Picornaviridae family

They are single-stranded, positive-sense, RNA viruses. This family has 9 different genera; 5 of these genera cause human diseases and the others cause animal diseases.

- Genus enterovirus
- Genus heparna virus (Hepatitis RNA virus)
- Genus rhinovirus

All of these may cause respiratory infections, GIT infections, paralysis, encephalitis, meningitis, fever with rash and many other clinical syndromes.

- Rhinoviruses cause common cold syndrome. They cause rhinitis with fever. It is a self-limiting disease. We have more than 120 different serotypes of this virus. In one season we could be infected with more than one serotype of this virus. We are not concerned about it because it is a mild, self-limiting disease.
- Hepatovirus (or Heparnavirus): Hepatitis RNA virus (i.e. Hepatitis A virus) will be discussed with the hepatitis viruses.

**Genus Enteroviruses; this genus has the following viruses:**

- Polio (types 1-3)
- Coxsackie A: 24 types
- Coxsackie B: 6 types
- Echoviruses (enteric cytopathic human orphan): 34 types
- Enteroviruses (types 68-71)
- Hepatitis A virus (Enterovirus 72)

**Poliovirus as a prototype of enteroviruses**

- It has a single-stranded, positive-sense RNA.
- It has four different viral proteins (VP₁, VP₂, VP₃, and VP4). We have 60 copies of each viral protein (i.e. we have 240 viral proteins in a single enterovirus). These proteins are structural proteins which make up the capsid.
- They are small viruses (20-30nm in diameter).
- They are non-enveloped viruses.

**Diseases Associated with Enterovirus Infections**

- Non-specific Febrile Illness (fever of unknown origin)
- Perinatal Infection
- Febrile Disease with Rash (we have to do differential diagnosis with Measles, Rubella, chickenpox)
- Meningitis
- Myocarditis
- Hepatitis
- Pleurodynia
- Poliomyelitis (by either Poliovirus or other viruses)
Background

The enteroviruses have been among the most intensively studied of all human pathogens. The war on poliomyelitis produced many breakthroughs (vaccine) in the science of virology.

Research on the enteroviruses has led to:

- Important discoveries in the replication of RNA viruses
- X-ray crystallographic characterization
- Fine structure mapping

There is no lipid in their structure so they are stable against treatment with ether, ethanol, and various detergents. They are also stable against gastric juices and bile salts; so they can pass through the stomach to the intestines and establish an infection there. Since they are heat and acid stable, they will stay viable for hours on surfaces.

Biological properties

- Found in feces & spread by fecal-oral route (respiratory route is another way of transmission)
- Grow in tissue culture with or without CPE
- Cause silent infections but also cause a number of important illnesses (e.g. poliomyelitis)
- 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.
- Isolation of Enteroviruses from the stool provides a basis for suspecting that the virus is responsible for the illness in question.

Viral Pathogenesis

- The virus enters the body through the mucosa of the oropharynx and upper respiratory tract, and then begins to multiply in the tissues around the oropharynx (first round of replication).
- 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.
- During the primary viremia, tissues are seeded according to the tropism of the virus.
  - VP1 determines the target tissue to be infected (e.g. Poliovirus infects neurons and Hepatitis A virus infects the liver)
Immunity

- Antibodies can be detected in the circulation by the seventh to tenth day after exposure, roughly the same time as the symptomatic disease and secondary viremia occur.
- With the exception of the gastrointestinal tract, viral replication in tissues soon slows to a halt. In contrast, gastrointestinal tract viral multiplication and fecal shedding can continue for weeks after the development of high neutralizing antibody titers.

Diseases

1. Aseptic meningitis
   - **Symptoms**: headache, neck ache, rigidity of neck and back, malaise
   - **Cause**: while several viruses can cause aseptic meningitis (enteroviruses, mumps, lymphocytic choriomeningitis, herpes, etc.), there are other causes of non-purulent (aseptic) meningitis (chlamydia, leptospira). Certain other bacteria and fungi may also cause non-purulent spinal fluids but with altered chemistry compared to viral meningitis.

2. Poliomyelitis
   - Poliovirus was once thought to be the main cause of paralysis before the advent of polio vaccines.
   - Poliovirus did account for a large portion of paralytic cases but many cases were caused by other agents or were due to unknown causes.
   - The vast majority of persons infected with poliovirus have an unapparent or silent infection.
   - The symptoms, locations, extent and persistence of paralysis depend on the degree of damage to the anterior horn neurons and the number of neurons affected.
   - If all neurons supplying a given muscle are irreversibly damaged, the result is permanent paralysis; but if the damage to the neurons is incomplete and reversible or if some neurons are spared, the muscle function can be restored or regained.
   - Paralytic disease (spinal form) may begin with excruciating pain or spasms which may precede paralysis of the extremities.
   - An especially serious form is bulbar polio as it involves cranial nerves and respiratory and circulatory centers in the medulla.
   - Post paralytic polio syndrome may occur many years after initial disease and reflects the continued loss of neurons with aging.
Prevention against poliovirus

- The Salk polio vaccine is a formalinized whole virus preparation. It is a killed vaccine given by injection. It is inconvenient that is why it is not used today.
- The Sabin polio vaccine is a live, attenuated virus. Attenuation means repeated passage of the virulent poliovirus in tissue culture to produce mutants which no longer are neurotrophic. The attenuated vaccine is not virulent but immunogenic. It stimulates production of IgA and IgG and it is a very effective vaccine up till now. Sabin vaccine is called a trivalent vaccine because it contains all three types of Poliovirus.
- If there is a break in the cold-chain of the vaccine or if it is subjected to heat, the virus will be inactivated. Sometimes there is reversion of the virus from the attenuated state causing the disease. These factors, along with others have caused questions to be raised about the Sabin vaccine in view of the alleged polio paralysis in a few recipients of the vaccine and their contacts.
- Immunity from Sabin vaccine seems to be life-long. Protection with the Salk vaccine requires multiple immunizations and boosters which can cause logistical problems.

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. (we have to do a differential diagnosis between this and measles because we have spots which resemble Koplik’s spots)
3. **Pleurodynia**: Coxsackie group B; characterized by acute sudden chest pain, fever, malaise (may present as 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. (maybe confused with coronary heart disease)
4. **Aseptic Meningitis**: No bacteria cultivated from CNS; caused by Coxsackie A or B; fever, malaise headache, anorexia, abdominal pain and sometimes mild muscle weakness and severe stiff neck.
5. **Neonatal Disease**: Mostly group B and some group A; ranges from unapparent infection to fatal disease.(differential diagnosis with Herpes simplex virus)
8. **Myocardioopathy**: Involves several Coxsackie B types.
9. **Sudden Onset Diabetes**: associated with Coxsackie B4 infection.

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