Virology

Lec (11)
Dr. Areej A. Hussein

Teaching Objectives:
1. Know general characteristic of Picornaviruses.
2. Recognize the mechanism of entry and replication.
3. Understand methods of diagnosis.
4. Know prevention methods.

Picornaviruses from Greek Pico which mean small and rna which mean RNA.

Classification: In the first classification, Picornaviridae contains five genera:
1-Enteroviruses: Human enteroviruses include polioviruses type 1-3, Coxasackie viruses A and B, Echoviruses type 1-33.

2-Rhinoviruses Human rhinovruses include > 100 antigenic types.

3-Hepatovirus [Hepatitis A virus].

4-Aphthovirus [Foot and mouth disease of cattle].

5-Cardiovirus [Cardioviruses of rodents].

-Picornaviridae family consist of two major groups of human pathogens.

-**Enteroviruses** are transient inhabitant of the human alimentary tract and may be isolated from the throat or lower intestine.

-Rhinoviruses are isolated chiefly from the nose and throat cause respiratory disease.

Important Properties of Picornaviruses

-Small, none enveloped viruses**,** measuring about 28-30 nm

-Composion RNA (30%) and protein (70%).

-Genome: Single strand RNA, linear, positive sense. Icosahedral symmetry and contain 60 subunits.

-Infectious genome contain genome -linked protein (Vpg)

-Proteins: Four major polypeptides, surface proteins VP1-VP3 are major antibody binding sites; internal protein VP4 is associated with viral RNA.

-Replication: in cytoplasm.

-Acid stability (ph3-5) for 1-3 hours.

-Causing various illnesses ranging from poliomyelitis to aseptic meningitis to the common cold.

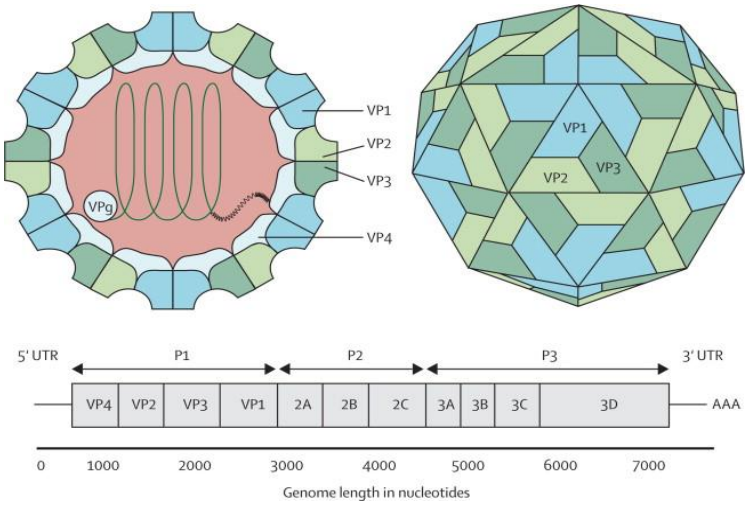

Figure 1: Genome of picornaviruses

Poliomyelitis: Polio, also called Poliomyelitis is a highly contagious infectious disease caused by one of three related, polio is a very serious disease, which can lead to paralysis or even death. One a person is exposed to polio it usually takes three to five days for symptoms to appear. The virus is inactivated by heating to 55°C for 30 min, poliovirus inactivated by concentration much highly, while it is not affected by ether or detergent.

Stereotypes

The antigenic structure of the virus is complex, but three distinct and stable stereotypes of poliovirus [type 1, 2 and 3] can be identified. Immunity following infection with poliovirus is lifelong but monotypic. The majority of outbreaks of paralytic polio are due to type 1, however, type 2 appears to be the most effective immunogenic.

Mode of infection

1-Direct contact with infected stool or throat secretion.

2-Indirect during eating or drinking contaminated food or water.

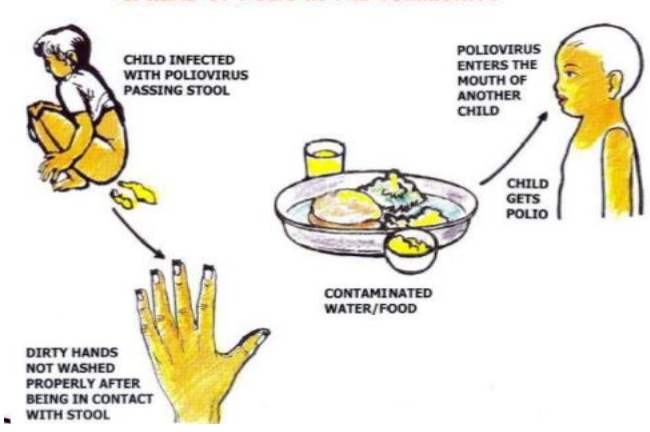

Figure 2: Spread of Polio in the Community

Pathogenesis and pathology:

The polio enters the body by ingestion or inhalation. They multiply in lymphatic tissue of alimentary canal (tonsils to Peyer's patches) then viruses are carried to blood stream and finally to spinal cord and brain. They destroy neuron with degeneration.

Clinical Findings

1-In apparent infection: (Incidence 90-95%) Clinical features (No clinical feature, the virus present in stool or throat or both of them).

2-Abortive poliomyelitis: (Incidence 4-8%) this is the most common form of the disease characterized by headache, nausea, vomiting, general discomfort, slight fever for up to three days.

3-Non paralytic poliomyelitis (Aseptic meningitis): (incidence 1-2%) illness similar to aseptic meningitis with stiff neck and back, fatigue and muscle pain last for 2-10 days, rapid recovery.

4-Paralytic poliomyelitis: (Incidence 0.1-2%) flaccid paralysis, painful muscle spasm occur, fever, constipation, the motor nerve damage is permanent.

5-Progressive post poliomyelitis: Muscle atrophy.

Factors Affecting Paralysis in Poliomyelitis include

- Age [less extensive and less common in infants].
- Trauma [injuries, hypodermic injections, tonsillectomy].
- Pregnancy [endocrine factors].

-Immunosuppression: infection with wild-type virus is much more severe in immunosuppressed patients. Vaccine related paralytic poliomyelitis may occur in immunocompromised individuals.

Prevention and Control

Two types of polio vaccines are in use throughout the world:

1- Attenuated live vaccine.

A- Live Polio vaccine (LPV).

B- Oral Polio vaccine (OPV) or Sabin vaccine.

C-Trivalent 1, 2, 3.

2 months, 4 and 6-18 months of age, and before school entry 4-6 years (4 doses).

2-Killed or inactivated vaccine (KPV, IPV) or Salk vaccine, 2, 4, 12-18 months, before school entry 4-6 years.

3-Recombinant DNA technology. Live polio vaccine that cannot mutant to increase neurovirulence.

4-Passive immunization: Immunoglobulin can provide protection for few weeks against paralytic disease; it is effective only if given shortly before infection.

Vaccine type	Advantages	Disadvantages
IPV	Safe, stable, no interference by other viruses	More expensive, difficult administration, required wide vaccine coverage. No detectable IgA in the intestinal tract.
OPV	Less expensive, easily administered, excellent herd immunity, provide immediate protection as interferes with wild poliovirus. Production of local IgA.	Less safe [can cause paralytic polio], less stable especially in tropics, some interference by enteroviruses.

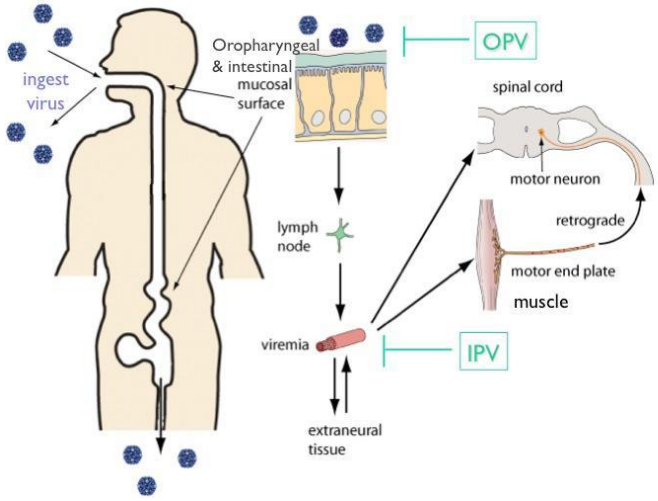

Figure 3: Method of Vaccination

Laboratory Diagnosis

-**Recovery of virus**: The virus can be recovered from throat swab taken soon after onset of illness or rectal swab or stool sample. No permanent carrier is known. Specimens should be kept frozen during transport to laboratory.

-**Cell culture**: Human embryonic fibroblast, monkey kidney cells then identification: by neutralizing test with specific antisera.

-**Serology**: Paired sample, neutralization test against 3 serotype.

Immunity: Passive immunity is transferred from mother to offspring, which are gradually disappearing during the first 6 months. Passively administered antibodies last only 3-5 weeks.

Virus-neutralizing Abs forms soon after exposure, often before onset of illness, and persists for life. It implies that viral multiplication occurs in the body before the invasion of the CNS. As the virus n the brain and spinal cord is not influenced by high titer in the blood. Immunization is of value only if it precedes the onset of symptoms referable to NS.

Important properties of Coxsackie viruses

- The virus was discovered in 1948-1949 by Dr. Gilbert Dalldorf a scientific working at the New York state department of health in Albany.

- Small viruses approximately 24-30 nm in diameter.

- Genome: Single strand RNA, linear, positive sense.

-They have a naked capsid structure with icosahedral symmetry.

- Four major polypeptides, [VP1-VP4] arranged in icosahedral symmetry around the genome.

-Acid stability (ph 3) for 1-3 hours.

- Coxsackievirus infections occur worldwide, primarily in the summer and fall, and divided into two groups depend on early observations of their pathogenicity in neonatal mice.

-Group A: 1-24 Types.

-Group B: 1-6 Types.

Mode of infection

1- Fecal-oral route (direct and indirect).

2- Respiratory aerosols.

Summary of Replicative Cycle

The virus replicate in the cytoplasm of the cells, first the virion attaches to specific receptor in the plasma membrane. The capsid proteins are then removed, after uncoating, the genome RNA function as mRNA and is translated into one very large polypeptide called noncapsid viral protein. This polypeptide is cleaved by a virus-encoded proteinase to form the capsid proteins of the progeny virions and several noncapsid protein, including the RNA polymerase that synthesizes the progeny RNA genome, then released upon death of the cell, they do not bud from cell membrane.

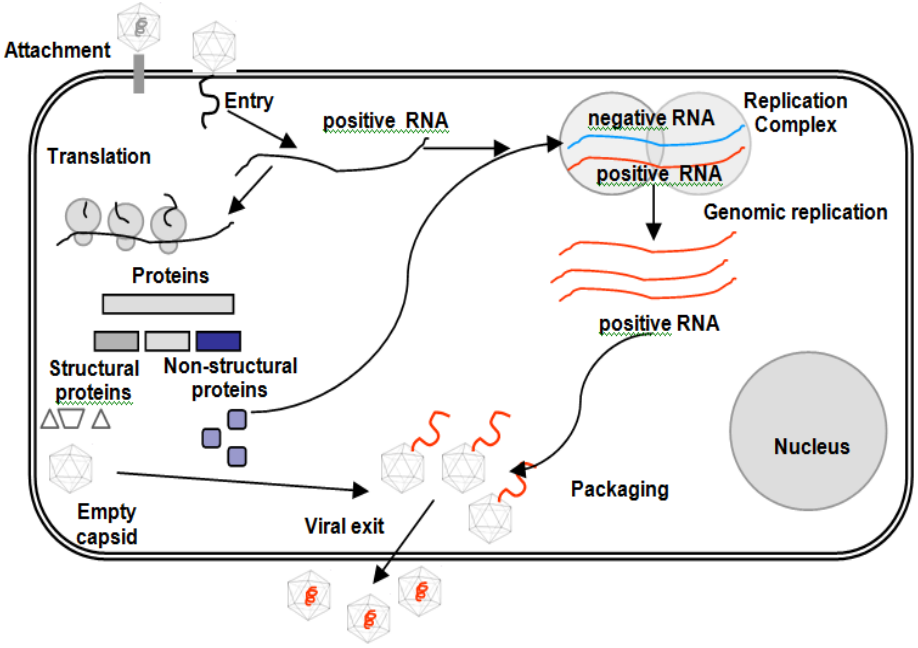

Figure 4: Replication cycle of Coxsackie viruses.

Clinical findings: Incubation period ranges from 2-9 days.

1- **Group A- specific disease.**

- **Herpangina** is characteristized by fever, sore throat and tender vesicles in oropharynx (pharynx, tonsils and tongue) occurs in children then recovery occurs.
- **Hand, foot and mouth diseases** is characteristized by a vesicular rash of the palm, soles may spread to hand and feet and ulcerations in the mouth mainly in children.
- **Gastrointestinal is characteristized by diarrhea in children.**
- **Ocular**: Acute hemorrhagic conjunctivitis associated with coxsackievirus. The patient has symptoms of pain, itching, and photophobia. The eye is red from prominent subconjunctival hemorrhage.

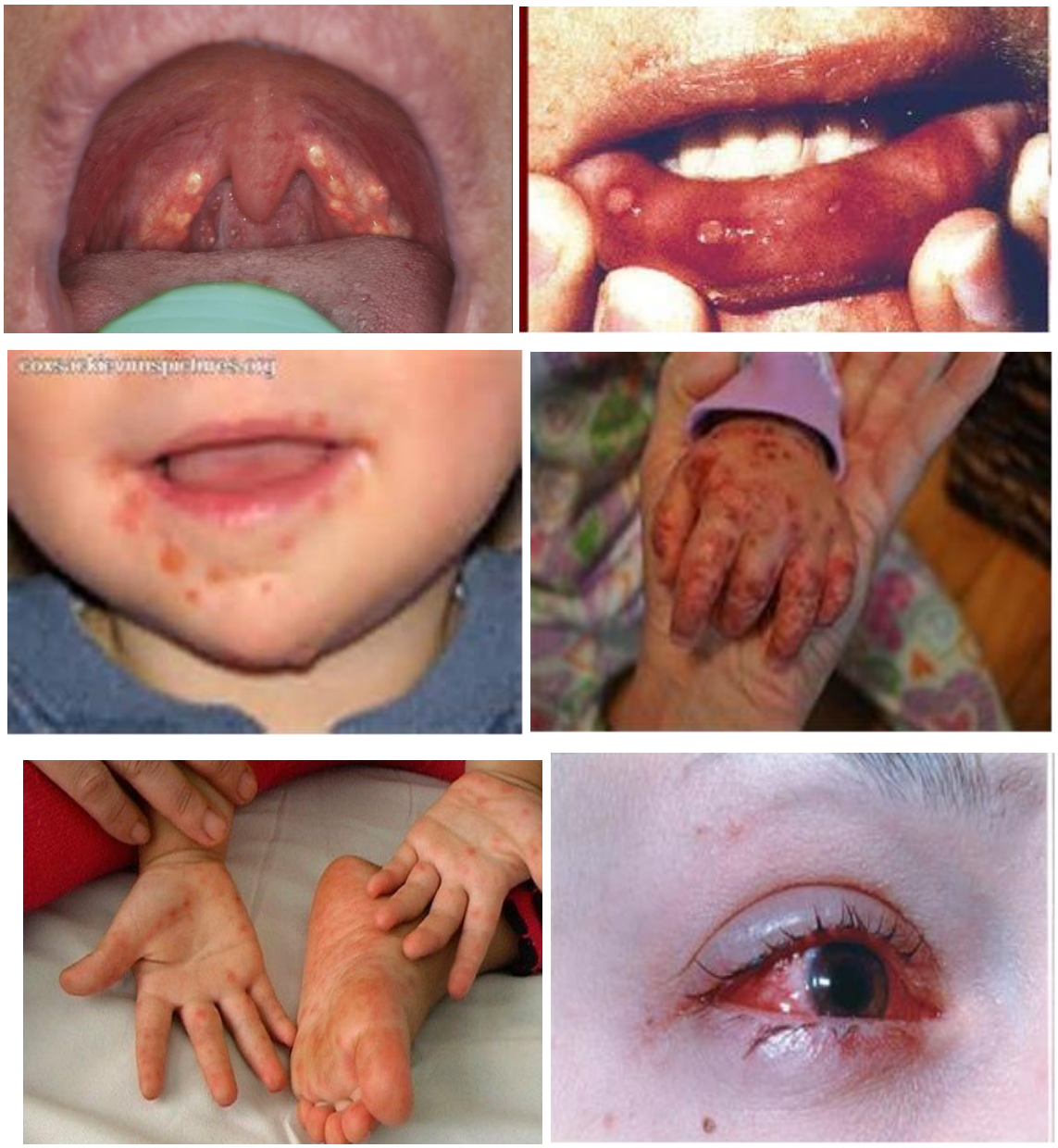

Figure 5: Clinical Findings of group A Coxsackievirus.

2- **Group B- specific Disease.**

- **Myocarditis** in adult as well as in children, 5% of all symptomatic coxsackie viruses infection induces heart disease, which is fatal in neonate.
- **Pleurodynia is** characteristized by fever; chest pain lasts for 2 days -2 weeks.
- **Diabetes** as a result of pancreatic damage.
- **Generalized disease** of infant, multiple organs involved like heart, liver, brain.

3- **Disease caused by both of them.**

- **Neurologic** (aseptic meningitis), mild paresis and acute flaccid paralysis similar to poliomyelitis, recovery occurs.
- **Respiratory infections:** upper respiratory tract infection (common cold).
- **Minor febrile illness**: with or without rash can occur also.

Lab diagnosis

1-Specimens, throat swab, stool, CSF, conjunctivital swab for viral culture then a cytopathic effect appears within 5-15 days.

2-Serological test for observing arise in titer of neutralizing antibody. However serologic testes are difficult to evaluate (because multiplicity of types).

3-Reverse transcription-PCR assay useful for detection due to rapid and sensitive test.

Treatment

There is neither antiviral drug therapy nor a vaccine available against these no passive immunization.