Adenoviruses are medium-sized (90–100 nm), no enveloped (naked) icosahedra viruses composed of a nucleocapsid and a double-stranded linear DNA genome. There are over 52 different serotypes in humans, which are responsible for 5–10% of upper respiratory infections in children, and many infections in adults as well.

Viruses of the family Adenoviridae infect various species of animals, including humans. Adenoviruses were first isolated in human adenoids, from which the name is derived, and are classified as group I under the Baltimore classification scheme.

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Virology

Classification

This family contains the following genera:

- Genus Aviadenovirus; type species: Fowl adenovirus A
- Genus Atadenovirus; type species: Ovine adenovirus D
- Genus Mast adenovirus; type species: Human adenovirus C; others include AD-36
- Genus Siadenovirus; type species: Frog adenovirus
Diversity

Classification of Adenoviridae can be complex.

In humans, there are 51 immunologically distinct human adenovirus serotypes (1-51) in six species (A-F).

- A: 12, 18, 31
- B: 3, 7, 11, 14, 16, 34, 35, 50
- C: 1, 2, 5, 6
- D: 8, 9, 10, 13, 15, 17, 19, 20, 22, 23, 24, 25, 26, 27, 28, 29, 30, 32, 33, 36, 37, 38, 39, 42, 43, 44, 45, 46, 47, 48, 49, 51
- E: 4
- F: 40, 41

Different serotypes are associated with different conditions:

- respiratory disease (mainly species HadV-B and C)
- conjunctivitis (Had-B and D)
- gastroenteritis (Had-F serotypes 40 and 41)

When not restricting the subject to human viruses, Adenoviridae can be divided into four genera: Mast adenovirus, Aviadenovirus, Atadenovirus, and Siadenovirus.

Structure

Adenoviruses represent the largest no enveloped viruses, because they are the maximum size able to be transported through the end some (i.e. envelope fusion is not necessary). The virion also has a unique "spike" or fiber associated with each pennon base of the capsid (see picture below) that aids in attachment to the host cell via the coxsackie-adenovirus receptor on the surface of the host cell.

Genome

Schematic diagram of the linear adenovirus genome, showing Early genes (E) and Late genes (L).
The adenovirus genome is linear, non-segmented double stranded (ds) DNA which is around 30–38 Kbp. This allows the virus to theoretically carry 30 to 40 genes. Although this is significantly larger than other viruses in its Baltimore group it is still a very simple virus and is heavily reliant on the host cell for survival and replication. An interesting feature of this viral genome is that it has a terminal 55 kDa protein associated with each of the 5’ ends of the linear dsDNA, these are used as primers in viral replication and ensure that the ends of the virus’ linear genome are adequately replicated.

**Replication**

Adenoviruses possess a linear dsDNA genome and are able to replicate in the nucleus of mammalian cells using the host’s replication machinery.

The structure of adenovirus. 1 = pennon capsomeres 2 = hexon capsomeres, and 3= viral genome (linear dsDNA)

Entry of adenoviruses into the host cell involves two sets of interactions between the virus and the host cell. Entry into the host cell is initiated by the knob domain of the fiber protein binding to the cell receptor. The two currently established receptors are: CD46 for the group B human adenovirus serotypes and the coxsackievirus adenovirus receptor (CAR) for all other serotypes. There are some reports suggesting MHC molecules and sialic acid residues functioning in this capacity as well. This is followed by a secondary interaction, where a specialized motif in the pennon base protein interacts with an integrin molecule. It is the co-receptor interaction that stimulates internalization of the adenovirus. This co-receptor molecule is αv integrin. Binding to αv integrin results in endocytosis of the virus particle via clathrin-coated pits. Attachment to αv integrin stimulates cell signaling and thus induces actin polymerization resulting in entry of the virion into the host cell within an endosome.²

Once the virus has successfully gained entry into the host cell the end some acidifies, which alters virus topology by causing capsid components to dissociate. These changes as well as the toxic nature of the pentons results in the release of the virion into the cytoplasm. With the help of cellular microtubules the virus is transported to the nuclear pore complex whereby the adenovirus particle disassembles. Viral DNA is subsequently released which can enter the nucleus via the nuclear pore.³ After this the DNA associates with histone molecules. Thus viral gene expression can occur and new virus particles can be generated.

The adenovirus life cycle is separated, by the DNA replication process, into two phases: an early and a late phase. In both phases a primary transcript is generated.
which is alternatively spliced to generate monocistronic mRNAs compatible with the host’s ribosome, allowing for the products to be translated.

The early genes are responsible for expressing mainly non-structural, regulatory proteins. The goal of these proteins is threefold: to alter the expression of host proteins that are necessary for DNA synthesis; to activate other virus genes (such as the virus-encoded DNA polymerase); and to avoid premature death of the infected cell by the host-immune defenses (blockage of apoptosis, blockage of interferon activity, and blockage of MHC class I translocation and expression).

Some adenoviruses under specialized conditions can transform cells using their early gene products. E1a (binds Retinoblastoma tumor suppressor protein) has been found to immortalize primary cells in vitro allowing E1b (binds p53 tumor suppressor) to assist and stably transform the cells. Nevertheless, they are reliant upon each other to successfully transform the host cell and form tumors.

DNA replication separates the early and late phases. Once the early genes have liberated adequate virus proteins, replication machinery and replication substrates, replication of the adenovirus genome can occur. A terminal protein that is covalently bound to the 5’ end of the adenovirus genome acts as a primer for replication. The viral DNA polymerase then uses a strand displacement mechanism, as opposed to the conventional Okazaki fragments used in mammalian DNA replication, to replicate the genome.

The late phase of the adenovirus life cycle is focused on producing sufficient quantities of structural protein to pack all the genetic material produced by DNA replication. Once the viral components have successfully been replicated the virus is assembled into its protein shells and released from the cell as a result of virally induced cell lysis.

**Epidemiology**

**Transmission**

Adenoviruses are unusually stable to chemical or physical agents and adverse pH conditions, allowing for prolonged survival outside of the body and water. Adenoviruses are primarily spread via respiratory droplets, however they can also be spread by fecal routes as well.

**Humans**

**Animals**

Two types of canine adenoviruses are well known, type 1 and 2. Type 1 causes infectious canine hepatitis, a potentially fatal disease involving vasculitis and hepatitis. Type 1 infection can also cause respiratory and eye infections. *Canine adenovirus* 2 (CA) is one of the potential causes of kennel cough. Core vaccines for dogs include attenuated live CA, which produces immunity to CA-1 and
CAdV-2. CAdV-1 was initially used in a vaccine for dogs, but corneal edema was a common complication.[4]

Adenoviruses are also known to cause respiratory infections in horses, cattle, pigs, sheep, and goats. Equine adenovirus 1 can also cause fatal disease in immunocompromised Arabian foals, involving pneumonia and destruction of pancreatic and salivary gland tissue.[4]

**Prevention**

In the past, US military recruits were vaccinated against two serotypes of adenoviruses, with a corresponding decrease in illnesses caused by those serotypes. The vaccine is no longer manufactured, and there are currently no vaccines available to protect against the adenovirus.

Good hygiene, including hand washing, is still the best way to avoid picking up the adenovirus from an infected person.

**Infections**

Most infections with adenovirus result in infections of the upper respiratory tract. Adenovirus infections often show up as conjunctivitis, tonsilitis (which may look exactly like strep throat and cannot be distinguished from strep except by throat culture), an ear infection, or croup. Adenoviruses can also cause gastroenteritis (stomach flu). A combination of conjunctivitis and tonsilitis is particularly common with adenovirus infections. Some children (especially small ones) can develop adenovirus bronchiolitis or pneumonia, both of which can be severe. In babies, adenoviruses can also cause coughing fits that look almost exactly like whooping cough. Adenoviruses can also cause viral meningitis or encephalitis. Rarely, adenovirus can cause cystitis (inflammation of the urinary bladder—a form of urinary tract infection—with blood in the urine).

Most people recover from adenovirus infections by themselves, but people with immunodeficiency sometimes die of adenovirus infections, and—rarely—even previously healthy people can die of these infections.[5]

Adenoviruses are often transmitted by coughed-out droplets, but can also be transmitted by contact with an infected person, or by virus particles left on objects such as towels and faucet handles. Some people with adenovirus gastroenteritis may shed the virus in their stools for months after getting over the symptoms. The virus can be passed from one person to another through some sexual practices, and through water in swimming pools that do not have enough chlorine in them. As with many other illnesses, good hand washing is one way to lessen the spread of adenoviruses from one person to another. Heat and bleach will kill adenoviruses on objects.

**Treatment**
There are no antiviral drugs to treat adenoviral infections, so treatment is largely directed at the symptoms (such as acetaminophen for fever). A doctor may give antibiotic eye drops for conjunctivitis, since it takes a while to test to see if the eye infection is bacterial or viral and to help prevent secondary bacterial infections.

References

4. ^a^b Fenner, Frank J.; Gibbs, E. Paul J.; Murphy, Frederick A.; Rott, Rudolph; Studdert, Michael J.; White, David O. (1993). *Veterinary Virology (2nd ed.)*. Academic Press, Inc. ISBN 0-12-253056-X.