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Non-Enveloped **DNA Viruses**:

Adenoviruses, Papillomaviruses Parvoviruses and Polyomaviruses

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.

Clinical Features of DNA Nonenveloped Viruses				
Virus	**Mode of Transmission**	**Types Cause Different Diseases**	**Certain Types Cause Cancer**	**Vaccine Available**
Adenovirus	Respiratory; fecal–oral	Yes	Yes, in animals but not humans	Yes, but used only in military
Human papillomavirus	Sexual; skin contact	Yes	Yes, in humans	Yes
Parvovirus B19	Respiratory; transplacental	No	No	No

Important Properties

Adenoviruses are **nonenveloped** viruses with double-stranded 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.

Summary of Replicative Cycle

After attachment to the cell surface via its fiber, the virus penetrates and uncoats, and the viral DNA moves to the nucleus. Host cell DNA-dependent RNA polymerase transcribes the early genes, and splicing enzymes remove the RNA representing the introns, resulting in functional mRNA. (Note that introns and exons, which are common in eukaryotic DNA, were first described for adenovirus DNA.) Early mRNA is translated into nonstructural proteins in the cytoplasm. After viral DNA replication in the nucleus, late mRNA is transcribed and then translated into structural virion proteins. Viral assembly occurs in the nucleus, and the virus is released by lysis of the cell, not by budding.

Transmission & Epidemiology

Adenoviruses are transmitted by several mechanisms: **aerosol** droplet, **fecal–oral** route, and **direct inoculation** of 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. Certain serotypes are associated with specific syndromes; e.g., types 3, 4, 7, and 21 cause respiratory diseases, especially in military recruits; types 8 and 19 cause epidemic keratoconjunctivitis; types 11 and 21 cause hemorrhagic cystitis; and types 40 and 41 cause infantile gastroenteritis.

Pathogenesis & Immunity

Adenoviruses infect the mucosal epithelium of several organs, e.g., the **respiratory tract** (both upper and lower), the **gastrointestinal tract,** and the **conjunctivas.** Immunity based on neutralizing antibody is type-specific and lifelong.

In addition to acute infection leading to death of the cells, adenoviruses cause a latent infection, particularly in the adenoidal and tonsillar tissues of the throat. In fact, these viruses were named for the adenoids, from which they were first isolated in 1953.

Clinical Findings

In the upper respiratory tract, adenoviruses cause such infections as pharyngitis, pharyngoconjunctival fever, and acute respiratory disease, characterized by fever, sore throat, coryza (runny nose), and conjunctivitis. In the lower respiratory tract, they cause bronchitis and atypical pneumonia. Hematuria and dysuria are prominent in hemorrhagic cystitis. Gastroenteritis with nonbloody diarrhea occurs mainly in children younger than 2 years of age. Most adenovirus infections resolve spontaneously. Approximately half of all adenovirus infections are asymptomatic.

Laboratory Diagnosis

- Detection of Antigen - a rapid diagnosis can be made by the detection of adenovirus antigen from nasopharyngeal aspirates and throat washings.
- Virus Isolation - virus may be readily isolated from nasopharyngeal aspirates, throat swabs, and faeces. cytopathic effect (roundish cells)
- Serology - a retrospective diagnosis may be made by serology. CFT most widely used.
- diagnosis: EM, ELISA or latex agglutination

Treatment: There is no antiviral therapy.

Prevention: Three live, nonattenuated vaccines against serotypes 4, 7, and 21 are available but are used only by the military. Each of the three vaccines is monovalent, i.e., each contains only one serotype. The viruses are administered separately because they interfere with each other when given together. The vaccines are delivered in an enteric-coated capsule, which protects the live virus from inactivation by stomach acid. The virus infects the gastrointestinal tract, where it causes an asymptomatic infection and induces immunity to respiratory disease. This vaccine is not available for civilian use.

Epidemic keratoconjunctivitis is an iatrogenic disease, preventable by strict asepsis and hand washing by health care personnel who examine eyes.

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.

Summary of Replicative Cycle: After adsorption to host cell receptors, the virion penetrates and moves to the nucleus, where replication occurs. The single-stranded genome DNA has "hairpin" loops at both of its ends that provide double-stranded areas for the cellular DNA polymerase to initiate the synthesis of the progeny genomes. The viral mRNA is synthesized by cellular RNA polymerase from the double-stranded DNA intermediate. The progeny virions are assembled in the nucleus. B19 virus replicates only when a cell is in S phase, which explains why the virus replicates in red cell precursors but not in mature red cells.

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.Humans are the natural reservoir; animals are not a source of human infection.

Pathogenesis & Immunity: B19 virus infects primarily two types of cells: **red blood cell precursors** (erythroblasts) in the bone marrow, which accounts for the aplastic anemia, and endothelial cells in the blood vessels, which accounts, in part, for the rash associated with erythema infectiosum. Immune complexes composed of virus and IgM or IgG also contribute to the pathogenesis of the rash and to the arthritis that is seen in some adults infected with B19 virus. Infection provides lifelong immunity against reinfection.

Hydrops fetalis manifests as massive edema of the fetus. This is secondary to congestive heart failure precipitated by severe anemia caused by the death of parvovirus B19—infected erythroblasts in the fetus.

Clinical Findings: There are five important clinical presentations.

Erythema Infectiosum (Slapped Cheek Syndrome, Fifth Disease); This is a mild disease, primarily of childhood, characterized by a bright red rash that is most prominent on the cheeks, accompanied by low-grade fever, runny nose (coryza), and sore throat. A "lacy," less intense, erythematous rash appears on the body. The symptoms resolve in about 1 week.

The disease in children is also called fifth disease. The five other macular or maculopapular rash diseases of childhood are measles, rubella, varicella, scarlet fever, and roseola (harpers 6).

Aplastic Anemia: Children with chronic anemia, such as sickle cell anemia, thalassemia, and spherocytosis, can have transient but severe aplastic anemia (aplastic crisis) when infected with B19 virus. People with normal red blood cells do not have clinically apparent anemia, although their red blood cell precursors are infected.

Fetal Infections; If a woman is infected with B19 virus during the first or second trimester of pregnancy, the virus may cross the placenta and infect the fetus. Infection during the first trimester is associated with fetal death, whereas infection during the second trimester leads to **hydrops fetalis.** Third-trimester infections do not result in important clinical findings. B19 virus is not a common cause of congenital abnormalities probably because the fetus dies when infected early in pregnancy.

Arthritis; Parvovirus B19 infection in adults, especially women, can cause arthritis mainly involving the small joints of the hands and feet bilaterally. It resembles rheumatoid arthritis. Other viral infections that cause an immune-complex–related arthritis include hepatitis B and rubella.

Chronic B19 Infection; People with immunodeficiencies, especially HIV-infected, chemotherapy, or transplant patients, can have chronic anemia, leukopenia, or thrombocytopenia as a result of chronic B19 infection.

Laboratory Diagnosis

Fifth disease and aplastic anemia are usually diagnosed by detecting IgM antibodies. B19 virus can be isolated from throat swabs, but this is not usually done. In immunocompromised patients, antibodies may not be detectable; therefore, viral DNA in the blood can be assayed by polymerase chain reaction (PCR) methods. Fetal infection can be determined by PCR analysis of amniotic fluid.

Treatment & Prevention; There is no specific treatment of B19 infection. Pooled immune globulins may have a beneficial effect on chronic B19 infection in patients with immunodeficiencies. There is no vaccine or chemoprophylaxis.