RNA Nonenveloped Viruses

PICORNAVIRUSES

-Picornaviruses are small (20–30 nm) **nonenveloped** viruses composed of an **icosahedral nucleocapsid** and a **singlestranded** RNA genome. The genome RNA has positive polarity (i.e., on entering the cell, it functions as the viral mRNA).

- There is no polymerase within the virion.

- Picornaviruses replicate in the cytoplasm of cells. They are not inactivated by lipid solvents, such as ether, because they do not have an envelope.

- The picornavirus family includes two groups of medical importance: the **enteroviruses** and the **rhinoviruses.** Among the major enteroviruses are poliovirus, Coxsackie viruses, echoviruses, and hepatitis A virus. Enteroviruses infect primarily the enteric tract, whereas rhinoviruses are found in the nose and throat (*rhino* = nose).

- Enteroviruses replicate optimally at 37°C, whereas rhinoviruses grow better at 33°C, in accordance with the lower temperature of the nose. Enteroviruses are stable under acid conditions (pH 3–5), which enables them to survive exposure to gastric acid, whereas rhinoviruses are acidlabile. This explains why rhinovirus infections are restricted to the nose and throat.

ENTEROVIRUSES

Poliovirus

Disease: This virus causes poliomyelitis.

Important Properties: The host range is limited to primates (i.e., humans and nonhuman **primates** such as apes and monkeys). This limitation is due to the binding of the viral capsid protein to a receptor found only on primate cell membranes. However, note that purified viral RNA (without the capsid protein) can enter and replicate in many nonprimate cells—the RNA can bypass the cell membrane receptor (i.e., it is “infectious RNA”). There are **three serologic (antigenic) types** based on different antigenic determinants on the outer capsid

proteins. Because there is little cross-reaction, protection from disease requires the presence of antibody against each of the three types.

Transmission: Poliovirus is transmitted by the **fecal–oral** route. It replicates in the oropharynx and intestinal tract. Humans are the only natural hosts.

Prevention: Poliomyelitis can be prevented by both the **killed** vaccine (Salk vaccine, inactivated vaccine, IPV) and the **live, attenuated** vaccine (Sabin vaccine, oral vaccine, OPV). Both vaccines induce humoral antibodies, which neutralize virus entering the blood and hence prevent central nervous system infection and disease. Both the killed and the live vaccines contain all three serotypes.

HEPATITIS A VIRUS (HAV)

Disease: HAV causes hepatitis A.

Important Properties: HAV is a typical **enterovirus** classified in the picornavirus family. It has a single-stranded RNA genome and a nonenveloped icosahedral nucleocapsid and replicates in the cytoplasm of the cell. It is also known as enterovirus. It has one serotype, and there is no antigenic relationship to HBV or other hepatitis viruses.

Transmission: HAV is transmitted by the **fecal–oral** route. Humans are

the reservoir for HAV. Virus appears in the feces roughly 2 weeks before the appearance of symptoms, so quarantine of patients is ineffective. **Children are the most frequently infected** group, and outbreaks occur in special living situations such as summer camps and boarding schools. Common-source outbreaks arise from fecally contaminated water or food such as oysters grown in polluted water and eaten raw. Unlike HBV, HAV is **rarely transmitted via the blood,** because the level of viremia is low and chronic infection does not occur.

RHINOVIRUSES

Disease: These viruses are the main cause of the common cold.

Important Properties: There are **more than 100 serologic types,** which explains why the common cold is so common. They **replicate better at 33C** than at 37°C, which explains why they affect primarily the nose and conjunctiva

rather than the lower respiratory tract. Because they are **acid-labile,** they are killed by gastric acid when swallowed. This explains why they do not infect the gastrointestinal tract, unlike the enteroviruses. The host range is limited to humans and chimpanzees.

Transmission: There are **two modes** of transmission for these viruses. In the past, it was accepted that they were transmitted directly from person to person via aerosols of respiratory droplets. However, now it appears that an indirect mode, in which respiratory droplets are deposited on the hands or on asurface such as a table and then transported by fingers to the nose or eyes, is also important. The common cold is reputed to be the most common human infection, although data are difficult to obtain because it is not a well-defined or notifiable disease. Millions of days of work and school are lost each year as a result of "colds." Rhinoviruses occur worldwide, causing disease particularly in the fall and winter. The reason for this seasonal variation is unclear. Low temperatures per se do not predispose to the common cold, but the crowding that occurs at schools. A few serotypes of rhinoviruses are prevalent during one season, only to be replaced by other serotypes during the following season. It appears that the population builds up immunity to the prevalent serotypes but remains susceptible to the others.

CALICIVIRUSES

- Caliciviruses are small, nonenveloped viruses with singlestranded RNA of positive polarity.

- Although they share those features with picornaviruses, caliciviruses are distinguished from picornaviruses by having a larger genome and having distinctive spikes on the surface.

- Norovirus is the main human pathogen in the calicivirus family.

REOVIRUSES

REO is an acronym for *r*espiratory *e*nteric *o*rphan; when the virus was discovered, it was isolated from the respiratory and enteric tracts and was not associated with any disease. Rotaviruses are the most important human pathogens in the reovirus family.

ROTAVIRUS

Disease: Rotavirus is a common cause of viral gastroenteritis, especially in young children.

Important Properties: Rotavirus has a segmented, double-stranded RNA genome surrounded by a double-layered icosahedral capsid without an envelope. The rotavirus genome has 11 segments. The virion contains an RNA-dependent RNA polymerase. A virion polymerase is required because human cells do not have an RNA polymerase that can synthesize mRNA from a double-stranded RNA template. Many domestic animals are infected with their own strains of rotaviruses, but these are not a source of human disease. There are at least six serotypes of human rotavirus. The outer surface protein (also known as the viral hemagglutinin) is the type-specific antigen and elicits protective antibody.

Transmission: Rotavirus is transmitted by the **fecal–oral** route. Infection occurs worldwide, and by age 6 years, most children have antibodies to at least one serotype.

Treatment & Prevention: There are two rotavirus vaccines available. Both contain live virus and are given orally. One is a live, attenuated vaccine (Rotarix), which contains the single most common rotavirus serotype (G1) causing disease in the United States. The other is a live reassortant vaccine (Rotateq), which contains five rotavirus strains. Patients with a history of intussusception should not receive either vaccine.

Tumor viruses

- Viruses can cause benign or malignant tumors in many species of animals (e.g., frogs, fishes, birds, and mammals).

- Despite the common occurrence of tumor viruses in animals, only a few viruses are associated with **human** tumors, and evidence that they are truly the causative agents exists for very few.

- Tumor viruses have no characteristic size, shape, or chemical composition. Some are large, and some are small; some are enveloped, and others are naked (i.e., nonenveloped); some have DNA as their genetic material, and others have RNA. The factor that unites all of them is their common ability to cause tumors.

- Tumor viruses are at the forefront of cancer research for two main reasons:

(1) They are more rapid, reliable, and efficient tumor producers than either chemicals or radiation. For example, many of these viruses can cause tumors in all susceptible animals in 1 or 2 weeks and can produce malignant transformation in cultured cells in just a few days.

(2) They have a small number of genes compared with a human cell (only three, four, or five for many retroviruses), and hence their role in the production of cancer can be readily analyzed and understood. To date, the genomes of many tumor viruses have been cloned and sequenced and the number of genes and their functions have been determined; all of this has provided important information.

Human Tumor Viruses

- Human T-Cell Lymphotropic Virus
- Hepatitis C Virus
- Human Papillomavirus
- Epstein–Barr Virus
- Human Herpesvirus 8
- Hepatitis B Virus
- Merkel Cell Polyomavirus