# DNA nonenveloped viruses

# ADENOVIRUSES

**Diseases:** Adenoviruses cause a variety of upper and lower respiratory tract diseases such as pharyngitis, conjunctivitis (“pink eye”), the common cold, and pneumonia. Keratoconjunctivitis, hemorrhagic cystitis, and gastroenteritis also occur. Some adenoviruses cause sarcomas in rodents.

**Important Properties**

- Adenoviruses are nonenveloped viruses with doublestranded linear DNA and an icosahedral nucleocapsid. They are the only viruses with a fiber protruding from each of the 12 vertices of the capsid. The fiber is the organ of attachment and is a hemagglutinin. When purified free of virions, the fiber is toxic to human cells.

- There are 41 known antigenic types; the fiber protein is the main type-specific antigen.

- All adenoviruses have a common group-specific antigen located on the hexon protein. Certain serotypes of human adenoviruses (especially 12, 18, and 31) cause sarcomas at the site of injection in laboratory rodents such as newborn hamsters.

- There is no evidence that adenoviruses cause tumors in humans.

**Transmission & Epidemiology**

Adenoviruses are transmitted by several mechanisms: aerosol droplet, fecal–oral route, and direct inoculationof conjunctivas by tonometers or fingers. The fecal–oral route is the most common mode of transmission among young children and their families. Many species of animals are infected by strains of adenovirus, but these strains are not pathogenic for humans. Adenovirus infections are endemic worldwide, but outbreaks occur among military recruits, apparently as a result of the close living conditions that facilitate transmission.

## PAPILLOMAVIRUSES

**Diseases:** Human papillomavirus causes papillomas, which are benign tumors of squamous cells (e.g., warts on the skin). Some HPV types, especially types 16 and 18, cause carcinoma of the cervix, penis, and anus.

**Important Properties:** Papillomaviruses are nonenveloped viruses with doublestranded circular DNA and an icosahedral nucleocapsid. Two of the early genes, ***E6*** and ***E7***, are implicated in carcinogenesis. They encode proteins that inactivate proteins encoded by tumor suppressor genes in human cells (e.g., the *p53* gene and the retinoblastoma [*RB*] gene, respectively). Inactivation of the p53 and RB proteins is an important step in the process by which a normal cell becomes a cancer cell.

There are at least 100 types of papillomaviruses, classified primarily on the basis of DNA restriction fragment analysis. There is a pronounced predilection of certain types to infect certain tissues. For example, skin warts are caused primarily by HPV-1 through HPV-4, whereas genital warts are usually caused by HPV-6 and HPV-11. Approximately 30 types of HPV infect the genital tract.

**Transmission & Epidemiology:** Papillomaviruses are transmitted primarily by skin-to-skin contact and by genital contact. Genital warts are among the most common sexually transmitted diseases. Skin warts are more common in children and young adults and tend to regress in older adults. HPV transmitted from an infected mother to the neonate during childbirth causes warts in the mouth and in the respiratory tract, especially on the larynx, of the infant. Many species of animals are infected with their own types of papillomaviruses, but these viruses are not an important source of human infection.

## PARVOVIRUSES

**Diseases:** Parvovirus B19 causes erythema infectiosum (slapped cheek syndrome, fifth disease), aplastic anemia (especially in patients with sickle cell anemia), and fetal infections, including hydrops fetalis.

**Important Properties:** Parvovirus B19 is a very small (22 nm) nonenveloped virus with a single-stranded DNA genome. The genome is negative-strand DNA, but there is no virion polymerase. The capsid has icosahedral symmetry. There is one serotype.

**Transmission & Epidemiology:** B19 virus is transmitted primarily by the respiratory route; transplacental transmission also occurs. Blood donated for transfusions also can transmit the virus. B19 virus infection occurs worldwide, and about half the people in the United States older than 18 years of age have antibodies to the virus. Humans are the natural reservoir; animals are not a source of human infection.

## POLYOMAVIRUSES

There are three members of the polyomavirus family that cause disease in humans, Merkel cell polyomavirus, JC virus, and BK virus. One member, SV40 virus, is a monkey virus that infected humans when it contaminated the poliovirus vaccine but has not caused human disease. Merkel cell polyomavirus causes carcinoma of the skin. JC virus is the cause of progressive multifocal leukoencephalopathy. BK virus causes nephropathy in renal transplant patients. SV40 virus causes no detectable disease in humans but does cause sarcomas in newborn hamsters.

# RNA Enveloped Viruses

## ORTHOMYXOVIRUSES

## INFLUENZA VIRUSES

- Influenza viruses are important human pathogens because they cause both outbreaks of influenza that sicken and kill thousands of people each year as well as infrequent but devastating worldwide epidemics (pandemics).

- Influenza viruses are the only members of the orthomyxovirus family. The orthomyxoviruses differ from the paramyxoviruses primarily in that the former have a segmented RNA genome (usually eight pieces), whereas the RNA genome of the latter consists of a single piece. The term *myxo* refers to the observation that these viruses interact with mucins (glycoproteins on the surface of cells). In addition, the orthomyxoviruses are smaller (110 nm in diameter) than the paramyxoviruses (150 nm in diameter).

- In 1997, an outbreak of human influenza (avian influenza, bird flu) caused by an H5N1 strain of influenza A virus began. In 2009, there was an outbreak of human influenza caused by an H1N1 influenza A virus of swine origin (swine-

origin influenza virus, S-OIV). In 2013, an outbreak of influenza caused by an H7N9 strain of influenza virus occurred.

## Human Influenza Virus

### Important Properties

- Influenza virus is composed of a **segmented** single stranded RNA genome, a helical nucleocapsid, and an outer lipoprotein envelope. The virion contains an RNA-dependent **RNA polymerase,** which transcribes the **negative-polarity** genome into mRNA. The envelope is covered with two different types of spikes, a **hemagglutinin** and a **neuraminidase.**

- Influenza A virus has 16 antigenically distinct types of hemagglutinin and 9 antigenically distinct types of neuraminidase. Some of these types cause disease in humans, but most of the types typically cause disease in other animal species such as birds, horses, and pigs.

- The function of the hemagglutinin is to bind to the cell surface receptor (neuraminic acid, sialic acid) to initiate infection of the cell. In the clinical laboratory, the hemagglutinin agglutinates red blood cells, which is the basis of a diagnostic test called the hemagglutination inhibition test. The hemagglutinin is also the target of neutralizing antibody (i.e., antibody against the hemagglutinin inhibits infection of the cell).

- The neuraminidase cleaves neuraminic acid (sialic acid) to release progeny virus from the infected cell. The hemagglutinin functions at the beginning of infection, whereas the neuraminidase functions at the end. Neuraminidase also degrades the protective layer of mucus in the respiratory tract. This enhances the ability of the virus to gain access to the respiratory epithelial cells.

- Influenza viruses, especially influenza A virus, show **changes in the antigenicity** of their hemagglutinin and neuraminidase proteins; this property contributes to their capacity to cause devastating **worldwide epidemics (pandemics).**

- There are two types of antigenic changes: (1) **antigenic shift,** which is a major change based on the reassortment of segments of the genome RNA; and (2) **antigenic drift,** which is a minor change based on mutations in the genome RNA. Influenza viruses have both **group-specific** and **type specific** antigens.

**(1)** The internal ribonucleoprotein is the group-specific antigen that distinguishes influenza A, B, and C viruses.

**(2)** The hemagglutinin and the neuraminidase are the type-specific antigens located on the surface. Antibody against the hemagglutinin neutralizes the infectivity of the virus (and prevents disease), whereas antibody against the group-specific antigen (which is located internally) does not. Antibody against the neuraminidase does not neutralize infectivity but does reduce disease by decreasing the amount of virus released from the infected cell and thus reducing spread of the virus to adjacent cells.

**Transmission**

The virus is transmitted by **airborne respiratory droplets.** The ability of influenza A virus to cause epidemics is dependent on antigenic changes in the hemagglutinin and neuraminidase.