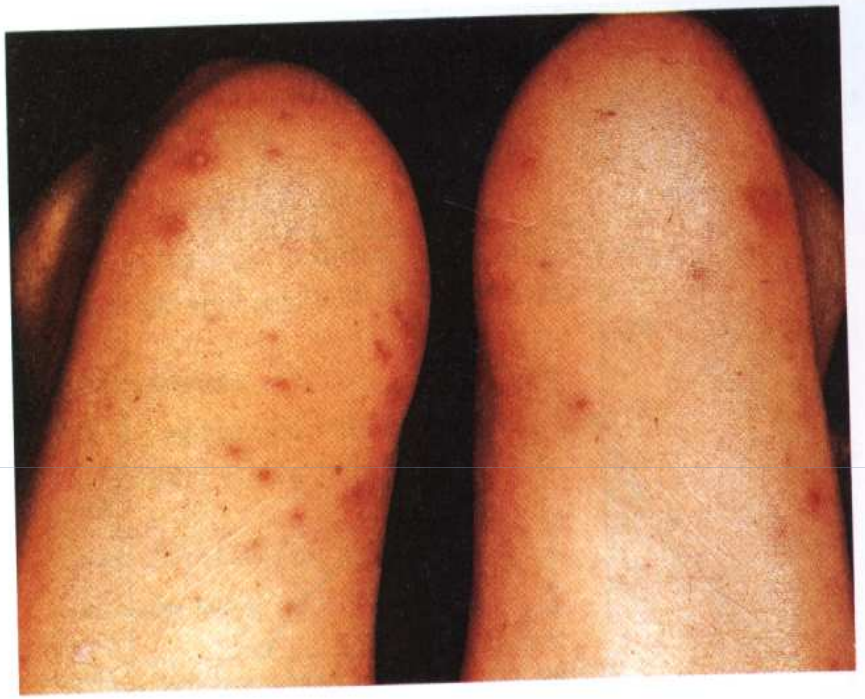

FIGURE 59-9 Hand-foot-and-mouth disease caused by coxsackie A virus. Lesions initially appear in the oral cavity and then develop within 1 day on the palms and, as seen here, soles. (From Habif TP: *Clinical dermatology: a color guide to diagnosis and therapy*, St Louis, 1985, Mosby.)

Echo virus

- Enteric cytopathic human orphan viruses
- Infect human only & their enteric tract
- Most infection are asymptomatic
- Fever with rash & aseptic meningitis sometimes as epidemic can be produced by several serotypes.
- Respiratory disease in children.

Enteroviruses

Serotypes	Disease
68	Pneumonia,brochitis
70	Acute hemorrhagic conjunctivitis
71	Meningitis
72	HAV

Rhinoviruses

- Causes common cold & are isolated commonly from nose & throat.
- They are named so because of their special adaptation to grow in the nose.
- Coryza is the common symptom .