

## **Polio, Common Cold, and Norwalk Virus** (Enteroviruses, Rhinoviruses, and Caliciviruses)

Reading: Schaechter's Mechanisms of Microbial Disease, Fourth Edition, Chapter 32 and Chapter 37 (pp. 374-375).

I. **Overview/Classification.** This first group of positive-strand RNA viruses includes etiologic agents of poliomyelitis, meningitis, hepatitis, myocarditis and the common cold.

A. *Picornaviridae* family of viruses encompasses a large group (>200 viruses) of human pathogens. This family's name is derived from *pico* (small) and *RNA* highlighting the fact that these are among the smallest viruses. Subdivided into five genera (three of which include human pathogens):

1. *Enterovirus*

- a) Polioviruses 1-3
- b) Coxsackieviruses A1-A24 (no A23), B1-B6
- c) Echoviruses 1-34 (no 10 or 28)
- d) Enteroviruses 68-71

2. *Rhinovirus*

- a) Rhinoviruses 1-110

3. *Hepatovirus*

- a) Hepatitis A virus (will be covered in the *RNA virus III: Hepatitis* Lecture)

B. *Caliciviridae* family includes several viruses that cause gastroenteritis, and one that causes hepatitis. The name of this family is derived from *calix* (cup) to describe the 32 cup-shaped depressions on the surface of the virion.

1. Norwalk virus

C. Hepevirus- Hepatitis E virus (will be covered in the *RNA virus III: Hepatitis* Lecture)

## II. **Biologic properties/virion structure/genome**

A. Biologic properties- common themes

- 1. Heat and detergent stable
- 2. Acid stability (ability to survive gastric acids following ingestion)
  - a. *Enterovirus*, *Hepatovirus*, and *Calicivirus* are acid-stable (pH >3)
  - b. *Rhinovirus* is acid-labile (pH <5)

B. Virion structure

- 1. *Picornaviridae*: nonenveloped icosahedral capsid, 30 nm in diameter, 60 protomers
- 2. *Caliciviridae*: nonenveloped icosahedral capsid, 30 – 38 nm, 90 capsomers; named for the 32 characteristic cup-shaped depressions on the virion surface

C. Genome structure

- 1. Linear, plus sense ssRNA, 7 – 8 kb
- 2. Protein primer at 5' end, polyadenylated at 3' end
- 3. Genome RNA is infectious

D. Replication

1. Attachment to receptor – canyon hypothesis
2. Virion RNA acts as mRNA and is translated into a polyprotein which auto-cleaves to yield non-structural (RNA dependent RNA polymerase) and structural proteins
3. Cytoplasmic site of replication
4. Virus inhibits cellular transcription, DNA replication & protein synthesis, cytotoxic.
5. Assembly of genome into capsids

### III. Diseases Mechanism

- A. Viruses ingested and enter via the oropharynx, intestinal mucosa or upper respiratory tract and infect the underlying lymphatic tissue; rhinoviruses are restricted to the upper respiratory tract.
- B. In the absence of serum antibody, enteroviruses spread by viremia to cells of a receptor-bearing target tissue.
- C. Different viruses bind to different receptors, many of which belong to the immunoglobulin superfamily (ie, ICAM-1).
- D. The infected target tissue determines the subsequent disease.
- E. Viral, rather than immune, pathologic effects are usually responsible for causing disease symptoms- cytopathic viruses.
- F. Serum antibody blocks viremic spread to target tissue, preventing symptoms.
- G. Enterovirus is shed in feces for long periods.
- H. Infection is often asymptomatic or causes mild flu-like or upper respiratory disease.
- I. Disease is often more severe in adults and asymptomatic in young children. (Except for coxsackievirus (newborns)).

### IV. Clinical Syndromes – Summary slide

- A. Neurologic
  1. Meningitis (“aseptic meningitis”)- acute illness, headache, fever, neck and back stiffness. May be a rash; recovery usually uneventful.
    - a) many enteroviruses (are most common cause of meningitis)
    - b) differential diagnosis with bacterial meningitis is very important
  2. Paralysis
    - a) Polioviruses 1, 2, 3
    - b) Enteroviruses
    - c) Coxsackievirus A and B
  3. Chronic meningoencephalitis/dermatomyositis
    - a) Echoviruses
  4. Outline of poliovirus infection
  5. Types of poliomyelitis: spinal and bulbar, predisposing factors- age, pregnancy, wound
- B. Cardiac and Muscular

1. Myocarditis - Coxsackievirus B
    - a) most severe in neonates, fever and sudden heart failure, high mortality. Brain, liver and pancreas also involved. Acute benign pericarditis in young adults.
    - b) some Coxsackievirus A and echoviruses
  2. Pleurodynia – (Bornhold's disease). Coxsackievirus B
    - a) Acute illness with sudden onset of fever and unilateral low thoracic, severe pleuritic chest pain. Lasts ~ 4 days, but may relapse.
- C. Skin and Mucosae
1. Herpangina - Coxsackievirus A
    - a) Fever, sore throat, pain on swallowing, anorexia and vomiting. Classic finding is vesicular ulcerated lesions on soft palate. Self limiting.
  2. Hand-foot-and-mouth disease - Coxsackieviruses A16
    - a) vesicular lesions on the hands, feet, mouth and tongue, mild fever, last 2-3 days.
- D. Respiratory
1. Colds- pH and temperature sensitivity restrict replication to upper respiratory tract; fever, runny nose, malaise, nasal obstruction; peaks at 3-4 days.
  2. 50% asymptomatic infection, transmitted by aerosols and fomites (hands)
  3. Immunity transient and many serotypes
  4. Drugs which bind canyon limit duration
    - a) Rhinoviruses – 50% of colds, >100 serotypes
    - b) Coxsackieviruses A
    - c) Echoviruses
    - d) Coxsackievirus B
- E. Ocular
1. Acute hemorrhagic conjunctivitis – extremely contagious, 24 hr incubation period, resolves within 1-2 weeks.
    - a) Enterovirus 70
    - b) Coxsackievirus A24
- F. Hepatitis
1. Hepatitis A virus
  2. Hepatitis E virus
- G. Gastroenteritis
1. Caliciviruses
  2. various enteroviruses
- H. Treatment/Vaccines. The polio vaccine represents an important milestone in vaccine technology
1. Salk vaccine – killed, inactivated (IPV and EIPV)
  2. Sabin vaccine – live attenuated (oral)
  3. Advantages and disadvantages of vaccines
  4. World-wide eradication effort

**V. Caliciviruses** - Caliciviruses (Norwalk agent- Cruise ship virus). Transmitted by fecal oral route. Incubation period 1-2 days; diarrhea, vomiting, abdominal cramps, nausea, fever; resolves in 1-3 days.