



# Viruses

For Grades 9-12

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5 ARTICLES

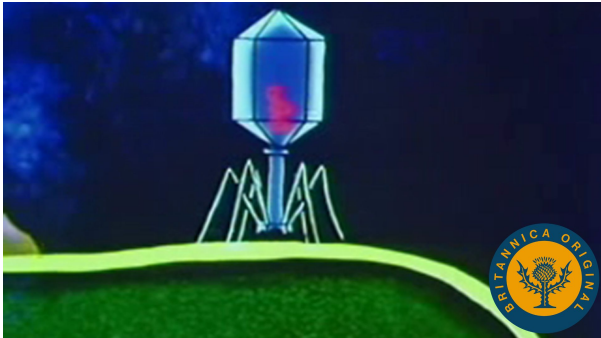
3 IMAGES

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## ARTICLE

# bacteriophage

also called phage or bacterial virus, any of a group of viruses that infect bacteria. Bacteriophages were discovered independently by Frederick W. Twort in Great Britain (1915) and Félix d'Hérelle in France (1917). D' Hérelle coined the term *bacteriophage*, meaning "bacteria eater," to describe the agent's bacteriocidal ability. Bacteriophages also infect the single-celled prokaryotic organisms known as archaea.



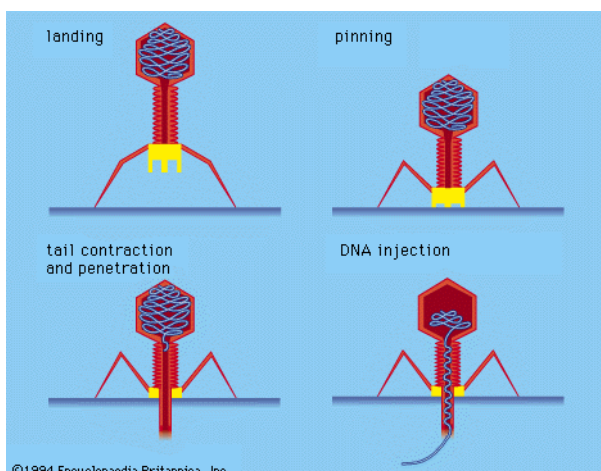
The cycle of infection results in the death of the host cell and the release of many virus particles, called virions.

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## Characteristics of bacteriophages

Thousands of varieties of phages exist, each of which may infect only one type or a few types of bacteria or archaea. Phages are classified in a number of virus families; some examples include Inoviridae, Microviridae, Rudiviridae, and Tectiviridae. Like all viruses, phages are simple organisms that consist of a core of genetic material (nucleic acid) surrounded by a protein capsid. The nucleic acid may be either DNA or RNA and may be double-stranded or single-stranded. There are three basic structural forms of phage: an icosahedral (20-sided) head with a tail, an icosahedral head without a tail, and a filamentous form.

## Life cycles of bacteriophages



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General structure of T4 bacteriophage and a model of its mode of attachment to, and injection of its DNA into, a bacterial cell.

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During infection a phage attaches to a bacterium and inserts its genetic material into the cell. A phage then usually follows one of two life cycles, lytic (virulent) or lysogenic (temperate). Lytic phages take over the machinery of the cell to make phage components. They then destroy, or lyse, the cell, releasing new phage particles. Lysogenic phages incorporate their nucleic acid into the chromosome of the host cell and replicate with it as a unit without destroying the cell. Under certain conditions lysogenic phages can be induced to follow a lytic cycle.

Other life cycles, including pseudolysogeny and chronic infection, also exist. In pseudolysogeny a bacteriophage enters a cell but neither co-opts cell-replication machinery nor integrates stably into the host genome. Pseudolysogeny occurs when a host cell encounters unfavourable growth conditions and appears to play an important role in phage survival by enabling the preservation of the phage genome until host growth conditions have become advantageous again. In chronic infection new phage particles are produced continuously over long periods of time but without apparent cell killing.

## Role in laboratory research

Phages have played an important role in laboratory research. The first phages studied were those designated type 1 (T1) to type 7 (T7). The T-even phages, T2, T4, and T6, were used as model systems for the study of virus multiplication. In 1952 Alfred Day Hershey and Martha Chase used the T2 bacteriophage in a famous experiment in which they demonstrated that only the nucleic acids of phage molecules were required for their replication within bacteria. The results of the experiment supported the theory that DNA is the genetic material. For his work with bacteriophages, Hershey was awarded the Nobel Prize for Physiology or Medicine in 1969. He shared the award with biologists Salvador Luria and Max Delbrück, whose experiments with the T1 phage in 1943 (the fluctuation test) showed that phage resistance in bacteria was the product of spontaneous mutation and not a direct response to environmental factors. Certain phages, such as lambda, Mu, and M13, are used in recombinant DNA technology. The phage  $\phi$ X174 was the first entity to have its entire nucleotide sequence determined, a feat that was accomplished by Frederick Sanger and colleagues in 1977.

In the 1980s American biochemist George P. Smith developed a technology known as phage display, which allowed for the generation of engineered proteins. Such proteins were produced by fusing foreign or engineered DNA fragments into phage gene III. Gene III encodes a protein expressed on the phage virion surface. Thus, gene III fusion proteins taken up by phages were displayed on the surfaces of virion particles. Researchers could then use antibodies developed to recognize the foreign protein fragment to purify fusion phage cultures, thereby effectively amplifying the foreign gene sequence for further study.

British biochemist Gregory P. Winter subsequently refined phage display technology for the development of human antibody proteins. Such proteins could be used to treat diseases in humans with less risk of inducing potentially dangerous immune reactions compared with previous therapeutic antibodies derived from animals. Adalimumab (Humira), used for the treatment of rheumatoid arthritis, was the first fully human antibody made via phage display to be approved by the U.S. Food and Drug Administration (approved in 2002). For their discoveries relating to phage display, Smith and Winter were awarded a share of the 2018 Nobel Prize in Chemistry.

## Phage therapy

Soon after making their discovery, Twort and d'Hérelle began to use phages in treating human bacterial diseases such as bubonic plague and cholera. Phage therapy initially was not successful. After the discovery of

antibiotics in the 1940s, it was virtually abandoned in many places, with the exception of eastern Europe, where it became widely used. In the early 21st century, with the rise of antibiotic-resistant bacteria, the therapeutic potential of phages received renewed attention in other parts of the world.

Because each phage targets a specific strain of bacteria, phage therapy is inherently a precision tool, relative to broad-spectrum antibiotics. In particular, the approach has shown promise in the treatment of drug-resistant infections involving *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Staphylococcus aureus*. However, while positive outcomes in antibiotic-resistant infections have been documented in case studies, animal models, and small clinical trials, phage therapy is still considered experimental in many countries, including the United States. Large-scale, controlled studies and established manufacturing standards are needed to confirm safety, efficacy, and best practices.

The Editors of Encyclopædia Britannica

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## ARTICLE

# herpesvirus

any virus belonging to the family Herpesviridae. These viruses are pathogenic (disease-causing) in a wide variety of animals, causing disease in humans, monkeys, birds, frogs, and fish.

The herpesviruses are characterized structurally by virions (virus particles) measuring approximately 150–200 nm (1 nm = 10<sup>-9</sup> metre) in diameter. The outer surface of the capsid (the protein shell surrounding the viral nucleic acids) is icosahedral and is composed of 162 capsomeres (capsid subunits). The capsid itself is surrounded by a lipid envelope containing glycoprotein spikes. Herpesviruses have genomes consisting of linear double-stranded DNA, which is integrated into the host cell chromosome upon infection.

There are three known subfamilies of herpesviruses: Alphaherpesvirinae, Betaherpesvirinae, and Gammaherpesvirinae. Alphaherpesvirinae contains the human herpes simplex viruses types 1 and 2, which are grouped in the genus *Simplexvirus*, along with bovine mamillitis virus and spider monkey herpesvirus. Other genera in the subfamily include *Varicellovirus*, which contains pseudorabies virus, equine herpesvirus, and varicella-zoster virus (the causative agent of chickenpox); *Mardivirus*, which contains Marek's disease viruses types 1 and 2 of chickens and turkey herpesvirus; and *Iltovirus*, which contains gallid herpesvirus 1. The alphaherpesviruses are distinguished from viruses of the other subfamilies by their fast rate of replication.

Betaherpesvirinae, members of which are noted for their relatively slow replication cycles, contains human, rhesus monkey, African green monkey, and chimpanzee cytomegaloviruses (genus *Cytomegalovirus*). Members of subfamily Gammaherpesvirinae, which is composed of the genera *Lymphocryptovirus*, *Macavirus*, *Percavirus*, and *Rhadinovirus*, include Epstein-Barr virus, baboon, orangutan, and gorilla herpesviruses, and herpesvirus saimiri. The replication rate of gammaherpesviruses is variable.

Among the best-characterized herpesviruses are those affecting humans, namely herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2). Whereas HSV-1 is transmitted orally and is responsible for cold sores and fever blisters, typically occurring around the mouth, HSV-2 is transmitted sexually and is the main cause of the condition known as genital herpes. HSV-1 may also infect the eye, causing corneal ulcers and visual impairment. Both viruses are highly contagious. HSV-2 may be transmitted by individuals who are lifelong carriers but who remain asymptomatic (and may not even know they are infected). HSV-2 infections have also been associated with the development of cervical cancer.

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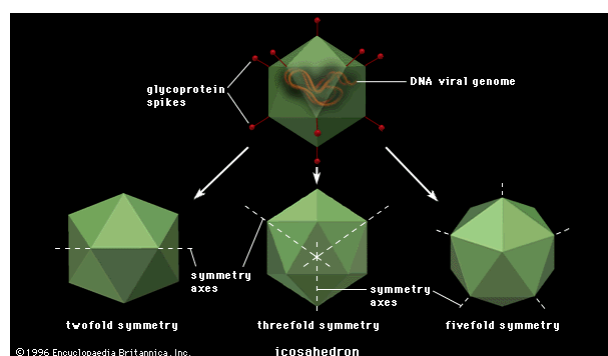
"Herpesvirus." *Britannica LaunchPacks: Viruses*, Encyclopædia Britannica, 22 Feb. 2010. packs.eb.com. Accessed 4 May. 2025.

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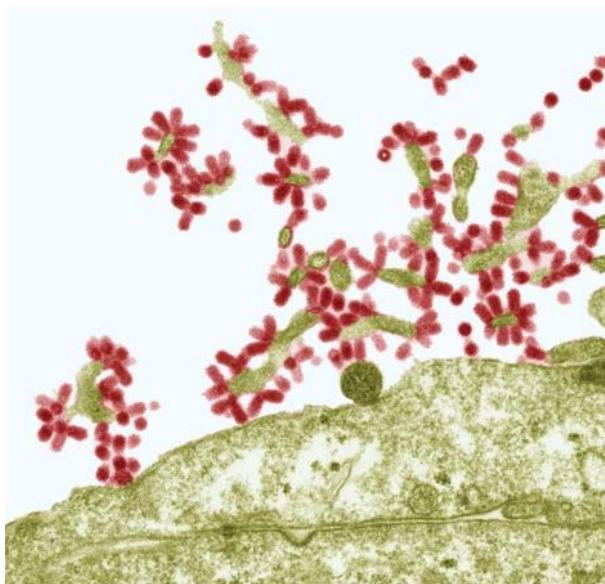
# virion

an entire virus particle, consisting of an outer protein shell called a capsid and an inner core of nucleic acid (either ribonucleic or deoxyribonucleic acid—RNA or DNA). The core confers infectivity, and the capsid provides specificity to the virus. In some virions the capsid is further enveloped by a fatty membrane, in which case the virion can be inactivated by exposure to fat solvents such as ether and chloroform. Many virions are spheroidal—actually icosahedral—the capsid having 20 triangular faces, with regularly arranged units called capsomeres, two to five or more along each side; and the nucleic acid is densely coiled within. Other virions have a capsid consisting of an irregular number of surface spikes and the nucleic acid loosely coiled within. Virions of most plant viruses are rod-shaped; the capsid is a naked cylinder (lacking a fatty membrane) within which lies a straight or helical rod of nucleic acid.



A virus icosahedron (20-sided structure) shown in the (left) twofold, (centre) threefold, and (right) fivefold axes of symmetry. Edges of the upper and lower surfaces are drawn in solid and broken lines, respectively.

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A coloured transmission electron micrograph showing influenza viruses (red) at the outer surface of a host cell.

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## ARTICLE

# virology

branch of microbiology that deals with the study of viruses.

Although diseases caused by viruses have been known since the 1700s and cures for many were (somewhat later) effected, the causative agent was not closely examined until 1892, when a Russian bacteriologist, D. Ivanovski, observed that the causative agent (later proved to be a virus) of tobacco mosaic disease could pass through a porcelain filter impermeable to bacteria. Modern virology began when two bacteriologists, Frederick William Twort in 1915 and Félix d'Hérelle in 1917, independently discovered the existence of bacteriophages (viruses that infect bacteria).

Direct visualization of viruses became possible after the electron microscope was introduced about 1940. In 1935 tobacco mosaic virus became the first virus to be crystallized; in 1955 the poliomyelitis virus was crystallized. (A virus "crystal" consists of several thousand viruses and, because of its purity, is well suited for chemical studies.) Virology is a discipline of immediate interest because many human diseases, including smallpox, influenza, the common cold, and AIDS, as well as a host of economically important plant and animal diseases, are caused by viruses.

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"Virology." *Britannica LaunchPacks: Viruses*, Encyclopædia Britannica, 20 Jul. 1998. packs.eb.com. Accessed 4 May. 2025.

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## ARTICLE

# virus

**Britannica Note:**

Viruses are not alive but they affect living things.

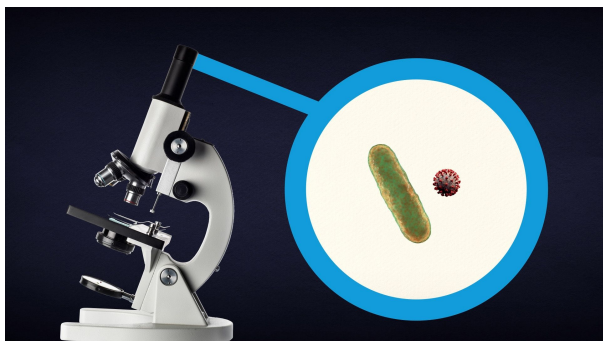
infectious agent of small size and simple composition that can multiply only in living cells of animals, plants, or bacteria. The name is from a Latin word meaning "slimy liquid" or "poison."



*Ebolavirus.*

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The earliest indications of the biological nature of viruses came from studies in 1892 by the Russian scientist Dmitry I. Ivanovsky and in 1898 by the Dutch scientist Martinus W. Beijerinck. Beijerinck first surmised that the virus under study was a new kind of infectious agent, which he designated *contagium vivum fluidum*, meaning that it was a live, reproducing organism that differed from other organisms. Both of these investigators found that a disease of tobacco plants could be transmitted by an agent, later called tobacco mosaic virus, passing through a minute filter that would not allow the passage of bacteria. This virus and those subsequently isolated would not grow on an artificial medium and were not visible under the light microscope. In independent studies in 1915 by the British investigator Frederick W. Twort and in 1917 by the French Canadian scientist Félix H. d' Hérelle, lesions in cultures of bacteria were discovered and attributed to an agent called bacteriophage ("eater of bacteria"), now known to be viruses that specifically infect bacteria.



Knowing the difference isn't just a technical distinction—it can save lives.

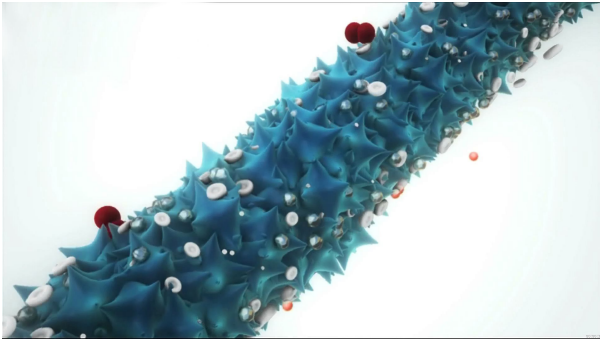
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The unique nature of these agents meant that new methods and alternative models had to be developed to study and classify them. The study of viruses confined exclusively or largely to humans, however, posed the formidable problem of finding a susceptible animal host. In 1933 the British investigators Wilson Smith, Christopher H. Andrewes, and Patrick P. Laidlaw were able to transmit influenza to ferrets, and the influenza virus was subsequently adapted to mice. In 1941 the American scientist George K. Hirst found that influenza virus grown in tissues of the chicken embryo could be detected by its capacity to agglutinate (draw together) red blood cells.

A significant advance was made by the American scientists John Enders, Thomas Weller, and Frederick Robbins, who in 1949 developed the technique of culturing cells on glass surfaces; cells could then be infected with the viruses that cause polio (poliovirus) and other diseases. (Until this time, the poliovirus could be grown only in the brains of chimpanzees or the spinal cords of monkeys.) Culturing cells on glass surfaces opened the way for diseases caused by viruses to be identified by their effects on cells (cytopathogenic effect) and by the presence of antibodies to them in the blood. Cell culture then led to the development and production of vaccines (preparations used to elicit immunity against a disease) such as the poliovirus vaccine.

Scientists were soon able to detect the number of bacterial viruses in a culture vessel by measuring their ability to break apart (lyse) adjoining bacteria in an area of bacteria (lawn) overlaid with an inert gelatinous substance called agar—viral action that resulted in a clearing, or “plaque.” The American scientist Renato Dulbecco in 1952 applied this technique to measuring the number of animal viruses that could produce plaques in layers of adjoining animal cells overlaid with agar. In the 1940s the development of the electron microscope permitted individual virus particles to be seen for the first time, leading to the classification of viruses and giving insight into their structure.

Advancements that have been made in chemistry, physics, and molecular biology since the 1960s have revolutionized the study of viruses. For example, electrophoresis on gel substrates gave a deeper understanding of the protein and nucleic acid composition of viruses. More-sophisticated immunologic procedures, including the use of monoclonal antibodies directed to specific antigenic sites on proteins, gave a better insight into the structure and function of viral proteins. The progress made in the physics of crystals that could be studied by X-ray diffraction provided the high resolution required to discover the basic structure of minute viruses. Applications of new knowledge about cell biology and biochemistry helped to determine how viruses use their host cells for synthesizing viral nucleic acids and proteins.



Learn how a benign bacterial virus can be used to improve the performance of lithium-oxygen storage batteries.

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The revolution that took place in the field of molecular biology allowed the genetic information encoded in nucleic acids of viruses—which enables viruses to reproduce, synthesize unique proteins, and alter cellular functions—to be studied. In fact, the chemical and physical simplicity of viruses has made them an incisive experimental tool for probing the molecular events involved in certain life processes. Their potential ecological significance was realized in the early 21st century, following the discovery of giant viruses in aquatic environments in different parts of the world.

This article discusses the fundamental nature of viruses: what they are, how they cause infection, and how they may ultimately cause disease or bring about the death of their host cells. For more-detailed treatment of specific viral diseases, see *infection*.

## General features

### Definition

Viruses occupy a special taxonomic position: they are not plants, animals, or prokaryotic bacteria (single-cell organisms without defined nuclei), and they are generally placed in their own kingdom. In fact, viruses should not even be considered organisms, in the strictest sense, because they are not free-living—i.e., they cannot reproduce and carry on metabolic processes without a host cell.

All true viruses contain nucleic acid—either DNA (deoxyribonucleic acid) or RNA (ribonucleic acid)—and protein. The nucleic acid encodes the genetic information unique for each virus. The infective, extracellular (outside the cell) form of a virus is called the virion. It contains at least one unique protein synthesized by specific genes in the nucleic acid of that virus. In virtually all viruses, at least one of these proteins forms a shell (called a capsid) around the nucleic acid. Certain viruses also have other proteins internal to the capsid; some of these proteins act as enzymes, often during the synthesis of viral nucleic acids. Viroids (meaning “viruslike”) are disease-causing organisms that contain only nucleic acid and have no structural proteins. Other viruslike particles called prions are composed primarily of a protein tightly complexed with a small nucleic acid molecule. Prions are very resistant to inactivation and appear to cause degenerative brain disease in mammals, including humans.

Viruses are quintessential parasites; they depend on the host cell for almost all of their life-sustaining functions. Unlike true organisms, viruses cannot synthesize proteins, because they lack ribosomes (cell organelles) for the translation of viral messenger RNA (mRNA; a complementary copy of the nucleic acid of the nucleus that associates with ribosomes and directs protein synthesis) into proteins. Viruses must use the ribosomes of their host cells to translate viral mRNA into viral proteins.

Viruses are also energy parasites; unlike cells, they cannot generate or store energy in the form of adenosine triphosphate (ATP). The virus derives energy, as well as all other metabolic functions, from the host cell. The

invading virus uses the nucleotides and amino acids of the host cell to synthesize its nucleic acids and proteins, respectively. Some viruses use the lipids and sugar chains of the host cell to form their membranes and glycoproteins (proteins linked to short polymers consisting of several sugars).

The true infectious part of any virus is its nucleic acid, either DNA or RNA but never both. In many viruses, but not all, the nucleic acid alone, stripped of its capsid, can infect (transfect) cells, although considerably less efficiently than can the intact virions.

The virion capsid has three functions: (1) to protect the viral nucleic acid from digestion by certain enzymes (nucleases), (2) to furnish sites on its surface that recognize and attach (adsorb) the virion to receptors on the surface of the host cell, and, in some viruses, (3) to provide proteins that form part of a specialized component that enables the virion to penetrate through the cell surface membrane or, in special cases, to inject the infectious nucleic acid into the interior of the host cell.

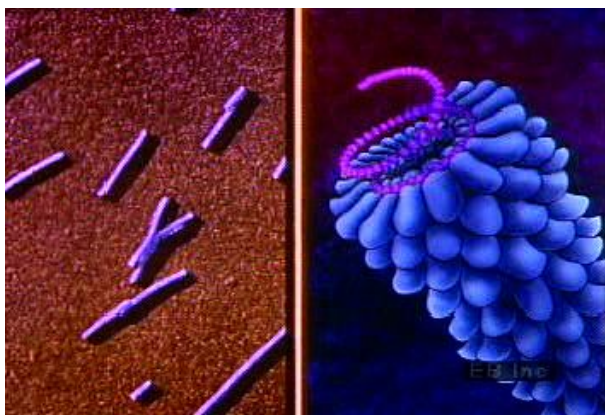
## Host range and distribution

Logic originally dictated that viruses be identified on the basis of the host they infect. This is justified in many cases but not in others, and the host range and distribution of viruses are only one criterion for their classification. It is still traditional to divide viruses into three categories: those that infect animals, plants, or bacteria.

Virtually all plant viruses are transmitted by insects or other organisms (vectors) that feed on plants. The hosts of animal viruses vary from protozoans (single-celled animal organisms) to humans. Many viruses infect either invertebrate animals or vertebrates, and some infect both. Certain viruses that cause serious diseases of animals and humans are carried by arthropods. These vector-borne viruses multiply in both the invertebrate vector and the vertebrate host.

Certain viruses are limited in their host range to the various orders of vertebrates. Some viruses appear to be adapted for growth only in ectothermic vertebrates (animals commonly referred to as cold-blooded, such as fishes and reptiles), possibly because they can reproduce only at low temperatures. Other viruses are limited in their host range to endothermic vertebrates (animals commonly referred to as warm-blooded, such as mammals).

## Size and shape



Animation and microphotography illustrating the structural diversity of viruses.

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The amount and arrangement of the proteins and nucleic acid of viruses determine their size and shape. The nucleic acid and proteins of each class of viruses assemble themselves into a structure called a nucleoprotein, or

nucleocapsid. Some viruses have more than one layer of protein surrounding the nucleic acid; still others have a lipoprotein membrane (called an envelope), derived from the membrane of the host cell, that surrounds the nucleocapsid core. Penetrating the membrane are additional proteins that determine the specificity of the virus to host cells. The protein and nucleic acid constituents have properties unique for each class of virus; when assembled, they determine the size and shape of the virus for that specific class. The genomes of Mimiviruses and Pandoraviruses, which are some of the largest known viruses, range from 1 to 2.5 Mb (1 Mb = 1,000,000 base pairs of DNA).

Most viruses vary in diameter from 20 nanometres (nm; 0.0000008 inch) to 250–400 nm; the largest, however, measure about 500 nm in diameter and are about 700–1,000 nm in length. Only the largest and most complex viruses can be seen under the light microscope at the highest resolution. Any determination of the size of a virus also must take into account its shape, since different classes of viruses have distinctive shapes.

Shapes of viruses are predominantly of two kinds: rods, or filaments, so called because of the linear array of the nucleic acid and the protein subunits; and spheres, which are actually 20-sided (icosahedral) polygons. Most plant viruses are small and are either filaments or polygons, as are many bacterial viruses. The larger and more-complex bacteriophages, however, contain as their genetic information double-stranded DNA and combine both filamentous and polygonal shapes. The classic T4 bacteriophage is composed of a polygonal head, which contains the DNA genome and a special-function rod-shaped tail of long fibres. Structures such as these are unique to the bacteriophages.

Animal viruses exhibit extreme variation in size and shape. The smallest animal viruses belong to the families Parvoviridae and Picornaviridae and measure about 20 nm and about 30 nm in diameter, respectively. Viruses of these two families are icosahedrons and contain nucleic acids with limited genetic information. Viruses of the family Poxviridae are about 250 to 400 nm in their longest dimension, and they are neither polygons nor filaments. Poxviruses are structurally more complex than simple bacteria, despite their close resemblance. Animal viruses that have rod-shaped (helical) nucleocapsids are those enclosed in an envelope; these viruses are found in the families Paramyxoviridae, Orthomyxoviridae, Coronaviridae, and Rhabdoviridae. Not all enveloped viruses contain helical nucleocapsids, however; those of the families Herpesviridae, Retroviridae, and Togaviridae have polygonal nucleocapsids. Most enveloped viruses appear to be spherical, although the rhabdoviruses are elongated cylinders.

The criteria used for classifying viruses into families and genera are primarily based on three structural considerations: (1) the type and size of their nucleic acid, (2) the shape and size of the capsids, and (3) the presence of a lipid envelope, derived from the host cell, surrounding the viral nucleocapsid.

## The nucleic acid

As is true in all forms of life, the nucleic acid of each virus encodes the genetic information for the synthesis of all proteins. In almost all free-living organisms, the genetic information is in the form of double-stranded DNA arranged as a spiral lattice joined at the bases along the length of the molecule (a double helix). In viruses, however, genetic information can come in a variety of forms, including single-stranded or double-stranded DNA or RNA.

The nucleic acids of virions are arranged into genomes. All double-stranded DNA viruses consist of a single large molecule, whereas most double-stranded RNA viruses have segmented genomes, with each segment usually representing a single gene that encodes the information for synthesizing a single protein. Viruses with single-

stranded genomic DNA are usually small, with limited genetic information. Some single-stranded DNA viruses are composed of two populations of virions, each consisting of complementary single-stranded DNA of polarity opposite to that of the other.

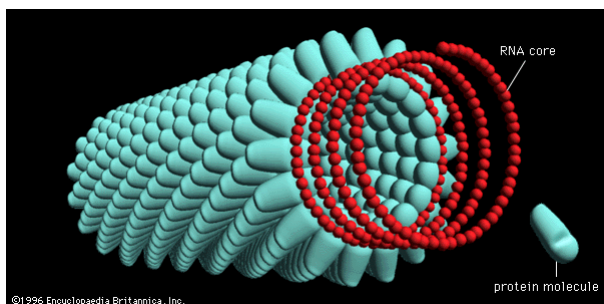
The virions of most plant viruses and many animal and bacterial viruses are composed of single-stranded RNA. In most of these viruses, the genomic RNA is termed a positive strand because the genomic RNA acts as mRNA for direct synthesis (translation) of viral protein. Several large families of animal viruses, and one that includes both plant and animal viruses (the Rhabdoviridae), however, contain genomic single-stranded RNA, termed a negative strand, which is complementary to mRNA. All of these negative-strand RNA viruses have an enzyme, called an RNA-dependent RNA polymerase (transcriptase), which must first catalyze the synthesis of complementary mRNA from the virion genomic RNA before viral protein synthesis can occur. These variations in the nucleic acids of viruses form one central criterion for classification of all viruses.

A distinctive large family of single-stranded RNA viruses is called Retroviridae; the RNA of these viruses is positive, but the viruses are equipped with an enzyme, called a reverse transcriptase, that copies the single-stranded RNA to form double-stranded DNA.

## The protein capsid

The protein capsid provides the second major criterion for the classification of viruses. The capsid surrounds the virus and is composed of a finite number of protein subunits known as capsomeres, which usually associate with, or are found close to, the virion nucleic acid.

There are two major classes of viruses based on the protein capsid: (1) those in which a single (or segmented) linear nucleic acid molecule with two free ends is essentially completely extended or somewhat coiled (a helix) and (2) those in which the nucleic acid, which may or may not be a covalently closed circle, is wound tightly into a condensed configuration, like a ball of yarn. These two classes of virus assume in the first case a long, extended rodlike structure and in the second case a symmetrical polygon.



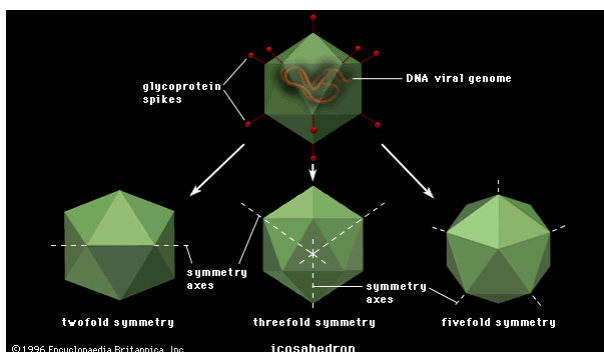
Schematic structure of the tobacco mosaic virus. The cutaway section shows the helical ribonucleic acid associated with protein molecules in a ratio of three nucleotides per protein molecule.

*Encyclopædia Britannica, Inc.*

By far the best-studied example of a helical rod-shaped virus is the tobacco mosaic virus, which was crystallized by Wendell Stanley in 1935. The tobacco mosaic virus contains a genome of single-stranded RNA encased by 2,130 molecules of a single protein; there are  $16\frac{1}{3}$  protein molecules for each turn of the RNA helix in the ratio of three nucleotides for each protein molecule.

Under the right environmental conditions, viral RNA and protein molecules in liquid suspension will assemble themselves into a perfectly formed and fully infectious virus. The length of the helical virus capsid is determined by the length of the nucleic acid molecule, which is the framework for the assembly of the capsid protein. The various helical viruses have different lengths and widths, depending on the size of the nucleic acid as well as on

the mass and shape of the protein molecule. Some of these helical viruses form rigid rods, while others form flexible rods, depending on the properties of the assembled proteins.



A virus icosahedron (20-sided structure) shown in the (left) twofold, (centre) threefold, and (right) fivefold axes of symmetry. Edges of the upper and lower surfaces are drawn in solid and broken lines, respectively.

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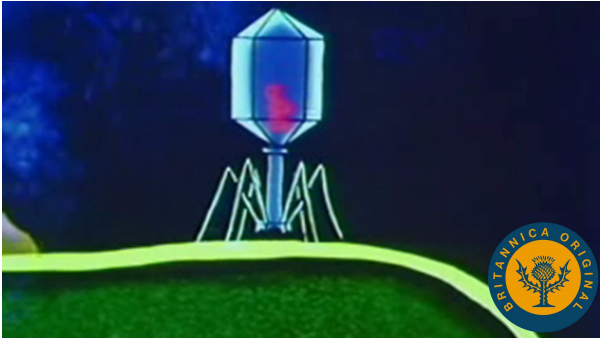
Polygonal viruses vary greatly in size, from 20 to 150 nm in diameter, essentially proportional to the size of the nucleic acid molecule coiled up inside the virion. Most, if not all, of the polygonal viruses are icosahedral; like a geodesic dome, they are formed by equilateral triangles, in this case 20. Each triangle is composed of protein subunits (capsomeres), often in the form of hexons (multiples of six) that are the building blocks of the capsid. There are 12 vertices (the apical junctions of these 20 triangles), each comprising a penton (five subunits). These icosahedral virions have three axes of fivefold, threefold, and twofold rotational symmetry. The number of capsomeres is a basis for taxonomic classification of these virus families. Certain icosahedral viruses, usually those that are more complex, contain internal proteins adhering to the nucleic acid that are not accessible at the surface of the virions.

## The lipoprotein envelope

Surrounding viruses of either helical or icosahedral symmetry are lipoprotein envelopes, unit membranes of two lipid layers interspersed with protein molecules (lipoprotein bilayer). These viral membranes are composed of phospholipids and neutral lipids (largely cholesterol) derived from cell membranes during the process known as budding. Virtually all proteins of the cell membrane, however, are replaced by proteins of viral origin during budding. Although all the viral envelope lipids originate from the cell, their relative proportions vary from those in the cell membrane because the viral proteins select only certain lipids during budding.

Associated with the virion membrane are “integral” glycoproteins, which completely traverse the lipid bilayer, and “peripheral” matrix proteins, which line the inner surface. The glycoproteins contain regions of amino acids that, in the first step of viral infection, recognize host-cell receptors. Matrix proteins appear to function in the selection of regions of the cell membrane to be used for the viral membrane, as well as to aid the virion in entering cells.

# The cycle of infection

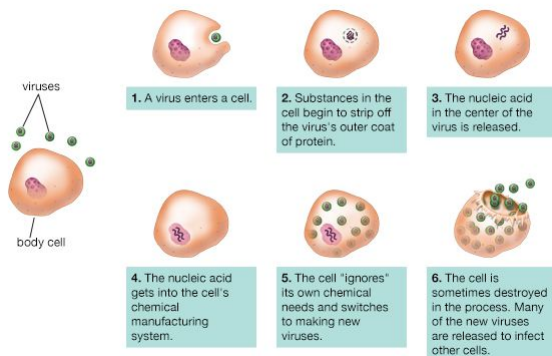


The cycle of infection results in the death of the host cell and the release of many virus particles, called virions.

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Viruses can reproduce only within a host cell. The parental virus (virion) gives rise to numerous progeny, usually genetically and structurally identical to the parent virus. The actions of the virus depend both on its destructive tendencies toward a specific host cell and on environmental conditions. In the vegetative cycle of viral infection, multiplication of progeny viruses can be rapid. This cycle of infection often results in the death of the cell and the release of many virus progeny. Certain viruses, particularly bacteriophages, are called temperate (or latent) because the infection does not immediately result in cell death. The viral genetic material remains dormant or is actually integrated into the genome of the host cell. Cells infected with temperate viruses are called lysogenic because the cells tend to be broken down when they encounter some chemical or physical factor, such as ultraviolet light. In addition, many animal and plant viruses, the genetic information of which is not integrated into the host DNA, may lie dormant in tissues for long periods of time without causing much, if any, tissue damage. Viral infection does not always result in cell death or tissue injury; in fact, most viruses lie dormant in tissue without ever causing pathological effects, or they do so only under other, often environmental, provocations.

How a virus invades a cell



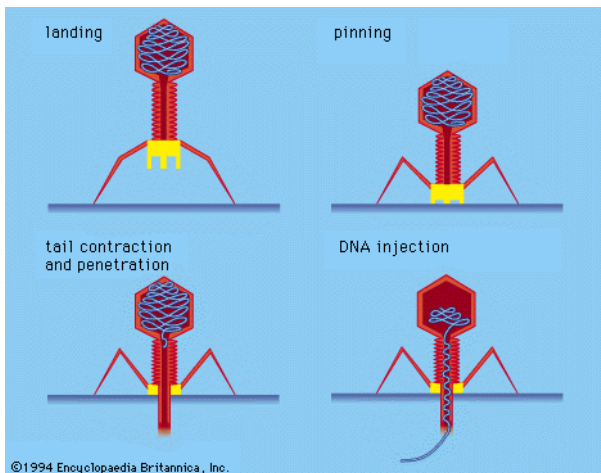
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The process by which a virus invades a cell and reproduces.

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Although the reproductive pathways of different viruses vary considerably, there are certain basic principles and a particular series of events in the cycle of infection for most, if not all, viruses. The first step in the cycle of infection is that the invading parental virus (virion) must attach to the surface of the host cell (adsorption). In the second step, the intact virion either penetrates the outer membrane and enters the cell's interior (cytoplasm) or injects the genetic material of the virus into the interior of the cell while the protein capsid (and envelope, if

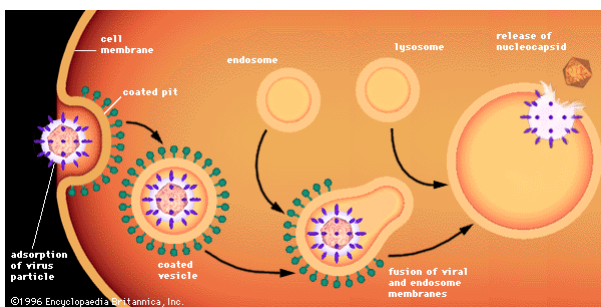
present) remains at the cell surface. In the case of whole-virion penetration, a subsequent process (uncoating) liberates the genetic material from the capsid and envelope, if present. In either case, the viral genetic material cannot begin to synthesize protein until it has emerged from the capsid or envelope.



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 General structure of T4 bacteriophage and a model of its mode of attachment to, and injection of its DNA into, a bacterial cell.  
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Certain bacterial viruses, such as the T4 bacteriophage, have evolved an elaborate process of infection: following adsorption and firm attachment of the virus’s tail to the bacterium surface by means of proteinaceous “pins,” the musclelike tail contracts, and the tail plug penetrates the cell wall and underlying membrane and injects virus (phage) DNA into the cell. Other bacteriophages penetrate the cell membrane by different means, such as injecting the nucleic acid through the male (sex) pili of the bacterium. In all bacterial viruses, penetration transmits the viral nucleic acid through a rigid bacterial cell wall.

Plant cells also have rigid cell walls, which plant viruses cannot ordinarily penetrate. Plant viruses, however, have not evolved their own systems for injecting nucleic acids into host cells, and so they are transmitted by the proboscis of insects that feed on plants. In the laboratory, plant viruses penetrate plant cells if the cell walls have been abraded with sandpaper or if cell protoplasts (plasma membrane, cytoplasm, and nucleus) are devoid of walls.



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 Adsorption to and entry into a cell of an enveloped animal virus by the process of endocytosis into clathrin-coated vesicles, which fuse with large vesicles (endosomes and lysosomes). The process triggered by the viral glycoprotein results in fusion and release of the viral nucleocapsid into the cytoplasm.  
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Penetration of animal cells by viruses involves different processes, because animal cells are enclosed not by walls but by a flexible lipoprotein bilayer membrane. Most animal viruses, whether or not they are encased in lipid envelopes, penetrate cells in an intact form by a process called endocytosis. The membrane invaginates and engulfs a virus particle adsorbed to a cell, usually in an area of the membrane called a coated pit, which is

lined by a special protein known as clathrin. As the coated pit invaginates, it is pinched off in the cytoplasm to form a coated vesicle. The coated vesicle fuses with cytoplasmic endosomes (membrane-enclosed vesicles) and then with cell organelles called lysosomes, which are membrane-enclosed vesicles containing enzymes. In an acidic environment, the membrane of an enveloped virus fuses with the endosome membrane, and the viral nucleocapsid is released into the cytoplasm. Nonenveloped viruses presumably undergo a similar process, by which the protein capsid is degraded, releasing the naked viral nucleic acid into the cytoplasm.

The order of the stages of viral replication that follow the uncoating of the genome varies for different virus classes. For many virus families the third step in the cycle of infection is transcription of the genome of the virus to produce viral mRNA, followed by the fourth step, translation of viral mRNA into proteins. For those viruses in which the genomic nucleic acid is an RNA that can serve as a messenger (i.e., positive-strand RNA viruses), the third step is the translation of the RNA to form viral proteins; some of these newly synthesized viral proteins are enzymes that synthesize nucleic acids (polymerases), which carry out a fourth step, the transcription of more mRNA from the viral genome. For the more complicated DNA viruses, such as adenoviruses and herpesviruses, some regions of the genome synthesize “early” mRNAs, which are translated into polymerases that initiate the transcription of “late” regions of the DNA into mRNAs, which are then translated into structural proteins.

Regardless of how the third and fourth steps proceed, the fifth step in the cycle of infection is replication (reproduction of the parental genome to make progeny genomes). The sixth step is the assembly of the newly replicated progeny genomes with structural proteins to make fully formed progeny virions. The seventh and last step is the release of progeny virions by lysis of the host cell through the process of either extrusion or budding, depending on the nature of the virus. In a host animal or cell culture, this seven-step process may be repeated many times; the progeny virions released from the original site of infection are then transmitted to other sites or to other individuals.

For most animal and plant RNA viruses, all replicative events take place in the cytoplasm; in fact, many of these RNA viruses can grow in host cells in which the nucleus has been removed. Replication of most animal and plant DNA viruses, as well as the RNA influenza virus, takes place in the nucleus. In these viruses, transcription takes place in the nucleus, the mRNA migrates to the cytoplasm, where it is translated, and these viral proteins migrate back to the nucleus, where they assemble with newly replicated progeny genomes. Migration of newly translated viral proteins from the cytoplasm to the nucleus is generally a function of specific amino acid sequences called “signals,” which translocate the protein through pores in the nucleus membrane.

## Viral DNA integration

### Lysogeny

Many bacterial and animal viruses lie dormant in the infected cell, and their DNA may be integrated into the DNA of the host cell chromosome. The integrated viral DNA replicates as the cell genome replicates; after cell division, the integrated viral DNA is duplicated and usually distributed equally to the two cells that result. The bacteria that carry the noninfective precursor phage, called the prophage, remain healthy and continue to grow until they are stimulated by some perturbing factor, such as ultraviolet light. The prophage DNA is then excised from the bacterial chromosome, and the phage replicates, producing many progeny phages and lysing the host bacterial cell. This process, originally discovered in temperate bacteriophages in 1950 by the French microbiologist André Lwoff, is called lysogeny.

The classic example of a temperate bacteriophage is called lambda ( $\lambda$ ) virus, which readily causes lysogeny in certain species of the bacterium *Escherichia coli*. The DNA of the  $\lambda$  bacteriophage is integrated into the DNA of the *E. coli* host chromosome at specific regions called attachment sites. The integrated prophage is the

inherited, noninfectious form of the virus; it contains a gene that represses the lytic functions of the phage and thus ensures that the host cell will continue to replicate the phage DNA along with its own and that it will not be destroyed by the virus. Ultraviolet light, or other factors that stimulate the replication of DNA in the host cell, causes the formation of a *recA* protease, an enzyme that breaks apart the  $\lambda$  phage repressor and induces  $\lambda$  phage replication and, eventually, destruction of the host cell.

Excision of the prophage DNA from the host chromosomal DNA (as an initial step in the synthesis of an infective, lytic virus) sometimes results in the removal of some of the host cell DNA, which is packaged into defective bacteriophages; part of the bacteriophage DNA is removed and replaced at the other end by a gene of the host bacterium. Such a virus particle is called a transducing phage because, when it infects a bacterial cell, it can transmit the gene captured by  $\lambda$  phage DNA into the next bacterial cell it infects. Transduction by bacteriophages is an efficient means for transferring the genetic information of one bacterial cell to another.

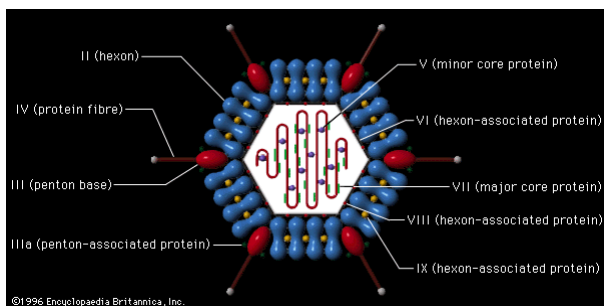
This means of transferring genetic information, called lysogenic conversion, imparts genes with special functions to bacterial cells without such functions. It is common in bacteria and is an important aspect of the epidemiology (incidence, distribution, and control) of infectious diseases. For example, the bacterium *Corynebacterium diphtheriae* is the causative agent of diphtheria, but only when it contains the prophage of bacteriophage  $\beta$ , which codes for the toxin that is responsible for the disease.

## Malignant transformation

A phenomenon analogous to bacterial cell lysogeny occurs in animal cells infected with certain viruses. These animal viruses do not generally cause disease immediately for certain animal cells. Instead, animal cells are persistently infected with such viruses, the DNA of which (provirus) is integrated into the chromosomal DNA of the host cell. In general, cells with integrated proviral DNA are converted into cancer cells, a phenomenon known as malignant transformation. As is the case with bacterial prophages, the transformed animal cell contains no infectious virus but only the integrated provirus DNA, which replicates along with the dividing cell's chromosomes. Therefore, following mitosis of the transformed cell, each new cell receives a copy of the proviral DNA. The hallmark of these transformed animal cells is that their growth is uncontrollable; unlike normal cells, their growth is not inhibited by contact with other cells, and they lose their capacity to adhere (anchor) to certain surfaces. Growth of normal tissues and organs is also controlled by a genetic phenomenon called programmed cell death, or apoptosis, in which a certain number of cells will die and be eliminated after a finite number of divisions. Malignant transformation can impede programmed cell death, thus allowing the cells to grow uncontrolled and resulting in cancer.

Among the animal viruses that cause malignant transformation by integration of proviral DNA are several families of DNA viruses and one large family of RNA viruses, the Retroviridae. Viruses of the family Polyomaviridae, a group of papovaviruses, were perhaps the first to be associated with malignancy (causing death or illness) in animals. Polyomaviruses are widespread in mice; they can infect other rodents, and they can cause tumours in infected animals. Another virus of the family Polyomaviridae is simian virus 40 (SV40), originally isolated from cells of the African green monkey (*Cercopithecus sabaeus*), where it grows rapidly and kills the cells. Infection of rodent or human cells, however, results in an abortive infection (an incompatibility between the virus and the host cell) but sometimes induces malignancy (sarcomas or lymphomas) in the occasional cell that is transformed. Viruses related to polyomavirus and SV40 have been isolated from humans, one of which, the JC virus, appears to be the causative agent of a fatal neurological disease called progressive multifocal leukoencephalopathy. In general, however, the human papovaviruses are not clearly associated with disease.

Other papovaviruses include the papillomaviruses (family Papillomaviridae), which are also small polygonal viruses containing circular double-stranded DNA. The papillomaviruses are associated with usually benign (nonthreatening) but widespread tumours, called papillomas or polyps, occurring in human skin and the genital tract. Specific papillomaviruses have been identified in humans in common warts and in genital warts (condylomata acuminata). Cancers of the human genital tract, particularly uterine cancer of the cervix, are frequently found in association with human papillomavirus type 16 (HPV 16); the virus undoubtedly is transmitted as a venereal disease.



The structure of an adenovirus showing its components and the polypeptides (proteins) exhibited by staining after electrophoresis.

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Certain viruses of the family Adenoviridae, originally found in the tonsils and adenoids of humans, cause malignant transformation in certain cells. This phenomenon of cancer induction under laboratory conditions has been studied widely, but there is no evidence that the common adenoviruses cause cancers in humans. The common viruses of the family Herpesviridae, however, including the common herpes simplex viruses that cause cold sores and the venereal disease genital herpes, are suspected of being causative agents of cancer. Like the adenoviruses, the herpesviruses can cause malignant transformations, and their DNA is integrated into the host cell chromosome. A herpesvirus known as the Epstein-Barr virus causes a frequently fatal childhood cancer called Burkitt lymphoma as well as the nonmalignant disease infectious mononucleosis. The herpesvirus cytomegalovirus lies dormant in the tissues of most humans and can be induced to cause fatal diseases in infants and immunocompromised adults. A different herpesvirus causes chickenpox (varicella); the same virus lies latent in the tissues for long periods of time (perhaps years or decades) and later undergoes recrudescence (the recurrence of symptoms after they have abated) to cause the painful skin and neurological disease called herpes zoster, or shingles. In addition, there are herpesviruses that cause disease in animals—for example, the widespread and usually fatal disease in chickens called Marek's disease. The widespread distribution of viruses of the family Herpesviridae is evident from other diseases in monkeys and frogs.

The viruses of the family Retroviridae are perhaps the most widely distributed of the transforming viruses that infect eukaryotic cells ranging from yeast to humans. It was suggested early in the 20th century that viruses cause leukemias and lymphomas in birds. In 1911 the American pathologist Peyton Rous first described a virus that causes sarcomas in chickens.

The virions of retroviruses are spherical (or polygonal) and are surrounded by a lipid membrane containing a glycoprotein that recognizes and binds to cell receptors of a particular species (type-specific glycoproteins). Retrovirus genomes consist of two identical RNA molecules, each with 7,000 to 10,000 nucleotides. Associated with the virion RNA is an enzyme, an RNA-dependent DNA polymerase, also called a reverse transcriptase. Using the virion RNA as a template, the reverse transcriptase catalyzes the synthesis of a linear DNA molecule complementary to the virion RNA. The new complementary strand of DNA also serves as a template for the reverse transcriptase, which makes a second anticomplementary DNA molecule, thus forming double-stranded DNA. The genomic RNA of fully infectious bird retroviruses, those that can replicate autonomously, has four

genes that code sequentially for group-specific antigens, the reverse transcriptase, the envelope glycoprotein, and the sarcoma-transforming protein. At each end of the genome are homologous flanking nucleotide sequences, known as long terminal repeats (LTR), which code for double-stranded DNA that can recognize host cell DNA sequences for integration of the proviral DNA into the host cell chromosome. Many retroviruses are defective and cannot replicate in cells without helper (nondefective) retroviruses. The helper retroviruses generally transform fibroblastic cells, resulting in malignant sarcomas, whereas the defective retroviruses transform blood-cell precursors, resulting in leukemias.

Many different retroviruses have been identified as causative agents of cancers in birds, rodents (particularly mice), domestic cats, monkeys, and humans. Certain lymphatic leukemias in humans are caused by human T-cell leukemia virus (HTLV); acquired immune deficiency syndrome (AIDS) is caused by a retrovirus called human immunodeficiency virus (HIV).

Retroviruses originated from genes in many different species of animals and even lower forms of life. Individual retroviruses are limited in their host range and do not readily cross species barriers. Virtually every retrovirus studied to date is analogous to the genes normally found in animals (including humans), known as proto-oncogenes, genes that are involved with regulating normal cell growth and development and that also have the potential to change into cancer-causing genes. These proto-oncogenes have deoxynucleotide sequences closely, but not entirely, homologous (i.e., of the same type and order) to the nucleotide sequences of a corresponding viral cancer-causing gene, called an oncogene. Integration of retrovirus DNA into cell chromosomes results in cancer, but the proto-oncogenes do not become cancer-causing genes unless triggered by another event. Cancers caused by chemical or physical carcinogens in the environment probably often, if not invariably, are due to alterations in the sequences of proto-oncogenes that have converted them to oncogenes. Some of the DNA tumour viruses, such as SV40 or adenoviruses, may induce malignant transformation when their DNA is integrated in proximity to the site of a proto-oncogene. All cancers studied to date appear to be due to either mutations in proto-oncogenes or the inheritance of mutated tumour suppressor genes, which normally regulate the function of proto-oncogenes.

## Disease

Although viruses were originally discovered and characterized on the basis of the diseases they cause, most viruses that infect bacteria, plants, and animals (including humans) do not cause disease. In fact, bacteriophages may be helpful in that they rapidly transfer genetic information from one bacterium to another, and viruses of plants and animals may convey genetic information between similar species, helping their hosts survive in hostile environments. In the future this could also be true for humans. Recombinant DNA biotechnology shows great promise for the repair of genetic defects. Afflicted persons are injected with cells transformed by viruses that carry a functional copy of the defective human gene. The virus integrates the normal gene into the DNA of the human cell.

Of those viruses that cause disease, some cause short-term (acute) diseases and others recurring or long-term (chronic) diseases. Some viruses cause acute disease from which there is fairly rapid recovery but may persist in the tissues, remaining dormant for long periods of time, and then become active again, bringing about serious disease decades later. Slowly progressive viruses have long incubation periods before the onset of disease. As mentioned above, the DNA of certain viruses becomes integrated into the genome of the host cell, often resulting in malignant transformation of cells, which become cancers.

The nature of the disease caused by a virus is generally a genetic property of the virus as well as of the host cells. Many viruses, however, can remain dormant in the tissues of the host (latency). Viruses that cause acute

disease are generally, but not always, those that rapidly harm or destroy cells (cytopathic effects) and have the capacity to shut off protein or nucleic acid synthesis within the host cell.

Human poliovirus and related picornaviruses that infect other animal species are examples of acute infectious agents that shut down protein synthesis in the host cell soon after infection; these picornaviruses also inhibit cellular RNA and DNA synthesis. Another virus that rapidly kills the infected cell is the negative-strand vesicular stomatitis virus (VSV) of the family Rhabdoviridae; viral RNA newly synthesized by infectious VSV rapidly shuts off cellular RNA synthesis and, to a somewhat lesser extent, cellular protein synthesis. In both poliovirus and VSV, the infected cell dies within hours of the inhibition of cellular RNA and protein synthesis. Influenza A viruses of the family Orthomyxoviridae, which cause a highly contagious respiratory disease in humans, inhibit cellular macromolecular synthesis by several unique mechanisms, including blocking the maturation of cellular mRNAs and cleaving off the ends of cellular mRNAs in the nucleus of infected cells. Other viruses that inhibit cellular macromolecule synthesis and produce acute infections include the poxviruses, reoviruses, togaviruses, adenoviruses, and herpesviruses; the latter two persist in host tissues for long periods of time and cause chronic infection as well.

Many, if not most, diseases resulting from viral infection of vertebrates are caused not by a direct effect of the virus but rather by a secondary immune response. Essentially all viral proteins are recognized by vertebrate animals as immunologically foreign, and the immune systems of these animals mount two kinds of immune response, humoral and cellular. In humoral immunity, B lymphocytes, usually triggered by helper T lymphocytes, make antibodies (proteins that recognize and bind foreign molecules) to the viral protein. The antibody synthesized as a result of the immune response against a specific viral antigen usually benefits the infected host because that antibody can neutralize the infectivity of the specific virus in the blood and tissues of the infected host. Viruses inside the cell are not accessible to the antibody, because it cannot cross the cell membrane barrier.

In cellular immunity, a killer T cell recognizes and kills a virus-infected cell because of the viral antigen on its surface, thus aborting the infection because a virus will not grow within a dead cell. If the virus-infected cells are not essential for host functions, the killer T cell can prevent the spread of the infecting virus to other cells and distant tissues. Not infrequently, the virus-specific T lymphocyte kills vital cells such as nerve cells (neurons), muscle cells, and liver cells, all of which carry out important functions. In addition, the death of cells results in an inflammatory response, which also can damage vital tissues. Therefore, the cellular immune response to a viral infection can cause disease. In general, diseases caused by chronic viral infections, but also occasionally by subacute (between acute and chronic) viral infections, are caused by cellular immune responses that damage the virus-infected tissue.

## Infectious patterns

Acute viral infections are of two types—local and systemic—both usually resulting from a direct effect of the invading virus on host tissue cells. Acute local infections generally occur at the site of viral infection. For example, acute respiratory infections include (1) the common cold, in which the rhinovirus infects only the nasal mucosa, (2) influenza, in which the virus is found in both nasal and bronchial mucosa, where severe damage can result in death, (3) flulike illnesses caused by adenoviruses localized in lymphoid tissue of the throat (although infection also can occur in the intestine and the eye or be spread to the heart), and (4) severe respiratory infections of infants and children, caused by parainfluenza viruses or respiratory syncytial viruses, which may be life-threatening. Examples of acute infections localized to the intestine include those that result in enteritis (bowel inflammation), which may be accompanied by diarrhea; these are often caused by rotaviruses and coronaviruses.

Many viruses transmitted by the respiratory route (from sneezes and coughs, for example) and limited to humans begin their cycle of infection in the upper respiratory tract (nose and throat) and then enter the bloodstream, where they are spread to distant tissues. Examples of such diseases are measles, mumps, and chickenpox, in which the growth of the specific virus in the mucosal cells of the throat during the first few days of infection usually results in mild fever and achiness; this stage is called the prodromal period of the illness. During the next few days, the virus enters the draining lymph nodes and then the bloodstream, where it is spread throughout the tissues of the body, resulting in fever and rash (in the case of measles and chickenpox) and inflammation of the parotid glands and, less frequently, the testes, ovaries, and joints (in the case of mumps). Varicella (chickenpox) virus rarely causes pneumonia, but all these viruses can cause meningitis and, rarely, encephalitis. A similar pattern of infection formerly occurred with smallpox, a disease that was more frequently fatal but now ostensibly has been eradicated.

A large number of viruses of the digestive tract (enteroviruses)—among them poliovirus, Coxsackie viruses, and echoviruses (enteric cytopathic human orphan virus)—also cause a two-phase illness. Enteroviruses grow initially in the intestinal tract and are transmitted by mouth through water, food, and other materials contaminated with feces. The viruses are resistant to the acid normally found in the stomach and thus reach the intestinal tract, where they multiply in living mucosal cells. This initial period of viral invasion and growth in the intestine causes either an initial mild febrile illness or is asymptomatic. Over the next few days these enteroviruses are spread from the intestinal mucosa to the draining lymph nodes, from which they invade the bloodstream, resulting in a condition known as viremia. From the bloodstream the viruses are widely spread to all tissues, but in most cases no symptomatic disease occurs. Poliovirus in less than 1 percent of cases affects the spinal cord or brain, resulting in paralysis or death. Different types of Coxsackie viruses and echoviruses can cause acute, usually nonfatal, illnesses such as meningitis, carditis, pleurisy, or rashes. Enteroviruses have also been linked to acute flaccid myelitis, a polio-like disease characterized by sudden muscle weakness and paralysis.

Many viral diseases are transmitted by bites of insects or other arthropods, and these infections usually begin in the skin or lymph nodes and rapidly invade the bloodstream. The nature of the disease caused by these arthropod-borne viruses (arboviruses) is determined by the affinity (tropism) of each virus for specific organs. Many that have an affinity for brain tissue cause encephalitis or meningitis, but others primarily infect the muscles, liver, heart, or kidneys. Virtually all these diseases are epidemic in character, and the viruses that cause them are the primary pathogens of birds and mammals. The insect, usually a certain species of mosquito, takes a blood meal from the infected host bird or mammal and shortly thereafter bites a human, thus transmitting the virus. These arboviruses do not ordinarily multiply in the insect but simply reside on its proboscis. Examples of human epidemic diseases resulting from transmission of these often fatal arboviruses are encephalitis caused by viruses of the family *Togaviridae* and *Flaviviridae*, yellow fever and dengue caused by viruses of the family *Flaviviridae*, and hemorrhagic fevers caused by viruses of the families *Bunyaviridae* and *Arenaviridae*. Of considerable interest and concern is the identification of new strains of viruses, particularly a hantavirus of the *Bunyaviridae* family that was responsible for an epidemic in the early 1990s in the southwestern United States that resulted in considerable numbers of fatal human infections.

## Latency

Inapparent infections (those that do not cause specific signs and symptoms) often result after exposure to picornaviruses, influenza viruses, rhinoviruses, herpesviruses, and adenoviruses but less frequently to measles and chickenpox viruses. In cases of inapparent infection, long-lasting immunity develops, but only to the strain of virus that has the same antigenic composition as the original infecting virus.

Certain of these viruses persist in the tissues of the host after the initial infection despite the presence of circulating antibodies to it in the blood and tissues. Such viruses probably reside inside cells, where they are

protected from antibodies that cannot penetrate the cell membrane. Among persistent viruses are adenoviruses, measles virus, and, in particular, many kinds of herpesviruses. The genetic information of herpesviruses and adenoviruses can be integrated into the genome of the host cell, but it is believed that these viruses frequently, and the measles virus invariably, reside in cells in the form of extrachromosomal genes (genes not integrated in chromosomes). These dormant viruses can be activated by many factors, such as trauma, another infection, emotional stress, menstruation, excessive exposure to sunlight, and various illnesses.

The phenomenon of latency and reactivation is particularly common among viruses of the family Herpesviridae, which cause chronic or recurrent diseases: (1) herpes simplex virus type 1, which causes recurrent cold sores, (2) herpes simplex virus type 2 in genital tissue, which causes repeated herpetic infections of the vagina or penis, (3) cytomegalovirus, which usually produces an inapparent infection activated by simultaneously occurring disease to cause severe liver, lung, or nervous-system disease, and (4) varicella virus, which is the causative agent of chickenpox but which can be activated decades later to produce herpes zoster (shingles). A rare, but invariably fatal, disease of the nervous system is subacute sclerosing panencephalitis (SSPE), which is a progressive degenerative condition caused by measles virus (a paramyxovirus) lying dormant in brain cells for many years and then reactivated, usually in adolescence. There is no simple explanation for why latent viruses, such as those in the family Herpesviridae, that are present in the tissues of most adult humans can be activated to cause disease in some people but not in others.

## Chronic and slowly progressive diseases

Although some viruses multiply slowly, this is not always the explanation for the chronicity or the slow progression of the diseases caused by these viruses. Hepatitis, for example, is a subacute or chronic disease, with a long latent period, that is caused by at least five viruses with different properties. Hepatitis A is caused by a picornavirus usually transmitted by the fecal-oral route in a manner similar to that of poliovirus. Hepatitis B is caused by a small DNA virus that contains its own DNA polymerase and is transmitted by transfusion of blood and other blood products, by the sharing of nonsterile hypodermic needles among drug users, by sexual intercourse, or from mother to neonate. Hepatitis B virus is classified with similar viruses of birds in the family Hepadnaviridae. Most cases of hepatitis spread by the transfusion of blood or blood products or by needles shared by drug users are caused by a third, completely distinct virus—originally called non-A, non-B hepatitis but now known to be a member of the virus family Flaviviridae—designated hepatitis C virus. A fourth unique agent that causes hepatitis is designated hepatitis delta virus, which has not yet been classified taxonomically but is a small enveloped virus containing a circular RNA genome; hepatitis B virus serves as a helper for replication of hepatitis delta virus, the virions of which contain hepatitis B surface antigen (HB<sub>s</sub>Ag). The fifth causative agent of viral hepatitis, largely occurring in Asia and Africa, is a small RNA virus tentatively classified as a member of the family Caliciviridae and designated hepatitis E virus.

Many other agents that appear to cause chronic and slowly progressive diseases, particularly those affecting the nervous system, have been identified. A fatal neurological disorder of sheep, called scrapie, has an incubation period of years and may be caused by a heat-resistant protein called a prion, which is self-replicating. Similar, rather obscure agents have been identified for two uncommon fatal disorders of the nervous system called Creutzfeldt-Jakob disease and kuru.

The disease now known as AIDS was first recognized in homosexuals and hemophiliacs about 1981 and continues to be disseminated throughout the world to become one of the most devastating epidemics of all time. AIDS is caused by HIV, a member of a genetically more complex group of the family Retroviridae called lentiviruses. Closely related viruses of monkeys and cats cause similar diseases. HIV is transmitted by blood and other body fluids and infects primarily helper T lymphocytes and other cells with CD4 surface receptors (cell

surface proteins that react with antigens), to which the virus binds. After the virus has been dormant for years, destruction of T lymphocytes results in drastic depression of the immune system. Death almost invariably results from “opportunistic” infections such as pneumonia—caused by ordinarily nonpathogenic organisms such as *Pneumocystis carinii*—or tuberculosis or by cancers such as Kaposi sarcoma and lymphomas.

## Prevention

The spread of many viral diseases can be prevented by hygienic factors such as efficient sanitation facilities, effective waste disposal, clean water, and personal cleanliness. Active immunization by vaccines (antigen-containing preparations that elicit the synthesis of antibodies and thus immunity) has been useful in preventing common epidemics caused by acutely infectious viruses.

The best example of such a preventable disease is smallpox, caused by a disease-producing virus that at one time was found worldwide. In 1796 the English physician Edward Jenner discovered that the milder cowpox virus could serve as a live vaccine (an antigenic preparation consisting of viruses whose disease-producing capacity has been weakened) for preventing smallpox; Jenner published his findings in 1798. The program of vaccination that resulted from Jenner’s discovery of a smallpox vaccine is one of the greatest success stories in the annals of medicine; in 1980 the World Health Organization declared that the disease had been eliminated.

A different prospect is presented by rabies, an invariably fatal viral disease mentioned in ancient Greek literature. Transmitted by the bite of dogs and other domestic and wild animals, the rabies virus is more difficult to eradicate because it is present in wild animals throughout the world, except in certain island countries such as Great Britain and Australia. Influenza virus is also distributed worldwide, but, of the three major immunologic types, only one (type A) is responsible for large epidemics. The worldwide epidemic (pandemic) of influenza at the end of World War I is estimated to have caused 20 million deaths, mostly of adolescents and young adults. Because of virus mutations that produce minor antigenic changes every year and major antigenic shifts about every 10 years, influenza viruses have the capacity to resist inactivation by antibodies acquired by previous infection or vaccination. Development of effective vaccines to combat influenza is a difficult task, although existing vaccines are partially effective and are recommended for people at high risk—i.e., the elderly and those with chronic disease of the respiratory or circulatory systems.

Vaccines are most successful when directed against those viruses that do not mutate and that infect only humans. In addition to smallpox, a successful vaccine program has been carried out against polio. Polioviruses exist in only three antigenic types, each of which has not changed significantly for decades. The vaccines available are the “killed” (Salk) vaccine, composed of inactivated virus of the three types, and the “live” (Sabin) vaccine, composed of genetically attenuated viruses of the three types. In developed countries these vaccines, which were introduced in the 1950s, have lowered the incidence of paralysis resulting from polio. The disease still occurs in developing countries and recurs in some developed countries where vaccination programs have not been enforced. Rare cases of polio occur from the Sabin vaccine strain of type-3 poliovirus, which is genetically unstable and occasionally reverts to the virulent form.

Vaccination can prevent diseases caused by strictly human viruses that exist in only one antigenic and stable type. Measles has been prevented in developed countries with routine vaccination. Measles, however, may still be the major cause of death in children in developing countries. Vaccination for mumps and chickenpox promises to be successful because the causative viruses of these diseases show little tendency to vary antigenically and are confined to humans. On the other hand, development of vaccines for the common cold caused by rhinoviruses, similar to polioviruses, will be a formidable, if not impossible, task because there are at least 100 antigenic types of the rhinovirus. Rhinoviruses and paralysis-inducing enteroviruses, however, depend on a protein in host cells called methyltransferase SETD3 for their replication; this discovery raised the possibility

of someday being able to suppress the protein therapeutically to protect individuals against infection by these viruses.

Also daunting is the task of developing a vaccine against HIV. The major antigenic component of this virus is a surface-membrane-inserted glycoprotein (gp120), which has a startling rate of mutation. The extreme antigenic diversity that results from the mutability of the gene that codes for this protein would prevent HIV from being identified and attacked by circulating antibodies or killer T lymphocytes.

## Treatment

Unlike bacteria, viruses mimic the metabolic functions of their host cells. Antibiotics are not effective against viruses. It is difficult to identify chemical compounds that inhibit the multiplication of viruses but do not slow the functions of, or are not toxic to, the host cell. Despite this difficulty, an effective antiviral drug has been developed against influenza virus. This drug targets a viral enzyme called the neuraminidase and is orders of magnitude less active against nonviral neuraminidases. These neuraminidase inhibitors are most effective when administered prophylactically or within the first 30 hours of symptom onset and can be used to limit the spread of influenza virus and to complement the administration of vaccines. Other chemicals that exert a selectively greater effect on viral replication than they do on cell replication include ribavirin, acyclovir, and zidovudine (azidothymidine [AZT]). These drugs have been partially effective in improving, if not curing, viral diseases without causing major toxic side effects. AZT has been used with some success in prolonging the lives of patients with AIDS.

Certain natural products of cells, called interferons, may have potential antiviral and anticancer properties. Interferons are proteins normally synthesized by the cells of vertebrates, including humans, either intrinsically and without stimulation or in response to certain viral infections, chemicals, or immune reactions. In general, the multiplication of viruses is inhibited by interferons, some to a much greater extent than others. Interferons are generally species-specific; i.e., they are effective in inhibiting viral infection only in cells of the same species that naturally synthesize the interferon.

There are three classes of interferons:  $\alpha$ -interferons, produced by blood leukocytes;  $\beta$ -interferons, produced by tissue cells and fibroblasts; and  $\gamma$ -interferons (also called immune interferons or interleukins), produced by immune reactions in blood lymphocytes. Interferons are now known to be a subset of a large group of natural cellular substances called cytokines, which signal cells to perform specific functions. Until recently, interferons were difficult to produce commercially because cells and tissues synthesize only small amounts of them. Through recombinant DNA technology, however, large amounts of interferon can be produced.

There has been some success in using interferons to treat viral diseases, such as colds caused by rhinoviruses, infections caused by herpesviruses, and benign tumours and warts caused by papillomaviruses. Local administration at the sites of viral infection affords the best results, although injections of large amounts of interferons can be harmful, probably because they tend to inhibit protein synthesis in the host cell.

## Evolution

### Evolutionary origins

Owing to their simplicity, viruses were at first considered to be the primordial life-forms. This concept is almost certainly incorrect, because viruses are completely devoid of the machinery for life processes; therefore, they could not have survived in the absence of cells. Viruses probably evolved from cells rather than cells from viruses. It seems likely that all viruses trace their origins to cellular genes and can be considered as pieces of

rogue nucleic acids. Although it is easier to imagine the cellular origin of DNA viruses than RNA viruses, the RNA viruses conceivably could have had their origins from cellular RNA transcripts made from cellular DNA. In fact, the discovery that many cells contain reverse transcriptase capable of converting RNA to DNA seems to suggest that conversion of RNA to DNA and DNA to RNA is not rare. Indeed, some speculate that RNA is the primordial genetic information from which DNA evolved to produce more-complex life-forms.

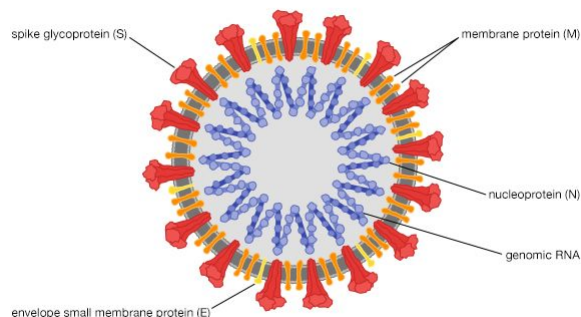
Other possible progenitors of viruses are the plasmids (small circular DNA molecules independent of chromosomes), which are more readily transferred from cell to cell than are chromosomes. Theoretically, plasmids could have acquired capsid genes, which coded for proteins to coat the plasmid DNA, converting it into a virus.

In brief, it is likely that viruses originated from the degradation of cellular nucleic acids, which acquired the property of being readily transferable from cell to cell during the process of evolution. The fact that normal proto-oncogenes of a cell have nucleic acid sequences that are almost identical to the oncogenes of retroviruses lends credence to the theory that viruses originated from cellular genes.

## Evolution of new virus strains

Viruses that infect animals can jump from one species to another, causing a new, usually severe disease in the new host. For example, in 2003 a virus in the Coronaviridae family jumped from an animal reservoir, believed to be horseshoe bats, to humans, causing a highly pathogenic disease in humans called severe acute respiratory syndrome (SARS). The ability of the SARS coronavirus to jump from horseshoe bats to humans undoubtedly required genetic changes in the virus. The changes are suspected to have occurred in the palmcivet, since the SARS virus present in horseshoe bats is unable to infect humans directly.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)



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The coronavirus SARS-CoV-2, the cause of the COVID-19 pandemic.

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Such newly emerged viruses often are highly infectious in humans, since they have not been previously encountered by the human immune system and thus humans have no immunity against them. The coronavirus that caused SARS, for example, spread quickly among humans, becoming a significant disease threat. The virus was quickly brought under control, owing to prohibitions on travel and quarantine measures. In late 2019 another type of coronavirus, called SARS-CoV-2, emerged in China and spread rapidly worldwide, giving rise to a pandemic. SARS-CoV-2 caused an illness known as coronavirus disease 2019 (COVID-19), which was very similar to SARS but caused significantly greater mortality, particularly among persons over age 65.

Influenza A viruses that infect humans can undergo a dramatic antigenic change, called antigenic shift, which generates viruses that cause pandemics. This dramatic change occurs because influenza A viruses have a large animal reservoir, wild aquatic birds. The RNA genome of influenza A viruses is in the form of eight segments. If

an intermediate host, probably the pig, is simultaneously infected with a human and an avian influenza A virus, the genome RNA segments can be reassorted, yielding a new virus that has a surface protein that is immunologically distinct from that of influenza A viruses that have been circulating in the human population. Because the human population will have little or no immunological protection against the new virus, a pandemic will result. This is what most likely occurred in the 1957 flu pandemic, the 1968 flu pandemic, and the influenza pandemic (H1N1) of 2009.

Pandemic influenza A viruses can also apparently arise by a different mechanism. It has been postulated that the strain that caused the influenza epidemic of 1918–19 derived all eight RNA segments from an avian virus and that this virus then underwent multiple mutations in the process of adapting to mammalian cells. The bird flu viruses, which have spread from Asia to Europe and Africa since the 1990s, appear to be taking this route to pandemic capability. These viruses, which have been directly transmitted from chickens to humans, contain only avian genes and are highly pathogenic in humans, causing a mortality rate higher than 50 percent. Bird flu viruses have not yet acquired the ability to transmit efficiently from humans to humans, and it is not known what genetic changes must take place for them to do so.

## Classification

### Distinguishing taxonomic features

Viruses are classified on the basis of their nucleic acid content, their size, the shape of their protein capsid, and the presence of a surrounding lipoprotein envelope.

The primary taxonomic division is into two classes based on nucleic acid content: DNA viruses or RNA viruses. The DNA viruses are subdivided into those that contain either double-stranded or single-stranded DNA. The RNA viruses also are divided into those that contain double-stranded or single-stranded RNA. Further subdivision of the RNA viruses is based on whether the RNA genome is segmented. If the viruses contain single-stranded RNA as their genetic information, they are divided into positive-strand viruses if the RNA is of messenger sense (directly translatable into proteins) or negative-strand viruses if the RNA must be transcribed by a polymerase into mRNA.

All viruses falling into one of these nucleic acid classifications are further subdivided on the basis of whether the nucleocapsid (protein coat and enclosed nucleic acid) assumes a rodlike or a polygonal (usually icosahedral) shape. The icosahedral viruses are further subdivided into families on the basis of the number of capsomeres making up the capsids. Finally, all viruses fall into two classes depending on whether the nucleocapsid is surrounded by a lipoprotein envelope.

Some virologists adhere to a division of viruses into those that infect bacteria, plants, or animals; these classifications have some validity, particularly for the unique bacterial viruses with tails, but there is otherwise so much overlap that taxonomy based on hosts seems unworkable. Classification based on diseases caused by viruses also is not tenable, because closely related viruses frequently do not cause the same disease. Eventually, it is likely that the classification of viruses will be based on their nucleotide sequences and their mode of replication rather than on structural components, as is now the case.

The basic taxonomic group is called a family, designated by the suffix *-viridae*. The major taxonomic disagreement among virologists is whether to segregate viruses within a family into a specific genus and further subdivide them into species names. In the first decade of the 21st century, there occurred a shift toward the use of binomial nomenclature, dividing viruses into italicized genera and species. This move was prompted in large part by the International Committee on Taxonomy of Viruses (ICTV), a member group of the International Union

of Microbiological Societies. The ICTV oversees the ongoing process of devising and maintaining a universal classification scheme for viruses. In the virus classification hierarchy, the ICTV recognizes orders, families, subfamilies, genera, and species. The placement of viruses in these groups is based on information provided by study groups composed of experts on specific types of viruses.

In the ICTV system, each species of virus is generally recognized as representing a group of isolates, or viruses with distinct nucleic acid sequences. Thus, a single species of virus may sometimes contain more than one isolate. Although the isolates of a species possess unique genetic sequences, they all descend from the same replicating lineage and therefore share particular genetic traits. Furthermore, isolates of a species also share in common the ability to thrive within a specific ecological niche. As scientists identify new isolates and species, the classification of viruses is expected to become increasingly complex. The following scheme presents examples of well-characterized DNA and RNA viruses as they are classified on the basis of the ICTV system.

Robert R. Wagner Robert M. Krug

## Annotated classification

**DNA viruses**

**Family Poxviridae** Large viruses of complex structure with dimensions of 400 × 250 nm, the genome of which is linear double-stranded DNA. Virions contain at least 40 proteins and lipids, as well as internal structures called lateral bodies. The 2 subfamilies are called Chordopoxvirinae, which infect vertebrates and are closely related antigenically, and Entomopoxvirinae, which infect arthropods. The Chordopoxvirinae are composed of groups called orthopoxviruses (vaccinia), parapoxviruses, avipoxviruses of birds, and many others that infect sheep, rabbits, and swine.

**Family Adenoviridae** Nonenveloped virions of icosahedral symmetry, about 80 nm in diameter, and capsids containing 252 capsomeres with 12 vertices to which are attached glycoprotein fibres 10–30 nm in length with knobs at the ends. The genome is linear double-stranded DNA. Classified in 2 subgroups: mastadenoviruses, which infect mammals, and aviadenoviruses, which infect birds. Common acute respiratory and gastrointestinal pathogens of humans, and some types cause malignant transformation of cultured cells and can cause cancer in animals.

**Family Herpesviridae** Icosahedral virions with capsid about 150–200 nm in diameter and 162 capsomeres surrounded by a floppy envelope containing glycoprotein spikes. Genome composed of linear double-stranded DNA. There are 3 known subfamilies: Alphaherpesvirinae, consisting of human herpes simplex viruses types 1 and 2, bovine mamillitis virus, SA8 virus and monkey B virus, pseudorabies virus, equine herpesvirus, and varicella-zoster virus; Betaherpesvirinae, composed of species of cytomegaloviruses; and Gammaherpesvirinae, composed of genera familiarly called Epstein-Barr virus, baboon herpesvirus, chimpanzee herpesvirus, Marek's disease virus of chickens, turkey herpesvirus, herpesvirus saimiri, and herpesvirus ateles.

**Family Iridoviridae** Large enveloped or nonenveloped icosahedral virions measuring 120–350 nm in diameter and containing linear double-stranded DNA. Genera include *Iridovirus*, which contains invertebrate iridescent virus 6, and *Lymphocystivirus*, which contains lymphocystis disease virus 1 of fish.

**Family Asfarviridae** Icosahedral, enveloped virions approximately 175–215 nm in diameter that contain linear double-stranded DNA. This family consists of one genus, *Asfivirus*, which contains the African swine fever virus.

**Family Hepadnaviridae** Small enveloped, spherical virions about 40–48 nm in diameter containing circular double-stranded DNA with a single-stranded DNA region and a DNA-dependent DNA polymerase that repairs the single-stranded DNA gap and is essential for replication. Also characteristic are the use of reverse transcriptase for replication and an abundance of a soluble protein (HB<sub>s</sub>Ag). Genera include *Orthohepadnavirus*, which consists of hepatitis B viruses that infect mammals, and *Avihepadnavirus*, which consists of hepatitis B viruses that infect birds.

**Family Papillomaviridae** Icosahedral, nonenveloped virions about 52–55 nm in diameter with 72 capsomeres. Virions contain covalently linked circular DNA. Papillomaviruses do not grow in cell culture, and they usually cause warts and benign papillomas; in some instances papillomas develop into cancers. The family contains multiple genera.

**Family Parvoviridae** Small icosahedral, nonenveloped virions with 32 capsomeres

measuring 18–26 nm in diameter that contain single-stranded DNA. Viruses of this family are divided into two subfamilies: Parvovirinae, which infect vertebrates, and Densovirinae, which infect insects. The vertebrate viruses fall into 2 classes: those that replicate autonomously and those that replicate only in the presence of helper adenoviruses or herpesviruses, designated adenoassociated viruses (AAV).

**Family Polyomaviridae**Icosahedral, nonenveloped virions 40–55 nm in diameter. Virions contain covalently linked circular double-stranded DNA. The family consists of one genus, *Polyomavirus*. The polyomaviruses produce malignant transformation of infected cells.

**RNA viruses**

**Family Picornaviridae**Small icosahedral, nonenveloped virions 20–30 nm in diameter, composed of 60 capsomeres and containing nonsegmented single-stranded, positive-sense RNA. Among the multiple recognized genera are *Enterovirus* (polioviruses), *Cardiovirus*, *Rhinovirus* (common cold viruses), and *Aphthovirus* (foot-and-mouth disease virus).

**Family Caliciviridae**Icosahedral, nonenveloped virions about 35–39 nm in diameter, composed of 32 capsomeres and 180 molecules of a single capsid protein. The genome consists of a single strand of positive-sense RNA. The prototype virus of this family is the vesicular exanthema of swine virus.

**Family Togaviridae**Enveloped virions spherical in shape with icosahedral nucleocapsid about 70 nm in diameter. The genome is single-stranded positive-sense RNA. There are 2 recognized genera: *Alphavirus* and *Rubivirus*. *Alphavirus* consists of viruses transmitted by arthropods (exclusively mosquitoes); prototypes include Sindbis virus and eastern and western equine encephalitis viruses. *Rubivirus* contains non-arthropod-borne viruses, including the causative agent of German measles.

**Family Flaviviridae**Viruses of this family are enveloped and spherical in shape, with a genome consisting of nonsegmented single-stranded positive-sense RNA. These viruses are transmitted by either insects or arachnids and cause severe diseases such as yellow fever, dengue, tick-borne encephalitis, and Japanese B encephalitis. Other members of this family include non-arthropod-borne hog cholera virus (pestivirus) and hepatitis C virus of humans.

**Family Coronaviridae**Enveloped virions 120 nm in diameter with a helical nucleocapsid containing a single strand of positive-sense RNA. Club-shaped glycoprotein spikes in envelope give crownlike (coronal) appearance. Viruses of this family are important agents of respiratory and gastrointestinal disease in humans, poultry, and bovines.

**Family Orthomyxoviridae**Enveloped virions about 80–120 nm in diameter with a helical nucleocapsid containing 8 segments of single-stranded negative-sense RNA and endogenous RNA polymerase. The lipoprotein envelope contains 2 glycoproteins, designated hemagglutinin (major antigen) and neuraminidase. The best-known viruses in this family are the 3 distinct antigenic types of influenza viruses: A, B, and C.

**Family Paramyxoviridae**Enveloped virions varying in size from 150 to 200 nm in diameter with a helical nucleocapsid containing a single strand of negative-sense nonsegmented RNA and an endogenous RNA polymerase. The lipoprotein envelope contains 2 glycoprotein spikes designated hemagglutinin-neuraminidase (HN) and fusion factor (F). The major subfamily is Paramyxovirinae, which contains the human parainfluenza viruses and mumps virus, as well as Newcastle disease virus of poultry. The genus *Morbillivirus*, within Paramyxovirinae, contains the agents that cause measles in humans, distemper in dogs and cats, and rinderpest in cattle. The second subfamily, Pneumovirinae, causes the serious respiratory syncytial virus disease in human infants.

**Family Rhabdoviridae**Enveloped virions, usually bullet-shaped, about 75 nm in diameter and 180 nm in length, containing a helical nucleocapsid with single-stranded negative-sense RNA and an endogenous RNA polymerase. The lipoprotein envelope contains a single glycoprotein, which is the type-specific antigen. Viruses of this family are widely infectious for plants and for animals varying from insects to humans. Genera that infect animals are *Vesiculovirus*, which includes the virus that causes vesicular stomatitis in cattle, swine, and equines, and *Lyssavirus*, which includes the causative agent of rabies.

**Family Filoviridae**Enveloped virions, variably elongated filaments 650–1,400 nm in length and pleomorphic in shape, containing a helical nucleocapsid with single-stranded negative-sense RNA (about 19 kilobases in length) and an endogenous RNA polymerase. Much like the Rhabdoviridae, the lipoprotein envelope contains a single glycoprotein, which is the type-specific antigen. The family consists of 2 genera: *Filovirus*, which contains the Marburg viruses, and *Ebolavirus*, which contains the Ebola viruses. These viruses have been isolated from African monkeys, and both are among the most dangerous pathogens. Some strains cause severe hemorrhagic fevers in humans; the mortality rate from

these diseases is as high as 90 percent. Human infections with Marburg virus have been traced to laboratory monkeys, but human outbreaks of fatal Ebola virus infection in Congo (Kinshasa) and Sudan have not been traced to monkeys. Instead, these infections are suspected to have been transmitted from fruit-eating bats.

**Family Arenaviridae** Enveloped virions 110–130 nm in diameter with a helical nucleocapsid in 2 segments containing negative-sense RNA, an endogenous RNA polymerase, and small amounts of ribosomal RNA. The family contains a single genus, *Arenavirus*, with species widely distributed in animals and causing serious human diseases. Many of these agents are transmitted by insects.

**Family Bunyaviridae** Enveloped virions about 80–120 nm in diameter with a 3-segment helical nucleocapsid containing single-stranded RNA of negative sense and endogenous RNA polymerase. Many viruses grouped in 5 genera: *Orthobunyavirus*, *Phlebovirus*, *Nairovirus*, *Tospovirus*, and *Hantavirus*. Most of these viruses are transmitted by arthropods and cause serious human disease.

**Family Retroviridae** Enveloped virions about 80–100 nm in diameter with 2 identical copies of single positive-strand RNA in nondefective virions and a reverse transcriptase, which promotes synthesis of double-stranded DNA from the viral RNA template. A hallmark of the virion RNA templates is long terminal repeat (LTR) nucleotide sequences, which serve for integration of the DNA in chromosomes of the host cell. Retroviridae cause cancers in many species of animals, including humans, and are probably derived from normal cell nucleotide sequences called proto-oncogenes. Certain retroviruses of the lentivirus group cause AIDS in humans, monkeys, felines, and cattle.

**Family Reoviridae** Nonenveloped icosahedral virions with outer and inner protein shells 60–80 nm in diameter and containing double-stranded RNA in 10 to 12 segments. Viruses in this family infect many species of plants and animals. Reoviridae genera containing species known to infect animals include *Orthoreovirus*, *Orbivirus* (widely distributed in insects and vertebrates, including bluetongue disease virus of sheep), *Rotavirus* (widespread causative agents of gastroenteritis in mammals, including humans), and *Cypovirus* (prototype causes cytoplasmic polyhedrosis disease in insects).

## Additional Reading

Descriptions of the diseases and their epidemiology are included in BERNARD N. FIELDS and DAVID M. KNIPE (eds.), *Fields Virology*, 2nd ed., 2 vol. (1990), a text on the structure, biological properties, replication, and immunology of virtually all human viruses of medical importance. DAVID O. WHITE and FRANK J. FENNER, *Medical Virology*, 4th ed. (1994), is intended for medical students and other health professionals. *The Viruses*, 24 vol. (1982–94), a monographic series, critically analyzes in detail the biology, chemistry, and physical properties of each family of viruses—e.g., BERNARD ROIZMAN and CARLOS LOPEZ (eds.), *The Herpesviruses*, 4 vol. (1982–85); and JAY A. LEVY (ed.), *The Retroviridae*, 3 vol. (1992–94). C.H. ANDREWES, *The Natural History of Viruses* (1967), offers a personal account by one of the pioneers in the field. ARNOLD J. LEVINE, *Viruses* (1992), a beautifully illustrated and well-written history and description of virology, provides insight into its scientific development. SHERWOOD CASJENS (ed.), *Virus Structure and Assembly* (1985), contains an illustrated series of essays by some of the major contributors to the understanding of the physical principles that determine the structure and assembly of viruses. ABNER LOUIS NOTKINS and MICHAEL B.A. OLDSTONE (eds.), *Concepts in Viral Pathogenesis* (1984), *Concepts in Viral Pathogenesis II* (1986), and *Concepts in Viral Pathogenesis III* (1989), contain a detailed series of chapters by leading investigators on the disease-causing properties of many pathogenetic viruses. The international classification of the families, genera, species, and strains of all viruses discovered by 1991 may be found in R.I.B. FRANCK *et al.* (eds.), *Classification and Nomenclature of Viruses* (1991). ROBERT G. WEBSTER and ALLAN GRANOFF (eds.), *Encyclopedia of Virology*, 3 vol. (1994), contains extremely well-annotated descriptions of every known virus in alphabetical order by common names with detailed indexes and tables.

Robert R. Wagner

Citation (MLA style):

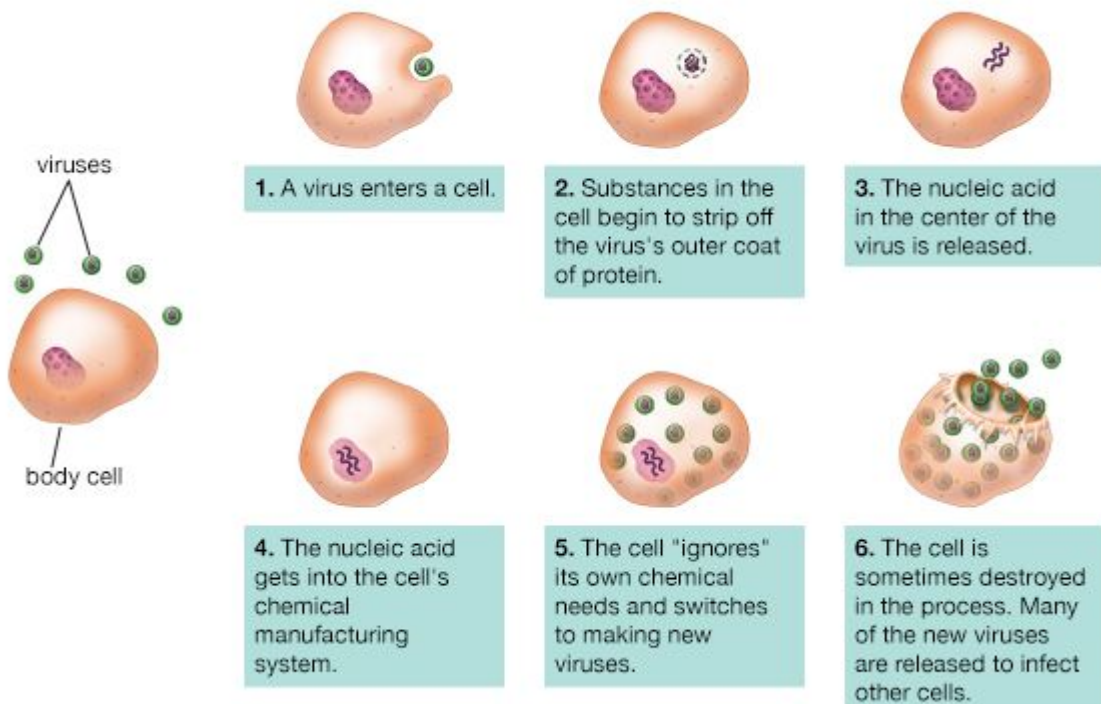
"Virus." *Britannica LaunchPacks: Viruses*, Encyclopædia Britannica, 14 Feb. 2025. packs.eb.com. Accessed 4 May. 2025.

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IMAGE

## virus: invasion of a cell

### How a virus invades a cell



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The process by which a virus invades a cell and reproduces.

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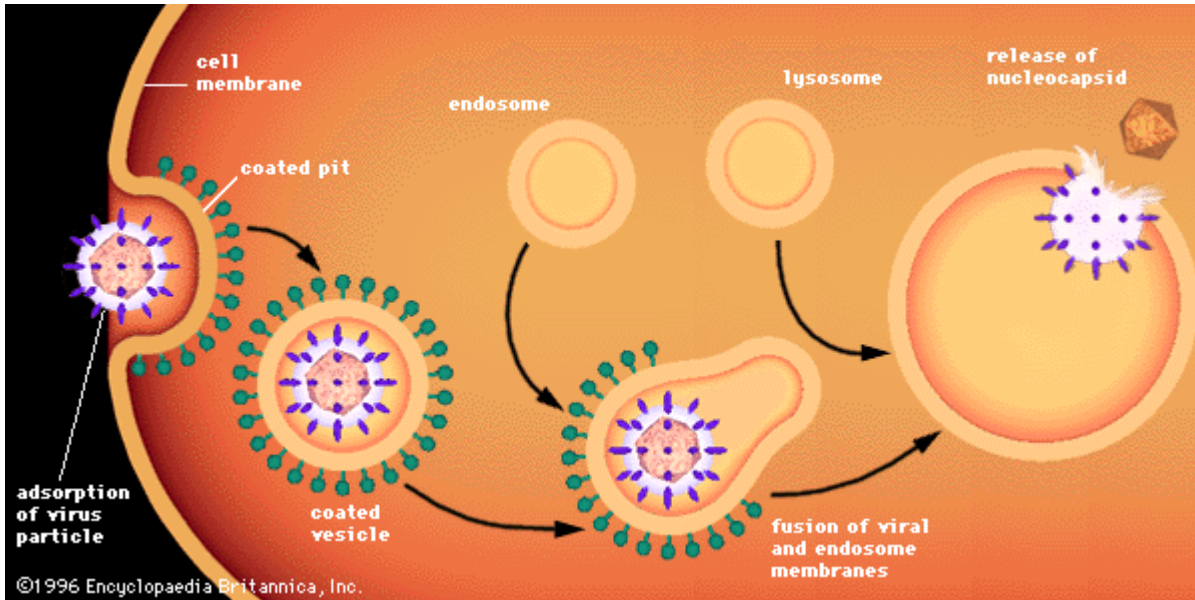
Citation (MLA style):

*Virus: invasion of a cell.* Image. *Britannica LaunchPacks: Viruses*, Encyclopædia Britannica, 23 Mar. 2025. packs.eb.com. Accessed 4 May. 2025.

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# endocytosis



Adsorption to and entry into a cell of an enveloped animal virus by the process of endocytosis into clathrin-coated vesicles, which fuse with large vesicles (endosomes and lysosomes). The process triggered by the viral glycoprotein results in fusion and release of the viral nucleocapsid into the cytoplasm.

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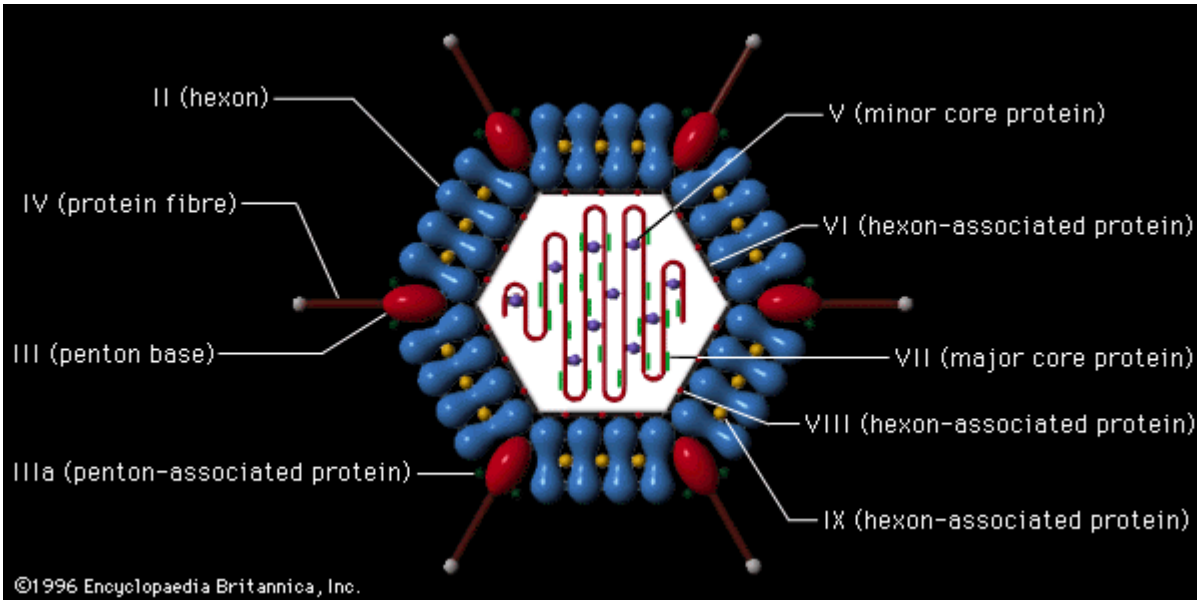
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# adenovirus



The structure of an adenovirus showing its components and the polypeptides (proteins) exhibited by staining after electrophoresis.

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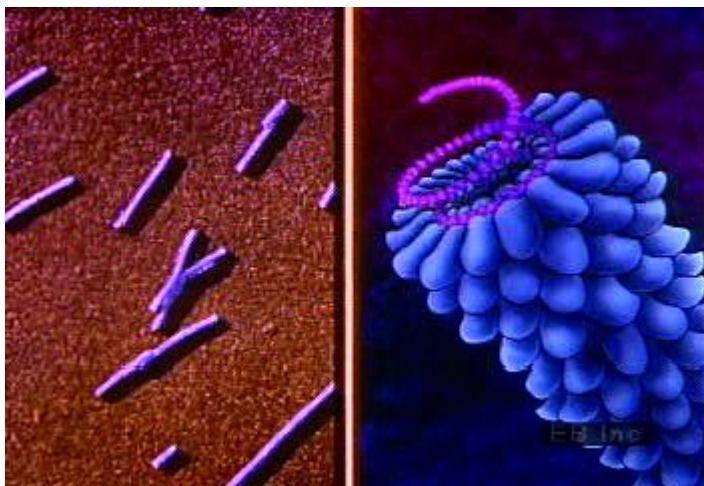
*Citation (MLA style):*

*Adenovirus.* Image. *Britannica LaunchPacks: Viruses*, Encyclopædia Britannica, 23 Mar. 2025. packs.eb.com. Accessed 4 May. 2025.

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## Dissect the anatomy of icosahedral, rod-shaped, and bacteriophage virus structures in electron micrographs



### Video Transcript

NARRATOR: Different viruses have different shapes. Some look roughly spherical under the electron microscope, but their exact geometry is an icosahedron, a figure with 20 triangular faces. There are also rod-shaped viruses. The rod has two layers wrapped together. At the center is a strand of nucleic acid; the outside shell is protein spirally wound in a long helix. Probably the most dramatically shaped viruses are called bacteriophages, or phages. The head of the phage is a hollow protein capsule that contains nucleic acid. Beneath that is a shaft called a sheath. Attached to the sheath are leglike tail fibers.

Animation and microphotography illustrating the structural diversity of viruses.

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*Citation (MLA style):*

*Dissect the anatomy of icosahedral, rod-shaped, and bacteriophage virus structures in electron micrographs.* Video. *Britannica LaunchPacks: Viruses*, Encyclopædia Britannica, 23 Mar. 2025. packs.eb.com. Accessed 4 May. 2025.

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