

# Virus

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A **virus** is a submicroscopic infectious agent that replicates only inside the living cells of an organism.<sup>[1]</sup> Viruses can infect all types of life forms, from animals and plants to microorganisms, including bacteria and archaea.<sup>[2]</sup> Since Dmitri Ivanovsky's 1892 article describing a non-bacterial pathogen infecting tobacco plants, and the discovery of the tobacco mosaic virus by Martinus Beijerinck in 1898,<sup>[3]</sup> more than 6,000 virus species have been described in detail,<sup>[4]</sup> of the millions of types of viruses in the environment.<sup>[5]</sup> Viruses are found in almost every ecosystem on Earth and are the most numerous type of biological entity.<sup>[6][7]</sup> The study of viruses is known as virology, a subspeciality of microbiology.

When infected, a host cell is forced to rapidly produce thousands of identical copies of the original virus. When not inside an infected cell or in the process of infecting a cell, viruses exist in the form of independent particles, or *virions*, consisting of: (i) the genetic material, i.e. long molecules of DNA or RNA that encode the structure of the proteins by which the virus acts; (ii) a protein coat, the *capsid*, which surrounds and protects the genetic material; and in some cases (iii) an outside envelope of lipids. The shapes of these virus particles range from simple helical and icosahedral forms to more complex structures. Most virus species have virions too small to be seen with an optical microscope as they are one hundredth the size of most bacteria.

The origins of viruses in the evolutionary history of life are unclear: some may have evolved from plasmids—pieces of DNA that can move between cells—while others may have evolved from bacteria. In evolution, viruses are an important means of horizontal gene transfer, which increases genetic diversity in a way analogous to sexual reproduction.<sup>[8]</sup> Viruses are considered by some biologists to be a life form, because they carry genetic material, reproduce, and evolve through natural selection, although they lack key characteristics (such as cell structure) that generally are considered necessary criteria for “life”. Because they possess some but not all such qualities, viruses have been described as “organisms at the edge of life”,<sup>[9]</sup> and as replicators.<sup>[10]</sup>

Viruses spread in many ways. One transmission pathway is through disease-bearing organisms known as vectors: for example, viruses are often transmitted from plant to plant by insects that feed on plant sap, such as aphids; and viruses in animals can be carried by blood-sucking insects. Influenza viruses are spread by coughing and sneezing. Norovirus and rotavirus, common causes of viral gastroenteritis, are transmitted by the faecal–oral route, passed by hand-to-mouth contact or in food or water. The infectious dose of norovirus required to produce infection in humans is less than 100 particles.<sup>[11]</sup> HIV is one of several viruses transmitted through sexual contact and by exposure to infected blood. The variety of host cells that a virus can infect is called its “host range”. This can be narrow, meaning a virus is capable of infecting few species, or broad, meaning it is capable of infecting many.<sup>[12]</sup>

<b>Virus</b>
SARS-CoV-2, a member of the family <i>Coronaviridae</i>
<b>Virus classification</b>
(unranked): <b>Virus</b>
<b>Subdivisions</b>
See text

Viral infections in animals provoke an immune response that usually eliminates the infecting virus. Immune responses can also be produced by vaccines, which confer an artificially acquired immunity to the specific viral infection. Some viruses, including those that cause AIDS, HPV infection, and viral hepatitis, evade these immune responses and result in chronic infections. Several antiviral drugs have been developed.

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## Etymology

The word is from the Latin neuter *vīrus* referring to poison and other noxious liquids, from the same Indo-European base as Sanskrit *viṣa*, Avestan *viša*, and ancient Greek *ἴός* (all meaning "poison"), first attested in English in 1398 in John Trevisa's translation of Bartholomeus Anglicus's *De Proprietatibus Rerum*.<sup>[13][14]</sup> Virulent, from Latin *virulentus* (poisonous), dates to c. 1400.<sup>[15][16]</sup> A meaning of "agent that causes infectious disease" is first recorded in 1728,<sup>[14]</sup> long before the discovery of viruses by Dmitri Ivanovsky in 1892. The English plural is viruses (sometimes also *vīra*)<sup>[17]</sup> whereas the Latin word is a mass noun, which has no classically attested plural (*vīra* is used in Neo-Latin<sup>[18]</sup>). The adjective *viral* dates to 1948.<sup>[19]</sup> The term *virion* (plural *virions*), which dates from 1959,<sup>[20]</sup> is also used to refer to a single viral particle that is released from the cell and is capable of infecting other cells of the same type.<sup>[21]</sup>

## History

Louis Pasteur was unable to find a causative agent for rabies and speculated about a pathogen too small to be detected by microscopes.<sup>[22]</sup> In 1884, the French microbiologist Charles Chamberland invented the Chamberland filter (or Pasteur-Chamberland filter) with pores small enough to remove all bacteria from a solution passed through it.<sup>[23]</sup> In 1892, the Russian biologist Dmitri Ivanovsky used this filter to study what is now known as the tobacco mosaic virus: crushed leaf extracts from infected tobacco plants remained infectious even after filtration to remove bacteria. Ivanovsky suggested the infection might be caused by a toxin produced by bacteria, but did not pursue the idea.<sup>[24]</sup> At the time it was thought that all infectious agents could be retained by filters and grown on a nutrient medium—this was part of the germ theory of disease.<sup>[3]</sup> In 1898, the Dutch microbiologist Martinus Beijerinck repeated the experiments and became convinced that the filtered solution contained a new form of infectious agent.<sup>[25]</sup> He observed that the agent multiplied only in cells that were dividing, but as his experiments did not show that it was made of particles, he called it a contagium vivum fluidum (soluble living germ) and re-introduced the word *virus*. Beijerinck maintained that viruses were liquid in nature, a theory later discredited by Wendell Stanley, who proved they were particulate.<sup>[24]</sup> In the same year Friedrich Loeffler and Paul Frosch passed the first animal virus through a similar filter: aphthovirus, the agent of foot-and-mouth disease.<sup>[26]</sup>



Martinus Beijerinck in his laboratory in 1921

In the early 20th century, the English bacteriologist Frederick Twort discovered a group of viruses that infect bacteria, now called bacteriophages<sup>[27]</sup> (or commonly 'phages'), and the French-Canadian microbiologist Félix d'Herelle described viruses that, when added to bacteria on an agar plate, would produce areas of dead bacteria. He accurately diluted a suspension of these viruses and discovered that the highest dilutions

(lowest virus concentrations), rather than killing all the bacteria, formed discrete areas of dead organisms. Counting these areas and multiplying by the dilution factor allowed him to calculate the number of viruses in the original suspension.<sup>[28]</sup> Phages were heralded as a potential treatment for diseases such as typhoid and cholera, but their promise was forgotten with the development of penicillin. The development of bacterial resistance to antibiotics has renewed interest in the therapeutic use of bacteriophages.<sup>[29]</sup>

By the end of the 19th century, viruses were defined in terms of their infectivity, their ability to pass filters, and their requirement for living hosts. Viruses had been grown only in plants and animals. In 1906, Ross Granville Harrison invented a method for growing tissue in lymph, and, in 1913, E. Steinhardt, C. Israeli, and R. A. Lambert used this method to grow vaccinia virus in fragments of guinea pig corneal tissue.<sup>[30]</sup> In 1928, H. B. Maitland and M. C. Maitland grew vaccinia virus in suspensions of minced hens' kidneys. Their method was not widely adopted until the 1950s when poliovirus was grown on a large scale for vaccine production.<sup>[31]</sup>

Another breakthrough came in 1931, when the American pathologist Ernest William Goodpasture and Alice Miles Woodruff grew influenza and several other viruses in fertilised chicken eggs.<sup>[32]</sup> In 1949, John Franklin Enders, Thomas Weller, and Frederick Robbins grew poliovirus in cultured cells from aborted human embryonic tissue,<sup>[33]</sup> the first virus to be grown without using solid animal tissue or eggs. This work enabled Hilary Koprowski, and then Jonas Salk, to make an effective polio vaccine.<sup>[34]</sup>

The first images of viruses were obtained upon the invention of electron microscopy in 1931 by the German engineers Ernst Ruska and Max Knoll.<sup>[35]</sup> In 1935, American biochemist and virologist Wendell Meredith Stanley examined the tobacco mosaic virus and found it was mostly made of protein.<sup>[36]</sup> A short time later, this virus was separated into protein and RNA parts.<sup>[37]</sup> The tobacco mosaic virus was the first to be crystallised and its structure could, therefore, be elucidated in detail. The first X-ray diffraction pictures of the crystallised virus were obtained by Bernal and Fankuchen in 1941. On the basis of her X-ray crystallographic pictures, Rosalind Franklin discovered the full structure of the virus in 1955.<sup>[38]</sup> In the same year, Heinz Fraenkel-Conrat and Robley Williams showed that purified tobacco mosaic virus RNA and its protein coat can assemble by themselves to form functional viruses, suggesting that this simple mechanism was probably the means through which viruses were created within their host cells.<sup>[39]</sup>

The second half of the 20th century was the golden age of virus discovery and most of the documented species of animal, plant, and bacterial viruses were discovered during these years.<sup>[40]</sup> In 1957, equine arterivirus and the cause of Bovine virus diarrhoea (a pestivirus) were discovered. In 1963, the hepatitis B virus was discovered by Baruch Blumberg,<sup>[41]</sup> and in 1965, Howard Temin described the first retrovirus. Reverse transcriptase, the enzyme that retroviruses use to make DNA copies of their RNA, was first described in 1970, independently by Temin and David Baltimore.<sup>[42]</sup> In 1983 Luc Montagnier's team at the Pasteur Institute in France, first isolated the retrovirus now called HIV.<sup>[43]</sup> In 1989 Michael Houghton's team at Chiron Corporation discovered Hepatitis C.<sup>[44][45]</sup>

## Origins

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Viruses are found wherever there is life and have probably existed since living cells first evolved.<sup>[46]</sup> The origin of viruses is unclear because they do not form fossils, so molecular techniques are used to investigate how they arose.<sup>[47]</sup> In addition, viral genetic material occasionally integrates into the germline of the host organisms, by which they can be passed on vertically to the offspring of the host for many generations. This provides an invaluable source of information for paleovirolologists to trace back ancient viruses that have existed up to millions of years ago. There are three main hypotheses that aim to explain the origins of viruses:<sup>[48][49]</sup>

### Regressive hypothesis

Viruses may have once been small cells that parasitised larger cells. Over time, genes not required by their parasitism were lost. The bacteria rickettsia and chlamydia are living cells that, like viruses, can reproduce only inside host cells. They lend support to this hypothesis, as their dependence on parasitism is likely to have caused the loss of genes that enabled them to survive outside a cell. This is also called the 'degeneracy hypothesis',<sup>[50][51]</sup> or 'reduction hypothesis'.<sup>[52]</sup>

### **Cellular origin hypothesis**

Some viruses may have evolved from bits of DNA or RNA that "escaped" from the genes of a larger organism. The escaped DNA could have come from plasmids (pieces of naked DNA that can move between cells) or transposons (molecules of DNA that replicate and move around to different positions within the genes of the cell).<sup>[53]</sup> Once called "jumping genes", transposons are examples of mobile genetic elements and could be the origin of some viruses. They were discovered in maize by Barbara McClintock in 1950.<sup>[54]</sup> This is sometimes called the 'vagrancy hypothesis',<sup>[50][55]</sup> or the 'escape hypothesis'.<sup>[52]</sup>

### **Co-evolution hypothesis**

This is also called the 'virus-first hypothesis'<sup>[52]</sup> and proposes that viruses may have evolved from complex molecules of protein and nucleic acid at the same time that cells first appeared on Earth and would have been dependent on cellular life for billions of years. Viroids are molecules of RNA that are not classified as viruses because they lack a protein coat. They have characteristics that are common to several viruses and are often called subviral agents.<sup>[56]</sup> Viroids are important pathogens of plants.<sup>[57]</sup> They do not code for proteins but interact with the host cell and use the host machinery for their replication.<sup>[58]</sup> The hepatitis delta virus of humans has an RNA genome similar to viroids but has a protein coat derived from hepatitis B virus and cannot produce one of its own. It is, therefore, a defective virus. Although hepatitis delta virus genome may replicate independently once inside a host cell, it requires the help of hepatitis B virus to provide a protein coat so that it can be transmitted to new cells.<sup>[59]</sup> In similar manner, the sputnik virophage is dependent on mimivirus, which infects the protozoan Acanthamoeba castellanii.<sup>[60]</sup> These viruses, which are dependent on the presence of other virus species in the host cell, are called 'satellites' and may represent evolutionary intermediates of viroids and viruses.<sup>[61][62]</sup>

In the past, there were problems with all of these hypotheses: the regressive hypothesis did not explain why even the smallest of cellular parasites do not resemble viruses in any way. The escape hypothesis did not explain the complex capsids and other structures on virus particles. The virus-first hypothesis contravened the definition of viruses in that they require host cells.<sup>[52]</sup> Viruses are now recognised as ancient and as having origins that pre-date the divergence of life into the three domains.<sup>[63]</sup> This discovery has led modern virologists to reconsider and re-evaluate these three classical hypotheses.<sup>[63]</sup>

The evidence for an ancestral world of RNA cells<sup>[64]</sup> and computer analysis of viral and host DNA sequences are giving a better understanding of the evolutionary relationships between different viruses and may help identify the ancestors of modern viruses. To date, such analyses have not proved which of these hypotheses is correct.<sup>[64]</sup> It seems unlikely that all currently known viruses have a common ancestor, and viruses have probably arisen numerous times in the past by one or more mechanisms.<sup>[65]</sup>

## **Microbiology**

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### **Life properties**

Scientific opinions differ on whether viruses are a form of life, or organic structures that interact with living organisms.<sup>[10]</sup> They have been described as "organisms at the edge of life",<sup>[9]</sup> since they resemble organisms in that they possess genes, evolve by natural selection,<sup>[66]</sup> and reproduce by creating multiple copies of themselves through self-assembly. Although they have genes, they do not have a cellular structure, which is often seen as the basic unit of life. Viruses do not have their own metabolism, and require a host cell to make new products. They therefore cannot naturally reproduce outside a host cell<sup>[67]</sup>—although bacterial species such as rickettsia and chlamydia are considered living organisms despite the same limitation.<sup>[68][69]</sup> Accepted forms of life use cell division to reproduce, whereas viruses spontaneously assemble within cells. They differ from autonomous growth of crystals as they inherit genetic mutations while being subject to natural selection. Virus self-assembly within host cells has implications for the study of the origin of life, as it lends further credence to the hypothesis that life could have started as self-assembling organic molecules.<sup>[2]</sup>

## Structure

Viruses display a wide diversity of shapes and sizes, called 'morphologies'. In general, viruses are much smaller than bacteria. Most viruses that have been studied have a diameter between 20 and 300 nanometres. Some filoviruses have a total length of up to 1400 nm; their diameters are only about 80 nm.<sup>[70]</sup> Most viruses cannot be seen with an optical microscope, so scanning and transmission electron microscopes are used to visualise them.<sup>[71]</sup> To increase the contrast between viruses and the background, electron-dense "stains" are used. These are solutions of salts of heavy metals, such as tungsten, that scatter the electrons from regions covered with the stain. When virions are coated with stain (positive staining), fine detail is obscured. Negative staining overcomes this problem by staining the background only.<sup>[72]</sup>

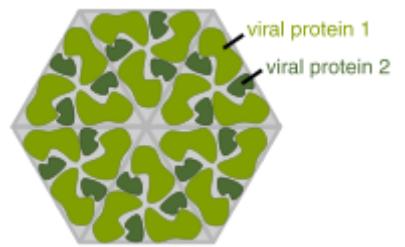


Diagram of how a virus capsid can be constructed using multiple copies of just two protein molecules

A complete virus particle, known as a **virion**, consists of nucleic acid surrounded by a protective coat of protein called a capsid. These are formed from identical protein subunits called capsomeres.<sup>[73]</sup> Viruses can have a lipid "envelope" derived from the host cell membrane. The capsid is made from proteins encoded by the viral genome and its shape serves as the basis for morphological distinction.<sup>[74][75]</sup> Virally-coded protein subunits will self-assemble to form a capsid, in general requiring the presence of the virus genome. Complex viruses code for proteins that assist in the construction of their capsid. Proteins associated with nucleic acid are known as nucleoproteins, and the association of viral capsid proteins with viral nucleic acid is called a nucleocapsid. The capsid and entire virus structure can be mechanically (physically) probed through atomic force microscopy.<sup>[76][77]</sup> In general, there are four main morphological virus types:

### Helical

These viruses are composed of a single type of capsomere stacked around a central axis to form a helical structure, which may have a central cavity, or tube. This arrangement results in rod-shaped or filamentous virions which can be short and highly rigid, or long and very flexible. The genetic material (typically single-stranded RNA, but ssDNA in some cases) is bound into the protein helix by interactions between the negatively charged nucleic acid and positive charges on the protein. Overall, the length of a helical capsid is related to the length of the nucleic acid contained within it, and the diameter is dependent on the size and arrangement of capsomeres. The well-studied tobacco mosaic virus is an example of a helical virus.<sup>[78]</sup>

### Icosahedral

Most animal viruses are icosahedral or near-spherical with chiral icosahedral symmetry. A regular icosahedron is the optimum way of forming a closed shell from identical sub-units. The minimum number of identical capsomeres required for each triangular face is 3, which gives 60 for the icosahedron. Many viruses, such as rotavirus, have more than 60 capsomeres and appear spherical but they retain this symmetry. To achieve this, the capsomeres at the apices are surrounded by five other capsomeres and are called pentons. Capsomeres on the triangular faces are surrounded by six others and are called hexons.<sup>[79]</sup> Hexons are in essence flat and pentons, which form the 12 vertices, are curved. The same protein may act as the subunit of both the pentamers and hexamers or they may be composed of different proteins.<sup>[80]</sup>

## Prolate

This is an icosahedron elongated along the fivefold axis and is a common arrangement of the heads of bacteriophages. This structure is composed of a cylinder with a cap at either end.<sup>[81]</sup>

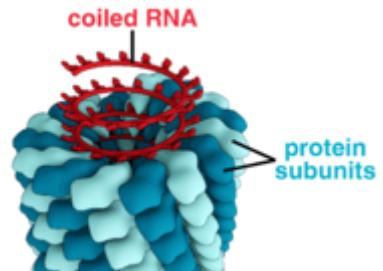
## Envelope

Some species of virus envelop themselves in a modified form of one of the cell membranes, either the outer membrane surrounding an infected host cell or internal membranes such as nuclear membrane or endoplasmic reticulum, thus gaining an outer lipid bilayer known as a viral envelope. This membrane is studded with proteins coded for by the viral genome and host genome; the lipid membrane itself and any carbohydrates present originate entirely from the host. The influenza virus and HIV use this strategy. Most enveloped viruses are dependent on the envelope for their infectivity.<sup>[82]</sup>

## Complex

These viruses possess a capsid that is neither purely helical nor purely icosahedral, and that may possess extra structures such as protein tails or a complex outer wall. Some bacteriophages, such as Enterobacteria phage T4, have a complex structure consisting of an icosahedral head bound to a helical tail, which may have a hexagonal base plate with protruding protein tail fibres. This tail structure acts like a molecular syringe, attaching to the bacterial host and then injecting the viral genome into the cell.<sup>[83]</sup>

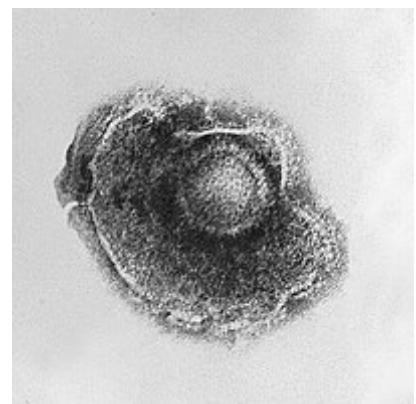
The poxviruses are large, complex viruses that have an unusual morphology. The viral genome is associated with proteins within a central disc structure known as a nucleoid. The nucleoid is surrounded by a membrane and two lateral bodies of unknown function. The virus has an outer envelope with a thick layer of protein studded over its surface. The whole virion is slightly pleomorphic, ranging from ovoid to brick-shaped.<sup>[84]</sup>



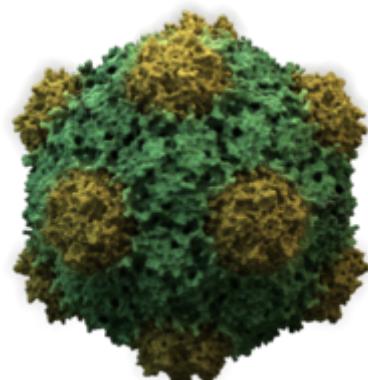
Structure of tobacco mosaic virus:  
RNA coiled in a helix of repeating  
protein sub-units



Structure of icosahedral  
adenovirus. Electron micrograph  
with an illustration to show shape



Structure of chickenpox virus.  
They have a lipid envelope



Structure of an icosahedral  
cowpea mosaic virus

## Giant viruses

Mimivirus is one of the largest characterised viruses, with a capsid diameter of 400 nm. Protein filaments measuring 100 nm project from the surface. The capsid appears hexagonal under an electron microscope, therefore the capsid is probably icosahedral.<sup>[85]</sup> In 2011, researchers discovered the largest then known virus in samples of water collected from the ocean floor off the coast of Las Cruces, Chile. Provisionally named Megavirus chilensis, it can be seen with a basic optical microscope.<sup>[86]</sup> In 2013, the Pandoravirus genus was discovered in Chile and Australia, and has genomes about twice as large as Megavirus and Mimivirus.<sup>[87]</sup> All giant viruses have dsDNA genomes and they are classified into several families: Mimiviridae, Pithoviridae, Pandoraviridae, Phycodnaviridae, and the Mollivirus genus.<sup>[88]</sup>

Some viruses that infect Archaea have complex structures unrelated to any other form of virus, with a wide variety of unusual shapes, ranging from spindle-shaped structures to viruses that resemble hooked rods, teardrops or even bottles. Other archaeal viruses resemble the tailed bacteriophages, and can have multiple tail structures.<sup>[89]</sup>

## Genome

An enormous variety of genomic structures can be seen among viral species; as a group, they contain more structural genomic diversity than plants, animals, archaea, or bacteria. There are millions of different types of viruses,<sup>[5]</sup> although only about 6,000 types have been described in detail.<sup>[90]</sup> As of September 2015, the NCBI Virus genome database has more than 75,000 complete genome sequences,<sup>[91]</sup> but there are doubtlessly many more to be discovered.<sup>[92][93]</sup>

A virus has either a DNA or an RNA genome and is called a DNA virus or an RNA virus, respectively. The vast majority of viruses have RNA genomes. Plant viruses tend to have single-stranded RNA genomes and bacteriophages tend to have double-stranded DNA genomes.<sup>[94]</sup>

Viral genomes are circular, as in the polyomaviruses, or linear, as in the adenoviruses. The type of nucleic acid is irrelevant to the shape of the genome. Among RNA viruses and certain DNA viruses, the genome is often divided up into separate parts, in which case it is called segmented. For RNA viruses, each segment often codes for only one protein and they are usually found together in one capsid. All segments are not required to be in the same virion for the virus to be infectious, as demonstrated by brome mosaic virus and several other plant viruses.<sup>[70]</sup>

A viral genome, irrespective of nucleic acid type, is almost always either single-stranded or double-stranded. Single-stranded genomes consist of an unpaired nucleic acid, analogous to one-half of a ladder split down the middle. Double-stranded genomes consist of two complementary paired nucleic acids, analogous to a ladder. The virus particles of some virus families, such as those belonging to the Hepadnaviridae, contain a genome that is partially double-stranded and partially single-stranded.<sup>[94]</sup>

For most viruses with RNA genomes and some with single-stranded DNA genomes, the single strands are said to be either positive-sense (called the 'plus-strand') or negative-sense (called the 'minus-strand'), depending on if they are complementary to the viral messenger RNA (mRNA). Positive-sense viral RNA is

Genomic diversity among viruses

Property	Parameters
Nucleic acid	<ul style="list-style-type: none"><li>▪ DNA</li><li>▪ RNA</li><li>▪ Both DNA and RNA (at different stages in the life cycle)</li></ul>
Shape	<ul style="list-style-type: none"><li>▪ Linear</li><li>▪ Circular</li><li>▪ Segmented</li></ul>
Strandedness	<ul style="list-style-type: none"><li>▪ Single-stranded</li><li>▪ Double-stranded</li><li>▪ Double-stranded with regions of single-strandedness</li></ul>
Sense	<ul style="list-style-type: none"><li>▪ Positive sense (+)</li><li>▪ Negative sense (-)</li><li>▪ Ambisense (+/-)</li></ul>

in the same sense as viral mRNA and thus at least a part of it can be immediately translated by the host cell. Negative-sense viral RNA is complementary to mRNA and thus must be converted to positive-sense RNA by an RNA-dependent RNA polymerase before translation. DNA nomenclature for viruses with single-sense genomic ssDNA is similar to RNA nomenclature, in that positive-strand viral ssDNA is identical in sequence to the viral mRNA and is thus a coding strand, while negative-strand viral ssDNA is complementary to the viral mRNA and is thus a template strand.<sup>[94]</sup> Several types of ssDNA and ssRNA viruses have genomes that are ambisense in that transcription can occur off both strands in a double-stranded replicative intermediate. Examples include geminiviruses, which are ssDNA plant viruses and arenaviruses, which are ssRNA viruses of animals.<sup>[95]</sup>

## Genome size

Genome size varies greatly between species. The smallest—the ssDNA circoviruses, family *Circoviridae*—code for only two proteins and have a genome size of only two kilobases;<sup>[96]</sup> the largest—the pandoraviruses—have genome sizes of around two megabases which code for about 2500 proteins.<sup>[97]</sup> Virus genes rarely have introns and often are arranged in the genome so that they overlap.<sup>[98]</sup>

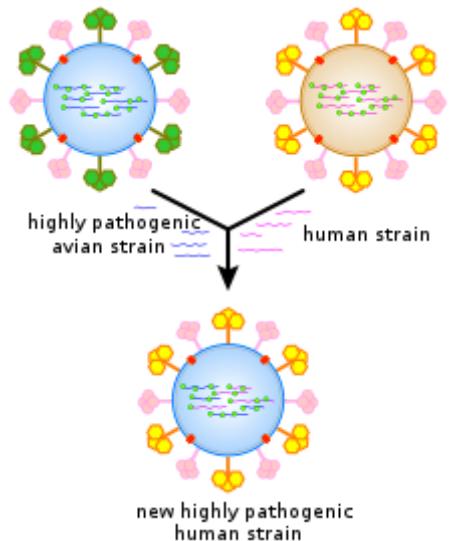
In general, RNA viruses have smaller genome sizes than DNA viruses because of a higher error-rate when replicating, and have a maximum upper size limit.<sup>[47]</sup> Beyond this, errors when replicating render the virus useless or uncompetitive. To compensate, RNA viruses often have segmented genomes—the genome is split into smaller molecules—thus reducing the chance that an error in a single-component genome will incapacitate the entire genome. In contrast, DNA viruses generally have larger genomes because of the high fidelity of their replication enzymes.<sup>[99]</sup> Single-strand DNA viruses are an exception to this rule, as mutation rates for these genomes can approach the extreme of the ssRNA virus case.<sup>[100]</sup>

## Genetic mutation

Viruses undergo genetic change by several mechanisms. These include a process called antigenic drift where individual bases in the DNA or RNA mutate to other bases. Most of these point mutations are "silent"—they do not change the protein that the gene encodes—but others can confer evolutionary advantages such as resistance to antiviral drugs.<sup>[101][102]</sup> Antigenic shift occurs when there is a major change in the genome of the virus. This can be a result of recombination or reassortment. When this happens with influenza viruses, pandemics might result.<sup>[103]</sup> RNA viruses often exist as quasispecies or swarms of viruses of the same species but with slightly different genome nucleoside sequences. Such quasispecies are a prime target for natural selection.<sup>[104]</sup>

Segmented genomes confer evolutionary advantages; different strains of a virus with a segmented genome can shuffle and combine genes and produce progeny viruses (or offspring) that have unique characteristics. This is called reassortment or 'viral sex'.<sup>[105]</sup>

Genetic recombination is the process by which a strand of DNA is broken and then joined to the end of a different DNA molecule. This can occur when viruses infect cells simultaneously and studies of viral evolution have shown that recombination has been rampant in the species studied.<sup>[106]</sup> Recombination is common to both RNA and DNA viruses.<sup>[107][108]</sup>



Antigenic shift, or reassortment, can result in novel and highly pathogenic strains of human flu

## Replication cycle

Viral populations do not grow through cell division, because they are acellular. Instead, they use the machinery and metabolism of a host cell to produce multiple copies of themselves, and they assemble in the cell.<sup>[109]</sup> When infected, the host cell is forced to rapidly produce thousands of identical copies of the original virus.<sup>[110]</sup>

Their life cycle differs greatly between species, but there are six basic stages in their life cycle:<sup>[111]</sup>

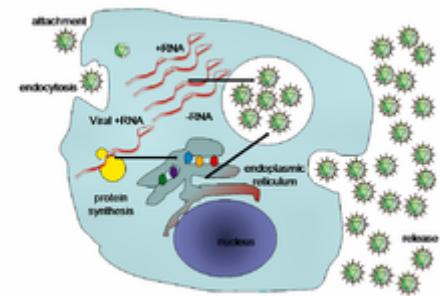
*Attachment* is a specific binding between viral capsid proteins and specific receptors on the host cellular surface. This specificity determines the host range and type of host cell of a virus. For example, HIV infects a limited range of human leucocytes. This is because its surface protein, gp120, specifically interacts with the CD4 molecule—a chemokine receptor—which is most commonly found on the surface of CD4+ T-Cells. This mechanism has evolved to favour those viruses that infect only cells in which they are capable of replication. Attachment to the receptor can induce the viral envelope protein to undergo changes that result in the fusion of viral and cellular membranes, or changes of non-enveloped virus surface proteins that allow the virus to enter.<sup>[112]</sup>

*Penetration* follows attachment: Virions enter the host cell through receptor-mediated endocytosis or membrane fusion in a process often known as viral entry. The infection of plant and fungal cells is different from that of animal cells. Plants have a rigid cell wall made of cellulose, and fungi one of chitin, so most viruses can get inside these cells only after trauma to the cell wall.<sup>[113]</sup> Nearly all plant viruses (such as tobacco mosaic virus) can also move directly from cell to cell, in the form of single-stranded nucleoprotein complexes, through pores called plasmodesmata.<sup>[114]</sup> Bacteria, like plants, have strong cell walls that a virus must breach to infect the cell. Given that bacterial cell walls are much thinner than plant cell walls due to their much smaller size, some viruses have evolved mechanisms that inject their genome into the bacterial cell across the cell wall, while the viral capsid remains outside.<sup>[115]</sup>

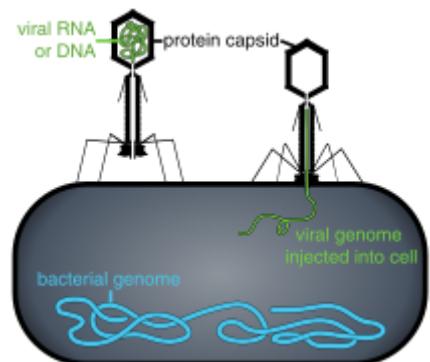
*Uncoating* is a process in which the viral capsid is removed: This may be by degradation by viral enzymes or host enzymes or by simple dissociation; the end-result is the releasing of the viral genomic nucleic acid.<sup>[116]</sup>

*Replication* of viruses involves primarily multiplication of the genome. Replication involves synthesis of viral messenger RNA (mRNA) from "early" genes (with exceptions for positive sense RNA viruses), viral protein synthesis, possible assembly of viral proteins, then viral genome replication mediated by early or regulatory protein expression. This may be followed, for complex viruses with larger genomes, by one or more further rounds of mRNA synthesis: "late" gene expression is, in general, of structural or virion proteins.<sup>[117]</sup>

*Assembly* – Following the structure-mediated self-assembly of the virus particles, some modification of the proteins often occurs. In viruses such as HIV, this modification (sometimes called maturation) occurs after the virus has been released from the host cell.<sup>[118]</sup>



A typical virus replication cycle



Some bacteriophages inject their genomes into bacterial cells (not to scale)

**Release** – Viruses can be released from the host cell by lysis, a process that kills the cell by bursting its membrane and cell wall if present: this is a feature of many bacterial and some animal viruses. Some viruses undergo a lysogenic cycle where the viral genome is incorporated by genetic recombination into a specific place in the host's chromosome. The viral genome is then known as a "provirus" or, in the case of bacteriophages a "prophage".<sup>[119]</sup> Whenever the host divides, the viral genome is also replicated. The viral genome is mostly silent within the host. At some point, the provirus or prophage may give rise to active virus, which may lyse the host cells.<sup>[120]</sup> Enveloped viruses (e.g., HIV) typically are released from the host cell by budding. During this process the virus acquires its envelope, which is a modified piece of the host's plasma or other, internal membrane.<sup>[121]</sup>

## Genome replication

The genetic material within virus particles, and the method by which the material is replicated, varies considerably between different types of viruses.

### DNA viruses

The genome replication of most DNA viruses takes place in the cell's nucleus. If the cell has the appropriate receptor on its surface, these viruses enter the cell either by direct fusion with the cell membrane (e.g., herpesviruses) or—more usually—by receptor-mediated endocytosis. Most DNA viruses are entirely dependent on the host cell's DNA and RNA synthesising machinery, and RNA processing machinery. Viruses with larger genomes may encode much of this machinery themselves. In eukaryotes the viral genome must cross the cell's nuclear membrane to access this machinery, while in bacteria it need only enter the cell.<sup>[122]</sup>

### RNA viruses

Replication of RNA viruses usually takes place in the cytoplasm. RNA viruses can be placed into four different groups depending on their modes of replication. The polarity (whether or not it can be used directly by ribosomes to make proteins) of single-stranded RNA viruses largely determines the replicative mechanism; the other major criterion is whether the genetic material is single-stranded or double-stranded. All RNA viruses use their own RNA replicase enzymes to create copies of their genomes.<sup>[123]</sup>

### Reverse transcribing viruses

Reverse transcribing viruses have ssRNA (Retroviridae, Metaviridae, Pseudoviridae) or dsDNA (Caulimoviridae, and Hepadnaviridae) in their particles. Reverse transcribing viruses with RNA genomes (retroviruses) use a DNA intermediate to replicate, whereas those with DNA genomes (pararetroviruses) use an RNA intermediate during genome replication. Both types use a reverse transcriptase, or RNA-dependent DNA polymerase enzyme, to carry out the nucleic acid conversion. Retroviruses integrate the DNA produced by reverse transcription into the host genome as a provirus as a part of the replication process; pararetroviruses do not, although integrated genome copies of especially plant pararetroviruses can give rise to infectious virus.<sup>[124]</sup> They are susceptible to antiviral drugs that inhibit the reverse transcriptase enzyme, e.g. zidovudine and lamivudine. An example of the first type is HIV, which is a retrovirus. Examples of the second type are the Hepadnaviridae, which includes Hepatitis B virus.<sup>[125]</sup>

## Cytopathic effects on the host cell

The range of structural and biochemical effects that viruses have on the host cell is extensive.<sup>[126]</sup> These are called 'cytopathic effects'.<sup>[127]</sup> Most virus infections eventually result in the death of the host cell. The causes of death include cell lysis, alterations to the cell's surface membrane and apoptosis.<sup>[128]</sup> Often cell

death is caused by cessation of its normal activities because of suppression by virus-specific proteins, not all of which are components of the virus particle.<sup>[129]</sup> The distinction between cytopathic and harmless is gradual. Some viruses, such as Epstein–Barr virus, can cause cells to proliferate without causing malignancy,<sup>[130]</sup> while others, such as papillomaviruses, are established causes of cancer.<sup>[131]</sup>

## Dormant and latent infections

Some viruses cause no apparent changes to the infected cell. Cells in which the virus is latent and inactive show few signs of infection and often function normally.<sup>[132]</sup> This causes persistent infections and the virus is often dormant for many months or years. This is often the case with herpes viruses.<sup>[133][134]</sup>

## Host range

Viruses are by far the most abundant biological entities on Earth and they outnumber all the others put together.<sup>[135]</sup> They infect all types of cellular life including animals, plants, bacteria and fungi.<sup>[90]</sup> Different types of viruses can infect only a limited range of hosts and many are species-specific. Some, such as smallpox virus for example, can infect only one species—in this case humans,<sup>[136]</sup> and are said to have a narrow host range. Other viruses, such as rabies virus, can infect different species of mammals and are said to have a broad range.<sup>[137]</sup> The viruses that infect plants are harmless to animals, and most viruses that infect other animals are harmless to humans.<sup>[138]</sup> The host range of some bacteriophages is limited to a single strain of bacteria and they can be used to trace the source of outbreaks of infections by a method called phage typing.<sup>[139]</sup>

## Classification

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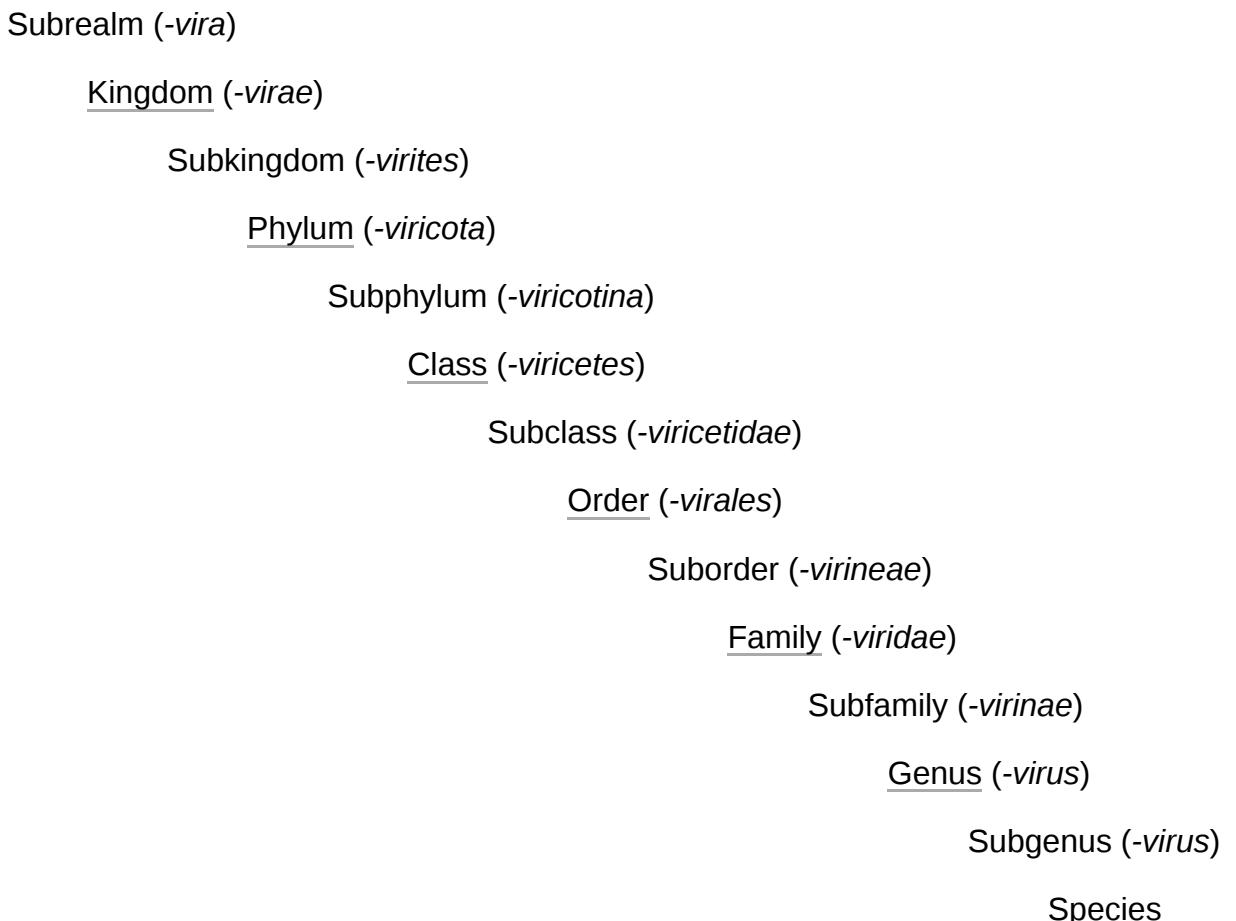
Classification seeks to describe the diversity of viruses by naming and grouping them on the basis of similarities. In 1962, André Lwoff, Robert Horne, and Paul Tournier were the first to develop a means of virus classification, based on the Linnaean hierarchical system.<sup>[140]</sup> This system based classification on phylum, class, order, family, genus, and species. Viruses were grouped according to their shared properties (not those of their hosts) and the type of nucleic acid forming their genomes.<sup>[141]</sup> In 1966, the International Committee on Taxonomy of Viruses (ICTV) was formed. The system proposed by Lwoff, Horne and Tournier was never fully accepted by the ICTV because small genome size viruses and their high rate of mutation makes it difficult to determine their ancestry beyond order. As such, the Baltimore classification is used to supplement the more traditional hierarchy.<sup>[142]</sup>

## ICTV classification

The International Committee on Taxonomy of Viruses (ICTV) developed the current classification system and wrote guidelines that put a greater weight on certain virus properties to maintain family uniformity. A unified taxonomy (a universal system for classifying viruses) has been established. Only a small part of the total diversity of viruses has been studied.<sup>[143]</sup> As of 2019, 4 realms, 9 kingdoms, 16 phyla, 2 subphyla, 36 classes, 55 orders, 8 suborders, 168 families, 103 subfamilies, 1,421 genera, 68 subgenera, and 6,589 species of viruses have been defined by the ICTV.<sup>[4]</sup>

The general taxonomic structure of taxon ranges and the suffixes used in taxonomic names are shown hereafter. As of 2019, the ranks of subrealm, subkingdom, and subclass are unused, whereas all other ranks are in use.

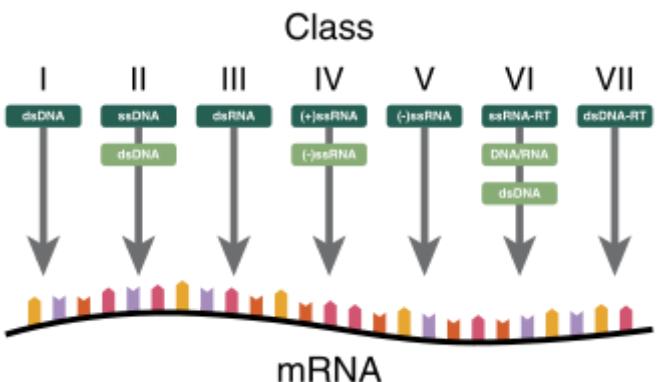
Realm (-viria)



## Baltimore classification

The Nobel Prize-winning biologist David Baltimore devised the Baltimore classification system.<sup>[42][144]</sup> The ICTV classification system is used in conjunction with the Baltimore classification system in modern virus classification.<sup>[145][146][147]</sup>

The Baltimore classification of viruses is based on the mechanism of mRNA production. Viruses must generate mRNAs from their genomes to produce proteins and replicate themselves, but different mechanisms are used to achieve this in each virus family. Viral genomes may be single-stranded (ss) or double-stranded (ds), RNA or DNA, and may or may not use reverse transcriptase (RT). In addition, ssRNA viruses may be either sense (+) or antisense (-). This classification places viruses into seven groups:



The Baltimore Classification of viruses is based on the method of viral mRNA synthesis

- I: **dsDNA viruses** (e.g. Adenoviruses, Herpesviruses, Poxviruses)
- II: **ssDNA viruses** (+ strand or "sense") DNA (e.g. Parvoviruses)
- III: **dsRNA viruses** (e.g. Reoviruses)
- IV: **(+)-ssRNA viruses** (+ strand or sense) RNA (e.g. Coronaviruses, Picornaviruses, Togaviruses)
- V: **(-)-ssRNA viruses** (- strand or antisense) RNA (e.g. Orthomyxoviruses, Rhabdoviruses)

- VI: **ssRNA-RT viruses** (+ strand or sense) RNA with DNA intermediate in life-cycle (e.g. Retroviruses)
- VII: **dsDNA-RT viruses** DNA with RNA intermediate in life-cycle (e.g. Hepadnaviruses)

As an example of viral classification, the chicken pox virus, varicella zoster (VZV), belongs to the order Herpesvirales, family Herpesviridae, subfamily Alphaherpesvirinae, and genus Varicellovirus. VZV is in Group I of the Baltimore Classification because it is a dsDNA virus that does not use reverse transcriptase.

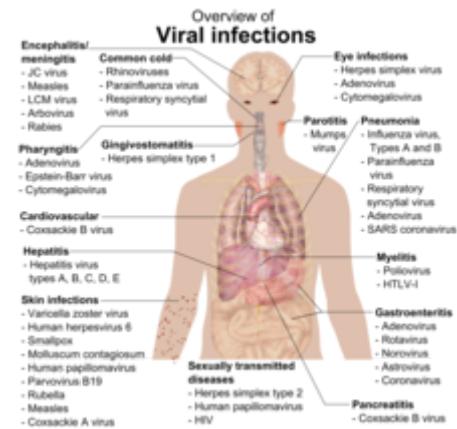
The complete set of viruses in an organism or habitat is called the virome; for example, all human viruses constitute the human virome.<sup>[148]</sup>

## Role in human disease

Examples of common human diseases caused by viruses include the common cold, influenza, chickenpox, and cold sores. Many serious diseases such as rabies, Ebola virus disease, AIDS (HIV), avian influenza, and SARS are caused by viruses. The relative ability of viruses to cause disease is described in terms of virulence. Other diseases are under investigation to discover if they have a virus as the causative agent, such as the possible connection between human herpesvirus 6 (HHV6) and neurological diseases such as multiple sclerosis and chronic fatigue syndrome.<sup>[150]</sup> There is controversy over whether the bornavirus, previously thought to cause neurological diseases in horses, could be responsible for psychiatric illnesses in humans.<sup>[151]</sup>

Viruses have different mechanisms by which they produce disease in an organism, which depends largely on the viral species. Mechanisms at the cellular level primarily include cell lysis, the breaking open and subsequent death of the cell. In multicellular organisms, if enough cells die, the whole organism will start to suffer the effects. Although viruses cause disruption of healthy homeostasis, resulting in disease, they may exist relatively harmlessly within an organism. An example would include the ability of the herpes simplex virus, which causes cold sores, to remain in a dormant state within the human body. This is called latency<sup>[152]</sup> and is a characteristic of the herpes viruses, including Epstein–Barr virus, which causes glandular fever, and varicella zoster virus, which causes chickenpox and shingles. Most people have been infected with at least one of these types of herpes virus.<sup>[153]</sup> These latent viruses might sometimes be beneficial, as the presence of the virus can increase immunity against bacterial pathogens, such as Yersinia pestis.<sup>[154]</sup>

Some viruses can cause lifelong or chronic infections, where the viruses continue to replicate in the body despite the host's defence mechanisms.<sup>[155]</sup> This is common in hepatitis B virus and hepatitis C virus infections. People chronically infected are known as carriers, as they serve as reservoirs of infectious virus.<sup>[156]</sup> In populations with a high proportion of carriers, the disease is said to be endemic.<sup>[157]</sup>



Overview of the main types of viral infection and the most notable species involved<sup>[149]</sup>

## Epidemiology

Viral epidemiology is the branch of medical science that deals with the transmission and control of virus infections in humans. Transmission of viruses can be vertical, which means from mother to child, or horizontal, which means from person to person. Examples of vertical transmission include hepatitis B virus

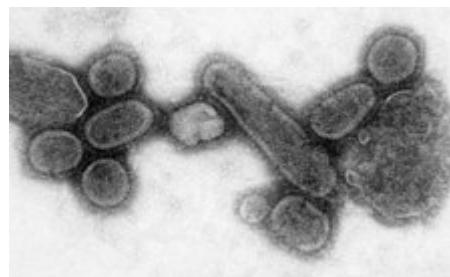
and HIV, where the baby is born already infected with the virus.<sup>[158]</sup> Another, more rare, example is the varicella zoster virus, which, although causing relatively mild infections in children and adults, can be fatal to the foetus and newborn baby.<sup>[159]</sup>

Horizontal transmission is the most common mechanism of spread of viruses in populations. Transmission can occur when: body fluids are exchanged during sexual activity, e.g., HIV; blood is exchanged by contaminated transfusion or needle sharing, e.g., hepatitis C; exchange of saliva by mouth, e.g., Epstein–Barr virus; contaminated food or water is ingested, e.g., norovirus; aerosols containing virions are inhaled, e.g., influenza virus; and insect vectors such as mosquitoes penetrate the skin of a host, e.g., dengue. The rate or speed of transmission of viral infections depends on factors that include population density, the number of susceptible individuals, (i.e., those not immune),<sup>[160]</sup> the quality of healthcare and the weather.<sup>[161]</sup>

Epidemiology is used to break the chain of infection in populations during outbreaks of viral diseases.<sup>[162]</sup> Control measures are used that are based on knowledge of how the virus is transmitted. It is important to find the source, or sources, of the outbreak and to identify the virus. Once the virus has been identified, the chain of transmission can sometimes be broken by vaccines. When vaccines are not available, sanitation and disinfection can be effective. Often, infected people are isolated from the rest of the community, and those that have been exposed to the virus are placed in quarantine.<sup>[163]</sup> To control the outbreak of foot-and-mouth disease in cattle in Britain in 2001, thousands of cattle were slaughtered.<sup>[164]</sup> Most viral infections of humans and other animals have incubation periods during which the infection causes no signs or symptoms.<sup>[165]</sup> Incubation periods for viral diseases range from a few days to weeks, but are known for most infections.<sup>[166]</sup> Somewhat overlapping, but mainly following the incubation period, there is a period of communicability—a time when an infected individual or animal is contagious and can infect another person or animal.<sup>[166]</sup> This, too, is known for many viral infections, and knowledge of the length of both periods is important in the control of outbreaks.<sup>[167]</sup> When outbreaks cause an unusually high proportion of cases in a population, community, or region, they are called epidemics. If outbreaks spread worldwide, they are called pandemics.<sup>[168]</sup>

## Epidemics and pandemics

A pandemic is a worldwide epidemic. The 1918 flu pandemic, which lasted until 1919, was a category 5 influenza pandemic caused by an unusually severe and deadly influenza A virus. The victims were often healthy young adults, in contrast to most influenza outbreaks, which predominantly affect juvenile, elderly, or otherwise-weakened patients.<sup>[169]</sup> Older estimates say it killed 40–50 million people,<sup>[170]</sup> while more recent research suggests that it may have killed as many as 100 million people, or 5% of the world's population in 1918.<sup>[171]</sup>



Transmission electron microscope image of a recreated 1918 influenza virus

Although viral pandemics are rare events, HIV—which evolved from viruses found in monkeys and chimpanzees—has been pandemic since at least the 1980s.<sup>[172]</sup> During the 20th century there were four pandemics caused by influenza virus and those that occurred in 1918, 1957 and 1968 were severe.<sup>[173]</sup> Most researchers believe that HIV originated in sub-Saharan Africa during the 20th century;<sup>[174]</sup> it is now a pandemic, with an estimated 37.9 million people now living with the disease worldwide.<sup>[175][175]</sup> There were about 770,000 deaths from AIDS in 2018.<sup>[176]</sup> The Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimate that AIDS has killed more than 25 million people since it was first recognised on 5 June 1981, making it one of the most destructive epidemics in recorded history.<sup>[177]</sup> In 2007 there were 2.7 million new HIV infections and 2 million HIV-related deaths.<sup>[178]</sup>

Several highly lethal viral pathogens are members of the *Filoviridae*. Filoviruses are filament-like viruses that cause viral hemorrhagic fever, and include ebolaviruses and marburgviruses. Marburg virus, first discovered in 1967, attracted widespread press attention in April 2005 for an outbreak in Angola.<sup>[179]</sup> Ebola virus disease has also caused intermittent outbreaks with high mortality rates since 1976 when it was first identified. The worst and most recent one is the 2013–2016 West Africa epidemic.<sup>[180]</sup>

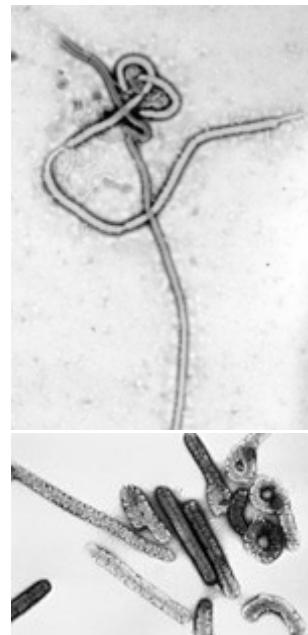
With the exception of smallpox, most pandemics are caused by newly evolved viruses. These "emergent" viruses are usually mutants of less harmful viruses that have circulated previously either in humans or other animals.<sup>[181]</sup>

Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) are caused by new types of coronaviruses. Other coronaviruses are known to cause mild infections in humans,<sup>[182]</sup> so the virulence and rapid spread of SARS infections—that by July 2003 had caused around 8,000 cases and 800 deaths—was unexpected and most countries were not prepared.<sup>[183]</sup>

A related coronavirus emerged in Wuhan, China in November 2019 and spread rapidly around the world. Thought to have originated in bats and subsequently named severe acute respiratory syndrome coronavirus 2, infections with the virus caused a pandemic in 2020.<sup>[184][185][186]</sup> Unprecedented restrictions in peacetime have been placed on international travel,<sup>[187]</sup> and curfews imposed in several major cities worldwide.<sup>[188]</sup>

## Cancer

Viruses are an established cause of cancer in humans and other species. Viral cancers occur only in a minority of infected persons (or animals). Cancer viruses come from a range of virus families, including both RNA and DNA viruses, and so there is no single type of "oncovirus" (an obsolete term originally used for acutely transforming retroviruses). The development of cancer is determined by a variety of factors such as host immunity<sup>[189]</sup> and mutations in the host.<sup>[190]</sup> Viruses accepted to cause human cancers include some genotypes of human papillomavirus, hepatitis B virus, hepatitis C virus, Epstein–Barr virus, Kaposi's sarcoma-associated herpesvirus and human T-lymphotropic virus. The most recently discovered human cancer virus is a polyomavirus (Merkel cell polyomavirus) that causes most cases of a rare form of skin cancer called Merkel cell carcinoma.<sup>[191]</sup> Hepatitis viruses can develop into a chronic viral infection that leads to liver cancer.<sup>[192][193]</sup> Infection by human T-lymphotropic virus can lead to tropical spastic paraparesis and adult T-cell leukaemia.<sup>[194]</sup> Human papillomaviruses are an established cause of cancers of cervix, skin, anus, and penis.<sup>[195]</sup> Within the *Herpesviridae*, Kaposi's sarcoma-associated herpesvirus causes Kaposi's sarcoma and body-cavity lymphoma, and Epstein–Barr virus causes Burkitt's lymphoma, Hodgkin's lymphoma, B lymphoproliferative disorder, and nasopharyngeal carcinoma.<sup>[196]</sup> Merkel cell polyomavirus closely related to SV40 and mouse polyomaviruses that have been used as animal models for cancer viruses for over 50 years.<sup>[197]</sup>



Ebola (top) and Marburg viruses (bottom)

## Host defence mechanisms

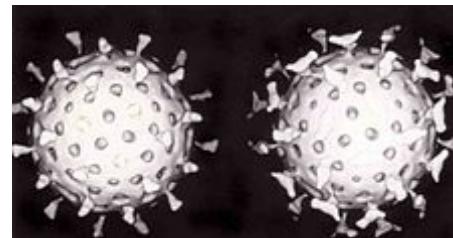
The body's first line of defence against viruses is the innate immune system. This comprises cells and other mechanisms that defend the host from infection in a non-specific manner. This means that the cells of the innate system recognise, and respond to, pathogens in a generic way, but, unlike the adaptive immune system, it does not confer long-lasting or protective immunity to the host.<sup>[198]</sup>

RNA interference is an important innate defence against viruses.<sup>[199]</sup> Many viruses have a replication strategy that involves double-stranded RNA (dsRNA). When such a virus infects a cell, it releases its RNA molecule or molecules, which immediately bind to a protein complex called a dicer that cuts the RNA into smaller pieces. A biochemical pathway—the RISC complex—is activated, which ensures cell survival by degrading the viral mRNA. Rotaviruses have evolved to avoid this defence mechanism by not uncoating fully inside the cell, and releasing newly produced mRNA through pores in the particle's inner capsid. Their genomic dsRNA remains protected inside the core of the virion.<sup>[200][201]</sup>

When the adaptive immune system of a vertebrate encounters a virus, it produces specific antibodies that bind to the virus and often render it non-infectious. This is called humoral immunity. Two types of antibodies are important. The first, called IgM, is highly effective at neutralising viruses but is produced by the cells of the immune system only for a few weeks. The second, called IgG, is produced indefinitely. The presence of IgM in the blood of the host is used to test for acute infection, whereas IgG indicates an infection sometime in the past.<sup>[202]</sup> IgG antibody is measured when tests for immunity are carried out.<sup>[203]</sup>

Antibodies can continue to be an effective defence mechanism even after viruses have managed to gain entry to the host cell. A protein that is in cells, called TRIM21, can attach to the antibodies on the surface of the virus particle. This primes the subsequent destruction of the virus by the enzymes of the cell's proteosome system.<sup>[204]</sup>

A second defence of vertebrates against viruses is called cell-mediated immunity and involves immune cells known as T cells. The body's cells constantly display short fragments of their proteins on the cell's surface, and, if a T cell recognises a suspicious viral fragment there, the host cell is destroyed by 'killer T' cells and the virus-specific T-cells proliferate. Cells such as the macrophage are specialists at this antigen presentation.<sup>[205]</sup> The production of interferon is an important host defence mechanism. This is a hormone produced by the body when viruses are present. Its role in immunity is complex; it eventually stops the viruses from reproducing by killing the infected cell and its close neighbours.<sup>[206]</sup>



Two rotaviruses: the one on the right is coated with antibodies that prevent its attachment to cells and infecting them.

Not all virus infections produce a protective immune response in this way. HIV evades the immune system by constantly changing the amino acid sequence of the proteins on the surface of the virion. This is known as "escape mutation" as the viral epitopes escape recognition by the host immune response. These persistent viruses evade immune control by sequestration, blockade of antigen presentation, cytokine resistance, evasion of natural killer cell activities, escape from apoptosis, and antigenic shift.<sup>[207]</sup> Other viruses, called 'neurotropic viruses', are disseminated by neural spread where the immune system may be unable to reach them.

## Prevention and treatment

Because viruses use vital metabolic pathways within host cells to replicate, they are difficult to eliminate without using drugs that cause toxic effects to host cells in general. The most effective medical approaches to viral diseases are vaccinations to provide immunity to infection, and antiviral drugs that selectively interfere with viral replication.

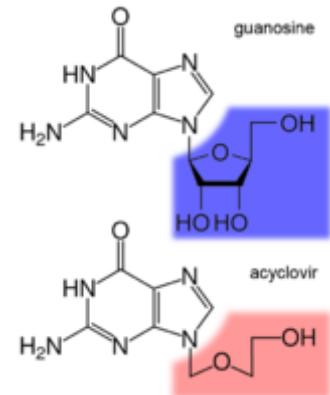
## Vaccines

Vaccination is a cheap and effective way of preventing infections by viruses. Vaccines were used to prevent viral infections long before the discovery of the actual viruses. Their use has resulted in a dramatic decline in morbidity (illness) and mortality (death) associated with viral infections such as polio, measles, mumps and rubella.<sup>[208]</sup> Smallpox infections have been eradicated.<sup>[209]</sup> Vaccines are available to prevent over thirteen viral infections of humans,<sup>[210]</sup> and more are used to prevent viral infections of animals.<sup>[211]</sup> Vaccines can consist of live-attenuated or killed viruses, or viral proteins (antigens).<sup>[212]</sup> Live vaccines contain weakened forms of the virus, which do not cause the disease but, nonetheless, confer immunity. Such viruses are called attenuated. Live vaccines can be dangerous when given to people with a weak immunity (who are described as immunocompromised), because in these people, the weakened virus can cause the original disease.<sup>[213]</sup> Biotechnology and genetic engineering techniques are used to produce subunit vaccines. These vaccines use only the capsid proteins of the virus. Hepatitis B vaccine is an example of this type of vaccine.<sup>[214]</sup> Subunit vaccines are safe for immunocompromised patients because they cannot cause the disease.<sup>[215]</sup> The yellow fever virus vaccine, a live-attenuated strain called 17D, is probably the safest and most effective vaccine ever generated.<sup>[216]</sup>

## Antiviral drugs

Antiviral drugs are often nucleoside analogues (fake DNA building-blocks), which viruses mistakenly incorporate into their genomes during replication. The life-cycle of the virus is then halted because the newly synthesised DNA is inactive. This is because these analogues lack the hydroxyl groups, which, along with phosphorus atoms, link together to form the strong "backbone" of the DNA molecule. This is called DNA chain termination.<sup>[217]</sup> Examples of nucleoside analogues are aciclovir for Herpes simplex virus infections and lamivudine for HIV and hepatitis B virus infections. Aciclovir is one of the oldest and most frequently prescribed antiviral drugs.<sup>[218]</sup> Other antiviral drugs in use target different stages of the viral life cycle. HIV is dependent on a proteolytic enzyme called the HIV-1 protease for it to become fully infectious. There is a large class of drugs called protease inhibitors that inactivate this enzyme.<sup>[219]</sup>

Hepatitis C is caused by an RNA virus. In 80% of people infected, the disease is chronic, and without treatment, they are infected for the remainder of their lives. There is now an effective treatment that uses the nucleoside analogue drug ribavirin combined with interferon.<sup>[220]</sup> The treatment of chronic carriers of the hepatitis B virus by using a similar strategy using lamivudine has been developed.<sup>[221]</sup>



The structure of the DNA base guanosine and the antiviral drug acyclovir

## Infection in other species

Viruses infect all cellular life and, although viruses occur universally, each cellular species has its own specific range that often infect only that species.<sup>[222]</sup> Some viruses, called satellites, can replicate only within cells that have already been infected by another virus.<sup>[60]</sup>

## Animal viruses

Viruses are important pathogens of livestock. Diseases such as foot-and-mouth disease and bluetongue are caused by viruses.<sup>[223]</sup> Companion animals such as cats, dogs, and horses, if not vaccinated, are susceptible to serious viral infections. Canine parvovirus is caused by a small DNA virus and infections are often fatal

in pups.<sup>[224]</sup> Like all invertebrates, the honey bee is susceptible to many viral infections.<sup>[225]</sup> Most viruses co-exist harmlessly in their host and cause no signs or symptoms of disease.<sup>[3]</sup>

## Plant viruses

There are many types of plant virus, but often they cause only a loss of yield, and it is not economically viable to try to control them. Plant viruses are often spread from plant to plant by organisms, known as vectors. These are usually insects, but some fungi, nematode worms, and single-celled organisms have been shown to be vectors. When control of plant virus infections is considered economical, for perennial fruits, for example, efforts are concentrated on killing the vectors and removing alternate hosts such as weeds.<sup>[226]</sup> Plant viruses cannot infect humans and other animals because they can reproduce only in living plant cells.<sup>[227]</sup>

Originally from Peru, the potato has become a staple crop worldwide.<sup>[228]</sup> The potato virus Y causes disease in potatoes and related species including tomatoes and peppers. In the 1980s, this virus acquired economical importance when it proved difficult to control in seed potato crops. Transmitted by aphids, this virus can reduce crop yields by up to 80 per cent, causing significant losses to potato yields.<sup>[229]</sup>

Plants have elaborate and effective defence mechanisms against viruses. One of the most effective is the presence of so-called resistance (R) genes. Each R gene confers resistance to a particular virus by triggering localised areas of cell death around the infected cell, which can often be seen with the unaided eye as large spots. This stops the infection from spreading.<sup>[230]</sup> RNA interference is also an effective defence in plants.<sup>[231]</sup> When they are infected, plants often produce natural disinfectants that kill viruses, such as salicylic acid, nitric oxide, and reactive oxygen molecules.<sup>[232]</sup>

Plant virus particles or virus-like particles (VLPs) have applications in both biotechnology and nanotechnology. The capsids of most plant viruses are simple and robust structures and can be produced in large quantities either by the infection of plants or by expression in a variety of heterologous systems. Plant virus particles can be modified genetically and chemically to encapsulate foreign material and can be incorporated into supramolecular structures for use in biotechnology.<sup>[233]</sup>

## Bacterial viruses

Bacteriophages are a common and diverse group of viruses and are the most abundant biological entity in aquatic environments—there are up to ten times more of these viruses in the oceans than there are bacteria,<sup>[234]</sup> reaching levels of 250,000,000 bacteriophages per millilitre of seawater.<sup>[235]</sup> These viruses infect specific bacteria by binding to surface receptor molecules and then entering the cell. Within a short amount of time, in some cases just minutes, bacterial polymerase starts translating viral mRNA into protein. These proteins go on to become either new virions within the cell, helper proteins, which help assembly of new virions, or proteins involved in cell lysis. Viral enzymes aid in the breakdown of the cell membrane, and, in the case of the T4 phage, in just over twenty minutes after injection over three hundred phages could be released.<sup>[236]</sup>

The major way bacteria defend themselves from bacteriophages is by producing enzymes that destroy foreign DNA. These enzymes, called restriction endonucleases, cut up the viral DNA that bacteriophages inject into bacterial cells.<sup>[237]</sup> Bacteria also contain a system that uses CRISPR sequences to retain fragments of the genomes of viruses that the bacteria have come into contact with in the past, which allows



Peppers infected by mild mottle virus

them to block the virus's replication through a form of RNA interference.<sup>[238][239]</sup> This genetic system provides bacteria with acquired immunity to infection.<sup>[240]</sup>

## Archaeal viruses

Some viruses replicate within archaea: these are double-stranded DNA viruses with unusual and sometimes unique shapes.<sup>[6][89]</sup> These viruses have been studied in most detail in the thermophilic archaea, particularly the orders Sulfolobales and Thermoproteales.<sup>[241]</sup> Defences against these viruses involve RNA interference from repetitive DNA sequences within archaean genomes that are related to the genes of the viruses.<sup>[242][243]</sup> Most archaea have CRISPR–Cas systems as an adaptive defence against viruses. These enable archaea to retain sections of viral DNA, which are then used to target and eliminate subsequent infections by the virus using a process similar to RNA interference.<sup>[244]</sup>



Transmission electron micrograph of multiple bacteriophages attached to a bacterial cell wall

## Role in aquatic ecosystems

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Viruses are the most abundant biological entity in aquatic environments<sup>[2]</sup> There are about ten million of them in a teaspoon of seawater.<sup>[245]</sup> Most of these viruses are bacteriophages infecting heterotrophic bacteria and cyanophages infecting cyanobacteria and they are essential to the regulation of saltwater and freshwater ecosystems.<sup>[246]</sup> Bacteriophages are harmless to plants and animals, and are essential to the regulation of marine and freshwater ecosystems<sup>[247]</sup> are important mortality agents of phytoplankton, the base of the foodchain in aquatic environments.<sup>[248]</sup> They infect and destroy bacteria in aquatic microbial communities, and are one of the most important mechanisms of recycling carbon and nutrient cycling in marine environments. The organic molecules released from the dead bacterial cells stimulate fresh bacterial and algal growth, in a process known as the viral shunt.<sup>[249]</sup> In particular, lysis of bacteria by viruses has been shown to enhance nitrogen cycling and stimulate phytoplankton growth.<sup>[250]</sup> Viral activity may also affect the biological pump, the process whereby carbon is sequestered in the deep ocean.<sup>[251]</sup>

Microorganisms constitute more than 90% of the biomass in the sea. It is estimated that viruses kill approximately 20% of this biomass each day and that there are 10 to 15 times as many viruses in the oceans as there are bacteria and archaea.<sup>[252]</sup> Viruses are also major agents responsible for the destruction of phytoplankton including harmful algal blooms,<sup>[253]</sup> The number of viruses in the oceans decreases further offshore and deeper into the water, where there are fewer host organisms.<sup>[251]</sup>

In January 2018, scientists reported that 800 million viruses, mainly of marine origin, are deposited daily from the Earth's atmosphere onto every square meter of the planet's surface, as the result of a global atmospheric stream of viruses, circulating above the weather system but below the altitude of usual airline travel, distributing viruses around the planet.<sup>[254][255]</sup>

Like any organism, marine mammals are susceptible to viral infections. In 1988 and 2002, thousands of harbour seals were killed in Europe by phocine distemper virus.<sup>[256]</sup> Many other viruses, including caliciviruses, herpesviruses, adenoviruses and parvoviruses, circulate in marine mammal populations.<sup>[251]</sup>

## Role in evolution

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Viruses are an important natural means of transferring genes between different species, which increases genetic diversity and drives evolution.<sup>[8]</sup> It is thought that viruses played a central role in early evolution, before the diversification of the last universal common ancestor into bacteria, archaea and eukaryotes.<sup>[257]</sup> Viruses are still one of the largest reservoirs of unexplored genetic diversity on Earth.<sup>[251]</sup>

## Applications

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### Life sciences and medicine

Viruses are important to the study of molecular and cell biology as they provide simple systems that can be used to manipulate and investigate the functions of cells.<sup>[258]</sup> The study and use of viruses have provided valuable information about aspects of cell biology.<sup>[259]</sup> For example, viruses have been useful in the study of genetics and helped our understanding of the basic mechanisms of molecular genetics, such as DNA replication, transcription, RNA processing, translation, protein transport, and immunology.

Geneticists often use viruses as vectors to introduce genes into cells that they are studying. This is useful for making the cell produce a foreign substance, or to study the effect of introducing a new gene into the genome. In a similar fashion, virotherapy uses viruses as vectors to treat various diseases, as they can specifically target cells and DNA. It shows promising use in the treatment of cancer and in gene therapy. Eastern European scientists have used phage therapy as an alternative to antibiotics for some time, and interest in this approach is increasing, because of the high level of antibiotic resistance now found in some pathogenic bacteria.<sup>[260]</sup> The expression of heterologous proteins by viruses is the basis of several manufacturing processes that are currently being used for the production of various proteins such as vaccine antigens and antibodies. Industrial processes have been recently developed using viral vectors and a number of pharmaceutical proteins are currently in pre-clinical and clinical trials.<sup>[261]</sup>



Scientist studying the H5N1 influenza virus

### Virotherapy

Virotherapy involves the use of genetically modified viruses to treat diseases.<sup>[262]</sup> Viruses have been modified by scientists to reproduce in cancer cells and destroy them but not infect healthy cells. Talimogene laherparepvec (T-VEC), for example, is a modified herpes simplex virus that has had a gene, which is required for viruses to replicate in healthy cells, deleted and replaced with a human gene (GM-CSF) that stimulates immunity. When this virus infects cancer cells, it destroys them and in doing so the presence of the GM-CSF gene attracts dendritic cells from the surrounding tissues of the body. The dendritic cells process the dead cancer cells and present components of them to other cells of the immune system.<sup>[263]</sup> Having completed successful clinical trials, the virus gained approval for the treatment of melanoma in late 2015.<sup>[264]</sup> Viruses that have been reprogrammed to kill cancer cells are called oncolytic viruses.<sup>[265]</sup>

### Materials science and nanotechnology

Current trends in nanotechnology promise to make much more versatile use of viruses. From the viewpoint of a materials scientist, viruses can be regarded as organic nanoparticles. Their surface carries specific tools that enable them to cross the barriers of their host cells. The size and shape of viruses and the number and

nature of the functional groups on their surface is precisely defined. As such, viruses are commonly used in materials science as scaffolds for covalently linked surface modifications. A particular quality of viruses is that they can be tailored by directed evolution. The powerful techniques developed by life sciences are becoming the basis of engineering approaches towards nanomaterials, opening a wide range of applications far beyond biology and medicine.<sup>[266]</sup>

Because of their size, shape, and well-defined chemical structures, viruses have been used as templates for organising materials on the nanoscale. Recent examples include work at the Naval Research Laboratory in Washington, D.C., using Cowpea mosaic virus (CPMV) particles to amplify signals in DNA microarray based sensors. In this application, the virus particles separate the fluorescent dyes used for signalling to prevent the formation of non-fluorescent dimers that act as quenchers.<sup>[267]</sup> Another example is the use of CPMV as a nanoscale breadboard for molecular electronics.<sup>[268]</sup>

## Synthetic viruses

Many viruses can be synthesised de novo ("from scratch") and the first synthetic virus was created in 2002.<sup>[269]</sup> Although somewhat of a misconception, it is not the actual virus that is synthesised, but rather its DNA genome (in case of a DNA virus), or a cDNA copy of its genome (in case of RNA viruses). For many virus families the naked synthetic DNA or RNA (once enzymatically converted back from the synthetic cDNA) is infectious when introduced into a cell. That is, they contain all the necessary information to produce new viruses. This technology is now being used to investigate novel vaccine strategies.<sup>[270]</sup> The ability to synthesise viruses has far-reaching consequences, since viruses can no longer be regarded as extinct, as long as the information of their genome sequence is known and permissive cells are available. As of November 2017, the full-length genome sequences of 7454 different viruses, including smallpox, are publicly available in an online database maintained by the National Institutes of Health.<sup>[271]</sup>

## Weapons

The ability of viruses to cause devastating epidemics in human societies has led to the concern that viruses could be weaponised for biological warfare. Further concern was raised by the successful recreation of the infamous 1918 influenza virus in a laboratory.<sup>[272]</sup> Smallpox virus devastated numerous societies throughout history before its eradication. There are only two centres in the world authorised by the WHO to keep stocks of smallpox virus: the State Research Center of Virology and Biotechnology VECTOR in Russia and the Centers for Disease Control and Prevention in the United States.<sup>[273]</sup> It may be used as a weapon,<sup>[273]</sup> as the vaccine for smallpox sometimes had severe side-effects, it is no longer used routinely in any country. Thus, much of the modern human population has almost no established resistance to smallpox and would be vulnerable to the virus.<sup>[273]</sup>

## See also

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- Cross-species transmission
- Glossary of virology
- Non-cellular life
- Viral metagenomics
- Viroplasm
- Zoonosis

## References

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## Notes

1. Wu, Katherine J. (15 April 2020). "There are more viruses than stars in the universe. Why do only some infect us? – More than a quadrillion quadrillion individual viruses exist on Earth, but most are not poised to hop into humans. Can we find the ones that are?" (<https://www.nationalgeographic.com/science/2020/04/factors-allow-viruses-infect-humans-coronavirus/>). *National Geographic Society*. Retrieved 18 May 2020.
2. Koonin EV, Senkevich TG, Dolja VV (September 2006). "The ancient Virus World and evolution of cells" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1594570>). *Biology Direct*. **1** (1): 29. doi:10.1186/1745-6150-1-29 (<https://doi.org/10.1186%2F1745-6150-1-29>). PMC 1594570 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1594570>). PMID 16984643 (<https://pubmed.ncbi.nlm.nih.gov/16984643>).
3. Dimmock p. 4
4. "Virus Taxonomy: 2019 Release" (<https://talk.ictvonline.org/taxonomy/>). *talk.ictvonline.org*. International Committee on Taxonomy of Viruses. Retrieved 25 April 2020.
5. Breitbart M, Rohwer F (June 2005). "Here a virus, there a virus, everywhere the same virus?". *Trends in Microbiology*. **13** (6): 278–84. doi:10.1016/j.tim.2005.04.003 (<https://doi.org/10.1016%2Fj.tim.2005.04.003>). PMID 15936660 (<https://pubmed.ncbi.nlm.nih.gov/15936660>).
6. Lawrence CM, Menon S, Eilers BJ, Bothner B, Khayat R, Douglas T, Young MJ (May 2009). "Structural and functional studies of archaeal viruses" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2675988>). *The Journal of Biological Chemistry*. **284** (19): 12599–603. doi:10.1074/jbc.R800078200 (<https://doi.org/10.1074%2Fjbc.R800078200>). PMC 2675988 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2675988>). PMID 19158076 (<https://pubmed.ncbi.nlm.nih.gov/19158076>).
7. Edwards RA, Rohwer F (June 2005). "Viral metagenomics". *Nature Reviews. Microbiology*. **3** (6): 504–10. doi:10.1038/nrmicro1163 (<https://doi.org/10.1038%2Fnrmicro1163>). PMID 15886693 (<https://pubmed.ncbi.nlm.nih.gov/15886693>). S2CID 8059643 (<https://api.semanticscholar.org/CorpusID:8059643>).
8. Canchaya C, Fournous G, Chibani-Chennoufi S, Dillmann ML, Brüssow H (August 2003). "Phage as agents of lateral gene transfer". *Current Opinion in Microbiology*. **6** (4): 417–24. doi:10.1016/S1369-5274(03)00086-9 (<https://doi.org/10.1016%2FS1369-5274%2803%290008-6-9>). PMID 12941415 (<https://pubmed.ncbi.nlm.nih.gov/12941415>).
9. Rybicki EP (1990). "The classification of organisms at the edge of life, or problems with virus systematics". *South African Journal of Science*. **86**: 182–86.
10. Koonin EV, Starokadomskyy P (October 2016). "Are viruses alive? The replicator paradigm sheds decisive light on an old but misguided question" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5406846>). *Studies in History and Philosophy of Biological and Biomedical Sciences*. **59**: 125–34. doi:10.1016/j.shpsc.2016.02.016 (<https://doi.org/10.1016%2Fj.shpsc.2016.02.016>). PMC 5406846 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5406846>). PMID 26965225 (<https://pubmed.ncbi.nlm.nih.gov/26965225>).
11. Robilotti, Elizabeth; Deresinski, Stan; Pinsky, Benjamin A. (2015). "Norovirus" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4284304>). *Clinical Microbiology Reviews*. **28** (1): 134–164. doi:10.1128/CMR.00075-14 (<https://doi.org/10.1128%2FCMR.00075-14>). PMC 4284304 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4284304>). PMID 25567225 (<https://pubmed.ncbi.nlm.nih.gov/25567225>).
12. Shors pp. 123–124
13. "Virus, n.". *OED Online*. Oxford University Press. March 2015.
14. Harper D (2011). "virus" (<http://www.etymonline.com/index.php?term=virus>). *The Online Etymology Dictionary*. Retrieved 19 December 2014.
15. "Virulent, adj.". *OED Online*. Oxford University Press. March 2015.
16. Harper D (2011). "virulent" (<http://www.etymonline.com/index.php?term=virulent>). *The Online Etymology Dictionary*. Retrieved 19 December 2014.

17. Buschard K, Thon R (2003). "Diabetic Animal Models". In Hau J, Van Hoosier Jr GL (eds.). *Handbook of Laboratory Animal Science. Animal Models.* II (Second ed.). CRC Press. pp. 163, 166.
18. William T. Stearn: *Botanical Latin. History, Grammar, Syntax, Terminology and Vocabulary.* David & Charles, third edition, 1983. Quote: "Virus: virus (s.n. II), gen. sing. viri, nom. pl. vira, gen. pl. vīrorum (to be distinguished from *virorum*, of men)."
19. Harper D (2011). "viral" (<http://www.etymonline.com/index.php?term=viral>). *The Online Etymology Dictionary*. Retrieved 19 December 2014.
20. Harper D (2011). "virion" (<http://www.etymonline.com/index.php?term=virion>). *The Online Etymology Dictionary*. Retrieved 19 December 2014.
21. Casjens S (2010). Mahy BW, Van Regenmortel MH (eds.). *Desk Encyclopedia of General Virology*. Boston: Academic Press. p. 167. ISBN 978-0-12-375146-1.
22. Bordenave G (May 2003). "Louis Pasteur (1822-1895)". *Microbes and Infection*. 5 (6): 553–60. doi:[10.1016/S1286-4579\(03\)00075-3](https://doi.org/10.1016/S1286-4579(03)00075-3) (<https://doi.org/10.1016%2FS1286-4579%2803%290007-5-3>). PMID [12758285](https://pubmed.ncbi.nlm.nih.gov/12758285) (<https://pubmed.ncbi.nlm.nih.gov/12758285>).
23. Shors pp. 74, 827
24. Collier p. 3
25. Dimmock pp. 4–5
26. Fenner F (2009). Mahy BW, Van Regenmortel MH (eds.). *Desk Encyclopedia of General Virology* (1 ed.). Oxford: Academic Press. p. 15. ISBN 978-0-12-375146-1.
27. Shors p. 827
28. D'Herelle F (September 2007). "On an invisible microbe antagonistic toward dysenteric bacilli: brief note by Mr. F. D'Herelle, presented by Mr. Roux. 1917". *Research in Microbiology*. 158 (7): 553–54. doi:[10.1016/j.resmic.2007.07.005](https://doi.org/10.1016/j.resmic.2007.07.005) (<https://doi.org/10.1016%2Fj.resmic.2007.07.005>). PMID [17855060](https://pubmed.ncbi.nlm.nih.gov/17855060) (<https://pubmed.ncbi.nlm.nih.gov/17855060>).
29. Domingo-Calap P, Georgel P, Bahram S (March 2016). "Back to the future: bacteriophages as promising therapeutic tools". *HLA*. 87 (3): 133–40. doi:[10.1111/tan.12742](https://doi.org/10.1111/tan.12742) (<https://doi.org/10.1111%2Ftan.12742>). PMID [26891965](https://pubmed.ncbi.nlm.nih.gov/26891965) (<https://pubmed.ncbi.nlm.nih.gov/26891965>).
30. Steinhardt E, Israeli C, Lambert RA (1913). "Studies on the cultivation of the virus of vaccinia" (<https://zenodo.org/record/1431761>). *The Journal of Infectious Diseases*. 13 (2): 294–300. doi:[10.1093/infdis/13.2.294](https://doi.org/10.1093/infdis/13.2.294) (<https://doi.org/10.1093%2Finfdis%2F13.2.294>).
31. Collier p. 4
32. Goodpasture EW, Woodruff AM, Buddingh GJ (October 1931). "The cultivation of vaccine and other viruses in the chorioallantoic membrane of chick embryos". *Science*. 74 (1919): 371–72. Bibcode:[1931Sci....74..371G](https://ui.adsabs.harvard.edu/abs/1931Sci....74..371G) (<https://ui.adsabs.harvard.edu/abs/1931Sci....74..371G>). doi:[10.1126/science.74.1919.371](https://doi.org/10.1126/science.74.1919.371) (<https://doi.org/10.1126%2Fscience.74.1919.371>). PMID [17810781](https://pubmed.ncbi.nlm.nih.gov/17810781) (<https://pubmed.ncbi.nlm.nih.gov/17810781>).
33. Thomas Huckle Weller (2004). *Growing Pathogens in Tissue Cultures: Fifty Years in Academic Tropical Medicine, Pediatrics, and Virology* (<https://books.google.com/books?id=jYbqLuOVJIEC&pg=PA57>). Boston Medical Library. p. 57. ISBN 978-0-88135-380-8.
34. Rosen FS (October 2004). "Isolation of poliovirus--John Enders and the Nobel Prize". *The New England Journal of Medicine*. 351 (15): 1481–83. doi:[10.1056/NEJMmp048202](https://doi.org/10.1056/NEJMmp048202) (<https://doi.org/10.1056%2FNEJMmp048202>). PMID [15470207](https://pubmed.ncbi.nlm.nih.gov/15470207) (<https://pubmed.ncbi.nlm.nih.gov/15470207>).
35. Frängsmyr T, Ekspång G, eds. (1993). *Nobel Lectures, Physics 1981–1990*. Singapore: World Scientific Publishing Co. Bibcode:[1993nlp..book.....F](https://ui.adsabs.harvard.edu/abs/1993nlp..book.....F) (<https://ui.adsabs.harvard.edu/abs/1993nlp..book.....F>).

- In 1887, Buist visualised one of the largest, Vaccinia virus, by optical microscopy after staining it. Vaccinia was not known to be a virus at that time. (Buist J.B. *Vaccinia and Variola: a study of their life history* Churchill, London)

36. Stanley WM, Loring HS (January 1936). "The Isolation of Crystalline Tobacco Mosaic Virus Protein From Diseased Tomato Plants". *Science*. **83** (2143): 85. Bibcode:1936Sci....83...85S (<https://ui.adsabs.harvard.edu/abs/1936Sci....83...85S>). doi:10.1126/science.83.2143.85 (<https://doi.org/10.1126%2Fscience.83.2143.85>). PMID 17756690 (<https://pubmed.ncbi.nlm.nih.gov/17756690>).
37. Stanley WM, Lauffer MA (April 1939). "Disintegration of Tobacco Mosaic Virus in Urea Solutions". *Science*. **89** (2311): 345–47. Bibcode:1939Sci....89..345S (<https://ui.adsabs.harvard.edu/abs/1939Sci....89..345S>). doi:10.1126/science.89.2311.345 (<https://doi.org/10.1126%2Fscience.89.2311.345>). PMID 17788438 (<https://pubmed.ncbi.nlm.nih.gov/17788438>).
38. Creager AN, Morgan GJ (June 2008). "After the double helix: Rosalind Franklin's research on Tobacco mosaic virus". *Isis; an International Review Devoted to the History of Science and Its Cultural Influences*. **99** (2): 239–72. doi:10.1086/588626 (<https://doi.org/10.1086%2F588626>). PMID 18702397 (<https://pubmed.ncbi.nlm.nih.gov/18702397>).
39. Dimmock p. 12
40. Norrby E (2008). "Nobel Prizes and the emerging virus concept". *Archives of Virology*. **153** (6): 1109–23. doi:10.1007/s00705-008-0088-8 (<https://doi.org/10.1007%2Fs00705-008-0088-8>). PMID 18446425 (<https://pubmed.ncbi.nlm.nih.gov/18446425>). S2CID 10595263 (<https://api.semanticscholar.org/CorpusID:10595263>).
41. Collier p. 745
42. Temin HM, Baltimore D (1972). "RNA-directed DNA synthesis and RNA tumor viruses". *Advances in Virus Research*. **17**: 129–86. doi:10.1016/S0065-3527(08)60749-6 (<https://doi.org/10.1016%2FS0065-3527%2808%2960749-6>). ISBN 9780120398171. PMID 4348509 (<https://pubmed.ncbi.nlm.nih.gov/4348509>).
43. Barré-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S, Gruest J, et al. (May 1983). "Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)". *Science*. **220** (4599): 868–71. Bibcode:1983Sci...220..868B (<https://ui.adsabs.harvard.edu/abs/1983Sci...220..868B>). doi:10.1126/science.6189183 (<https://doi.org/10.1126%2Fscience.6189183>). PMID 6189183 (<https://pubmed.ncbi.nlm.nih.gov/6189183>).
44. Choo QL, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M (April 1989). "Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome". *Science*. **244** (4902): 359–62. Bibcode:1989Sci...244..359C (<https://ui.adsabs.harvard.edu/abs/1989Sci...244..359C>). CiteSeerX 10.1.1.469.3592 (<https://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.469.3592>). doi:10.1126/science.2523562 (<https://doi.org/10.1126%2Fscience.2523562>). PMID 2523562 (<https://pubmed.ncbi.nlm.nih.gov/2523562>).
45. Houghton M (November 2009). "The long and winding road leading to the identification of the hepatitis C virus" (<http://www.journal-of-hepatology.eu/article/S0168-8278%2809%2900535-2/fulltext>). *Journal of Hepatology*. **51** (5): 939–48. doi:10.1016/j.jhep.2009.08.004 (<https://doi.org/10.1016%2Fj.jhep.2009.08.004>). PMID 19781804 (<https://pubmed.ncbi.nlm.nih.gov/19781804>).
46. Iyer LM, Balaji S, Koonin EV, Aravind L (April 2006). "Evolutionary genomics of nucleocytoplasmic large DNA viruses" (<https://zenodo.org/record/1259447>). *Virus Research*. **117** (1): 156–84. doi:10.1016/j.virusres.2006.01.009 (<https://doi.org/10.1016%2Fj.virusres.2006.01.009>). PMID 16494962 (<https://pubmed.ncbi.nlm.nih.gov/16494962>).
47. Sanjuán R, Nebot MR, Chirico N, Mansky LM, Belshaw R (October 2010). "Viral mutation rates" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2937809>). *Journal of Virology*. **84** (19): 9733–48. doi:10.1128/JVI.00694-10 (<https://doi.org/10.1128%2FJVI.00694-10>). PMC 2937809 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2937809>). PMID 20660197 (<https://pubmed.ncbi.nlm.nih.gov/20660197>).
48. Shors pp. 14–16
49. Collier pp. 11–21
50. Dimmock p. 16
51. Collier p. 11

52. Mahy WJ, Regenmortel MH, eds. (2009). *Desk Encyclopedia of General Virology*. Oxford: Academic Press. p. 24. [ISBN 978-0-12-375146-1](#).
53. Shors p. 810
54. McClintock B (June 1950). "The origin and behavior of mutable loci in maize" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1063197>). *Proceedings of the National Academy of Sciences of the United States of America*. **36** (6): 344–55. Bibcode:1950PNAS...36..344M (<https://ui.adsabs.harvard.edu/abs/1950PNAS...36..344M>). doi:10.1073/pnas.36.6.344 (<https://doi.org/10.1073/pnas.36.6.344>). PMC 1063197 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1063197>). PMID 15430309 (<https://pubmed.ncbi.nlm.nih.gov/15430309>).
55. Collier pp. 11–12
56. Dimmock p. 55
57. Shors pp. 791
58. Tsagris EM, Martínez de Alba AE, Gozmanova M, Kalantidis K (November 2008). "Viroids". *Cellular Microbiology*. **10** (11): 2168–79. doi:10.1111/j.1462-5822.2008.01231.x (<https://doi.org/10.1111/j.1462-5822.2008.01231.x>). PMID 18764915 (<https://pubmed.ncbi.nlm.nih.gov/18764915>).
59. Shors pp. 460
60. La Scola B, Desnues C, Pagnier I, Robert C, Barrassi L, Fournous G, et al. (September 2008). "The virophage as a unique parasite of the giant mimivirus". *Nature*. **455** (7209): 100–04. Bibcode:2008Natur.455..100L (<https://ui.adsabs.harvard.edu/abs/2008Natur.455..100L>). doi:10.1038/nature07218 (<https://doi.org/10.1038/nature07218>). PMID 18690211 (<https://pubmed.ncbi.nlm.nih.gov/18690211>).
61. Collier p. 777
62. Dimmock pp. 55–57
63. Mahy WJ, Van Regenmortel MH, eds. (2009). *Desk Encyclopedia of General Virology*. Oxford: Academic Press. p. 28. [ISBN 978-0-12-375146-1](#).
64. Mahy WJ, Regenmortel MH, eds. (2009). *Desk Encyclopedia of General Virology*. Oxford: Academic Press. p. 26. [ISBN 978-0-12-375146-1](#).
65. Dimmock pp. 15–16
66. Holmes EC (October 2007). "Viral evolution in the genomic age" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1994994>). *PLOS Biology*. **5** (10): e278. doi:10.1371/journal.pbio.0050278 (<https://doi.org/10.1371/journal.pbio.0050278>). PMC 1994994 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1994994>). PMID 17914905 (<https://pubmed.ncbi.nlm.nih.gov/17914905>).
67. Wimmer E, Mueller S, Tumpey TM, Taubenberger JK (December 2009). "Synthetic viruses: a new opportunity to understand and prevent viral disease" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819212>). *Nature Biotechnology*. **27** (12): 1163–72. doi:10.1038/nbt.1593 (<https://doi.org/10.1038/nbt.1593>). PMC 2819212 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819212>). PMID 20010599 (<https://pubmed.ncbi.nlm.nih.gov/20010599>).
68. Horn M (2008). "Chlamydiae as symbionts in eukaryotes". *Annual Review of Microbiology*. **62**: 113–31. doi:10.1146/annurev.micro.62.081307.162818 (<https://doi.org/10.1146/annurev.micro.62.081307.162818>). PMID 18473699 (<https://pubmed.ncbi.nlm.nih.gov/18473699>).
69. Ammerman NC, Beier-Sexton M, Azad AF (November 2008). "Laboratory maintenance of *Rickettsia rickettsii*" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725428>). *Current Protocols in Microbiology*. **11** (1): 3A.5.1–3A.5.21. doi:10.1002/9780471729259.mc03a05s11 (<https://doi.org/10.1002/9780471729259.mc03a05s11>). ISBN 978-0471729259. PMC 2725428 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725428>). PMID 19016440 (<https://pubmed.ncbi.nlm.nih.gov/19016440>).
70. Collier pp. 33–55
71. Collier pp. 33–37

72. Kiselev NA, Sherman MB, Tsuprun VL (1990). "Negative staining of proteins". *Electron Microscopy Reviews*. **3** (1): 43–72. doi:10.1016/0892-0354(90)90013-1 ([https://doi.org/10.1016/0892-0354\(90\)90013-1](https://doi.org/10.1016/0892-0354(90)90013-1)). PMID 1715774 (<https://pubmed.ncbi.nlm.nih.gov/1715774/>).
73. Collier p. 40
74. Caspar DL, Klug A (1962). "Physical principles in the construction of regular viruses". *Cold Spring Harbor Symposia on Quantitative Biology*. **27**: 1–24. doi:10.1101/sqb.1962.027.001.005 (<https://doi.org/10.1101/sqb.1962.027.001.005>). PMID 14019094 (<https://pubmed.ncbi.nlm.nih.gov/14019094/>).
75. Crick FH, Watson JD (March 1956). "Structure of small viruses". *Nature*. **177** (4506): 473–75. Bibcode:1956Natur.177..473C (<https://ui.adsabs.harvard.edu/abs/1956Natur.177..473C>). doi:10.1038/177473a0 (<https://doi.org/10.1038/177473a0>). PMID 13309339 (<https://pubmed.ncbi.nlm.nih.gov/13309339/>).
76. Falvo MR, Washburn S, Superfine R, Finch M, Brooks FP, Chi V, Taylor RM (March 1997). "Manipulation of individual viruses: friction and mechanical properties" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1184522>). *Biophysical Journal*. **72** (3): 1396–403. Bibcode:1997BpJ....72.1396F (<https://ui.adsabs.harvard.edu/abs/1997BpJ....72.1396F>). doi:10.1016/S0006-3495(97)78786-1 ([https://doi.org/10.1016/S0006-3495\(97\)78786-1](https://doi.org/10.1016/S0006-3495(97)78786-1)). PMC 1184522 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1184522>). PMID 9138585 (<https://pubmed.ncbi.nlm.nih.gov/9138585/>).
77. Kuznetsov YG, Malkin AJ, Lucas RW, Plomp M, McPherson A (September 2001). "Imaging of viruses by atomic force microscopy". *The Journal of General Virology*. **82** (Pt 9): 2025–34. doi:10.1099/0022-1317-82-9-2025 (<https://doi.org/10.1099/0022-1317-82-9-2025>). PMID 11514711 (<https://pubmed.ncbi.nlm.nih.gov/11514711/>).
78. Collier p. 37
79. Collier pp. 40, 42
80. Wilson DP (2016). "Protruding Features of Viral Capsids Are Clustered on Icosahedral Great Circles" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4821576>). *PLOS ONE*. **11** (4): e0152319. Bibcode:2016PLoS..1152319W (<https://ui.adsabs.harvard.edu/abs/2016PLoS..1152319W>). doi:10.1371/journal.pone.0152319 (<https://doi.org/10.1371/journal.pone.0152319>). PMC 4821576 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4821576>). PMID 27045511 (<https://pubmed.ncbi.nlm.nih.gov/27045511/>).
81. Casens S (2009). *Desk Encyclopedia of General Virology*. Boston: Academic Press. pp. 167–74. ISBN 978-0-12-375146-1.
82. Collier pp. 42–43
83. Rossmann MG, Mesyanzhinov VV, Arisaka F, Leiman PG (April 2004). "The bacteriophage T4 DNA injection machine". *Current Opinion in Structural Biology*. **14** (2): 171–80. doi:10.1016/j.sbi.2004.02.001 (<https://doi.org/10.1016/j.sbi.2004.02.001>). PMID 15093831 (<https://pubmed.ncbi.nlm.nih.gov/15093831/>).
84. Long GW, Nobel J, Murphy FA, Herrmann KL, Lourie B (September 1970). "Experience with electron microscopy in the differential diagnosis of smallpox" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC376966>). *Applied Microbiology*. **20** (3): 497–504. doi:10.1128/AEM.20.3.497-504.1970 (<https://doi.org/10.1128/AEM.20.3.497-504.1970>). PMC 376966 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC376966>). PMID 4322005 (<https://pubmed.ncbi.nlm.nih.gov/4322005/>).
85. Suzan-Monti M, La Scola B, Raoult D (April 2006). "Genomic and evolutionary aspects of Mimivirus". *Virus Research*. **117** (1): 145–55. doi:10.1016/j.virusres.2005.07.011 (<https://doi.org/10.1016/j.virusres.2005.07.011>). PMID 16181700 (<https://pubmed.ncbi.nlm.nih.gov/16181700/>).

86. Arslan D, Legendre M, Seltzer V, Abergel C, Claverie JM (October 2011). "Distant Mimivirus relative with a larger genome highlights the fundamental features of Megaviridae" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3198346>). *Proceedings of the National Academy of Sciences of the United States of America*. **108** (42): 17486–91. Bibcode:2011PNAS..10817486A (<https://ui.adsabs.harvard.edu/abs/2011PNAS..10817486A>). doi:10.1073/pnas.1110889108 (<https://doi.org/10.1073%2Fpnas.1110889108>). PMC 3198346 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3198346>). PMID 21987820 (<https://pubmed.ncbi.nlm.nih.gov/21987820>).
87. Philippe N, Legendre M, Doutre G, Couté Y, Poirot O, Lescot M, et al. (July 2013). "Pandoraviruses: amoeba viruses with genomes up to 2.5 Mb reaching that of parasitic eukaryotes" (<https://hal-cea.archives-ouvertes.fr/cea-00862677/file/phi.pdf>) (PDF). *Science*. **341** (6143): 281–86. Bibcode:2013Sci...341..281P (<https://ui.adsabs.harvard.edu/abs/2013Sci...341..281P>). doi:10.1126/science.1239181 (<https://doi.org/10.1126%2Fscience.1239181>). PMID 23869018 (<https://pubmed.ncbi.nlm.nih.gov/23869018>). S2CID 16877147 (<https://api.semanticscholar.org/CorpusID:16877147>).
88. Brandes N, Linial M (April 2019). "Giant Viruses-Big Surprises" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6563228>). *Viruses*. **11** (5): 404. doi:10.3390/v11050404 (<https://doi.org/10.3390%2Fv11050404>). PMC 6563228 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6563228>). PMID 31052218 (<https://pubmed.ncbi.nlm.nih.gov/31052218>).
89. Prangishvili D, Forterre P, Garrett RA (November 2006). "Viruses of the Archaea: a unifying view". *Nature Reviews Microbiology*. **4** (11): 837–48. doi:10.1038/nrmicro1527 (<https://doi.org/10.1038%2Fnrmicro1527>). PMID 17041631 (<https://pubmed.ncbi.nlm.nih.gov/17041631>).
90. Dimmock p. 49
91. "NCBI Viral Genome database" (<https://www.ncbi.nlm.nih.gov/genome/viruses/>). ncbi.nlm.nih.gov. Retrieved 15 January 2017.
92. Pennisi E (March 2011). "Microbiology. Going viral: exploring the role of viruses in our bodies". *Science*. **331** (6024): 1513. Bibcode:2011Sci...331.1513P (<https://ui.adsabs.harvard.edu/abs/2011Sci...331.1513P>). doi:10.1126/science.331.6024.1513 (<https://doi.org/10.1126%2Fscience.331.6024.1513>). PMID 21436418 (<https://pubmed.ncbi.nlm.nih.gov/21436418>).
93. Shi M, Lin XD, Tian JH, Chen LJ, Chen X, Li CX, et al. (December 2016). "Redefining the invertebrate RNA virosphere". *Nature*. **540** (7634): 539–43. Bibcode:2016Natur.540..539S (<https://ui.adsabs.harvard.edu/abs/2016Natur.540..539S>). doi:10.1038/nature20167 (<https://doi.org/10.1038%2Fnature20167>). PMID 27880757 (<https://pubmed.ncbi.nlm.nih.gov/27880757>).
94. Collier pp. 96–99
95. Saunders VA, Carter J (2007). *Virology: principles and applications*. Chichester: John Wiley & Sons. p. 72. ISBN 978-0-470-02387-7.
96. Belyi VA, Levine AJ, Skalka AM (December 2010). "Sequences from ancestral single-stranded DNA viruses in vertebrate genomes: the parvoviridae and circoviridae are more than 40 to 50 million years old" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2976387>). *Journal of Virology*. **84** (23): 12458–62. doi:10.1128/JVI.01789-10 (<https://doi.org/10.1128%2FJVI.01789-10>). PMC 2976387 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2976387>). PMID 20861255 (<https://pubmed.ncbi.nlm.nih.gov/20861255>).
97. Philippe N, Legendre M, Doutre G, Couté Y, Poirot O, Lescot M, et al. (July 2013). "Pandoraviruses: amoeba viruses with genomes up to 2.5 Mb reaching that of parasitic eukaryotes" (<https://hal-cea.archives-ouvertes.fr/cea-00862677/file/phi.pdf>) (PDF). *Science*. **341** (6143): 281–86. Bibcode:2013Sci...341..281P (<https://ui.adsabs.harvard.edu/abs/2013Sci...341..281P>). doi:10.1126/science.1239181 (<https://doi.org/10.1126%2Fscience.1239181>). PMID 23869018 (<https://pubmed.ncbi.nlm.nih.gov/23869018>). S2CID 16877147 (<https://api.semanticscholar.org/CorpusID:16877147>).

98. Brandes N, Linial M (May 2016). "Gene overlapping and size constraints in the viral world" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4875738>). *Biology Direct.* **11** (1): 26. doi:10.1186/s13062-016-0128-3 (<https://doi.org/10.1186%2Fs13062-016-0128-3>). PMC 4875738 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4875738>). PMID 27209091 (<https://pubmed.ncbi.nlm.nih.gov/27209091>).
99. Pressing J, Reanney DC (1984). "Divided genomes and intrinsic noise" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7087551>). *Journal of Molecular Evolution.* **20** (2): 135–46. Bibcode:1984JMolE..20..135P (<https://ui.adsabs.harvard.edu/abs/1984JMolE..20..135P>). doi:10.1007/BF02257374 (<https://doi.org/10.1007%2FBF02257374>). PMC 7087551 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7087551>). PMID 6433032 (<https://pubmed.ncbi.nlm.nih.gov/6433032>).
00. Duffy S, Holmes EC (June 2009). "Validation of high rates of nucleotide substitution in geminiviruses: phylogenetic evidence from East African cassava mosaic viruses" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4091138>). *The Journal of General Virology.* **90** (Pt 6): 1539–47. doi:10.1099/vir.0.009266-0 (<https://doi.org/10.1099%2Fvir.0.009266-0>). PMC 4091138 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4091138>). PMID 19264617 (<https://pubmed.ncbi.nlm.nih.gov/19264617>).
01. Sandbulte MR, Westgeest KB, Gao J, Xu X, Klimov AI, Russell CA, et al. (December 2011). "Discordant antigenic drift of neuraminidase and hemagglutinin in H1N1 and H3N2 influenza viruses" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3251064>). *Proceedings of the National Academy of Sciences of the United States of America.* **108** (51): 20748–53. Bibcode:2011PNAS..10820748S (<https://ui.adsabs.harvard.edu/abs/2011PNAS..10820748S>). doi:10.1073/pnas.1113801108 (<https://doi.org/10.1073%2Fpnas.1113801108>). PMC 3251064 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3251064>). PMID 22143798 (<https://pubmed.ncbi.nlm.nih.gov/22143798>).
02. Moss RB, Davey RT, Steigbigel RT, Fang F (June 2010). "Targeting pandemic influenza: a primer on influenza antivirals and drug resistance". *The Journal of Antimicrobial Chemotherapy.* **65** (6): 1086–93. doi:10.1093/jac/dkq100 (<https://doi.org/10.1093%2Fjac%2Fdq100>). PMID 20375034 (<https://pubmed.ncbi.nlm.nih.gov/20375034>).
03. Hampson AW, Mackenzie JS (November 2006). "The influenza viruses". *The Medical Journal of Australia.* **185** (S10): S39–43. doi:10.5694/j.1326-5377.2006.tb00705.x (<https://doi.org/10.5694%2Fj.1326-5377.2006.tb00705.x>). PMID 17115950 (<https://pubmed.ncbi.nlm.nih.gov/17115950>).
04. Metzner KJ (December 2006). "Detection and significance of minority quasispecies of drug-resistant HIV-1". *Journal of HIV Therapy.* **11** (4): 74–81. PMID 17578210 (<https://pubmed.ncbi.nlm.nih.gov/17578210>).
05. Goudsmit, Jaap. *Viral Sex.* Oxford Univ Press, 1998. ISBN 978-0-19-512496-5, 0-19-512496-0
06. Worobey M, Holmes EC (October 1999). "Evolutionary aspects of recombination in RNA viruses". *The Journal of General Virology.* **80** (10): 2535–43. doi:10.1099/0022-1317-80-10-2535 (<https://doi.org/10.1099%2F0022-1317-80-10-2535>). PMID 10573145 (<https://pubmed.ncbi.nlm.nih.gov/10573145>).
07. Lukashev AN (2005). "Role of recombination in evolution of enteroviruses". *Reviews in Medical Virology.* **15** (3): 157–67. doi:10.1002/rmv.457 (<https://doi.org/10.1002%2Frmv.457>). PMID 15578739 (<https://pubmed.ncbi.nlm.nih.gov/15578739>).
08. Umene K (July 1999). "Mechanism and application of genetic recombination in herpesviruses". *Reviews in Medical Virology.* **9** (3): 171–82. doi:10.1002/(SICI)1099-1654(199907/09)9:3<171::AID-RMV243>3.0.CO;2-A (<https://doi.org/10.1002%2F%28SICI%291099-1654%28199907%2F09%299%3A3%3C171%3A%3AAID-RMV243%3E3.0.CO%3B2-A>). PMID 10479778 (<https://pubmed.ncbi.nlm.nih.gov/10479778>).

09. Freed EO (August 2015). "HIV-1 assembly, release and maturation" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6936268>). *Nature Reviews. Microbiology*. **13** (8): 484–96. doi:10.1038/nrmicro3490 (<https://doi.org/10.1038%2Fnrmicro3490>). PMC 6936268 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6936268>). PMID 26119571 (<https://pubmed.ncbi.nlm.nih.gov/26119571>).
10. Yin J, Redovich J (June 2018). "Kinetic Modeling of Virus Growth in Cells" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5968458>). *Microbiology and Molecular Biology Reviews : MMBR*. **82** (2). doi:10.1128/MMBR.00066-17 (<https://doi.org/10.1128%2FMMBR.00066-17>). PMC 5968458 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5968458>). PMID 29592895 (<https://pubmed.ncbi.nlm.nih.gov/29592895>).
11. Collier pp. 75–91
12. Más V, Melero JA (2013). "Entry of enveloped viruses into host cells: membrane fusion". *Structure and Physics of Viruses. Subcellular Biochemistry*. **68**. pp. 467–87. doi:10.1007/978-94-007-6552-8\_16 ([https://doi.org/10.1007%2F978-94-007-6552-8\\_16](https://doi.org/10.1007%2F978-94-007-6552-8_16)). ISBN 978-94-007-6551-1. PMC 7121288 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7121288>). PMID 23737062 (<https://pubmed.ncbi.nlm.nih.gov/23737062>).
13. Dimmock p. 70
14. Boevink P, Opalka KJ (August 2005). "Virus-host interactions during movement processes" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1183373>). *Plant Physiology*. **138** (4): 1815–21. doi:10.1104/pp.105.066761 (<https://doi.org/10.1104%2Fpp.105.066761>). PMC 1183373 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1183373>). PMID 16172094 (<https://pubmed.ncbi.nlm.nih.gov/16172094>).
15. Dimmock p. 71
16. Blaas D (May 2016). "Viral entry pathways: the example of common cold viruses" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4871925>). *Wiener Medizinische Wochenschrift*. **166** (7–8): 211–26. doi:10.1007/s10354-016-0461-2 (<https://doi.org/10.1007%2Fs10354-016-0461-2>). PMC 4871925 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4871925>). PMID 27174165 (<https://pubmed.ncbi.nlm.nih.gov/27174165>).
17. Isomura H, Stinski MF (February 2013). "Coordination of late gene transcription of human cytomegalovirus with viral DNA synthesis: recombinant viruses as potential therapeutic vaccine candidates". *Expert Opinion on Therapeutic Targets*. **17** (2): 157–66. doi:10.1517/14728222.2013.740460 (<https://doi.org/10.1517%2F14728222.2013.740460>). PMID 23231449 (<https://pubmed.ncbi.nlm.nih.gov/23231449>). S2CID 11448687 (<https://api.semanticscholar.org/CorpusID:11448687>).
18. Barman S, Ali A, Hui EK, Adhikary L, Nayak DP (September 2001). "Transport of viral proteins to the apical membranes and interaction of matrix protein with glycoproteins in the assembly of influenza viruses". *Virus Research*. **77** (1): 61–69. doi:10.1016/S0168-1702(01)00266-0 (<https://doi.org/10.1016%2FS0168-1702%2801%2900266-0>). PMID 11451488 (<https://pubmed.ncbi.nlm.nih.gov/11451488>).
19. Shors pp. 836
20. Dimmock, Chapter 15, *Mechanisms in virus latency*, pp. 243–59
21. Dimmock 185–87
22. Shors p. 118; Collier p. 78
23. Collier p. 79
24. Staginnus C, Richert-Poggeler KR (October 2006). "Endogenous pararetroviruses: two-faced travelers in the plant genome". *Trends in Plant Science*. **11** (10): 485–91. doi:10.1016/j.tplants.2006.08.008 (<https://doi.org/10.1016%2Fj.tplants.2006.08.008>). PMID 16949329 (<https://pubmed.ncbi.nlm.nih.gov/16949329>).
25. Collier pp. 88–89
26. Collier pp. 115–46
27. Collier p. 115

28. Roulston A, Marcellus RC, Branton PE (1999). "Viruses and apoptosis". *Annual Review of Microbiology*. **53**: 577–628. doi:10.1146/annurev.micro.53.1.577 (<https://doi.org/10.1146%2Fannurev.micro.53.1.577>). PMID 10547702 (<https://pubmed.ncbi.nlm.nih.gov/10547702>).
29. Alwine JC (2008). "Modulation of host cell stress responses by human cytomegalovirus". *Current Topics in Microbiology and Immunology*. **325**: 263–79. doi:10.1007/978-3-540-77349-8\_15 ([https://doi.org/10.1007%2F978-3-540-77349-8\\_15](https://doi.org/10.1007%2F978-3-540-77349-8_15)). ISBN 978-3-540-77348-1. PMID 18637511 (<https://pubmed.ncbi.nlm.nih.gov/18637511>).
30. Barozzi P, Potenza L, Riva G, Vallerini D, Quadrelli C, Bosco R, et al. (December 2007). "B cells and herpesviruses: a model of lymphoproliferation". *Autoimmunity Reviews*. **7** (2): 132–36. doi:10.1016/j.autrev.2007.02.018 (<https://doi.org/10.1016%2Fj.autrev.2007.02.018>). PMID 18035323 (<https://pubmed.ncbi.nlm.nih.gov/18035323>).
31. Subramanya D, Grivas PD (November 2008). "HPV and cervical cancer: updates on an established relationship". *Postgraduate Medicine*. **120** (4): 7–13. doi:10.3810/pgm.2008.11.1928 (<https://doi.org/10.3810%2Fpgm.2008.11.1928>). PMID 19020360 (<https://pubmed.ncbi.nlm.nih.gov/19020360>). S2CID 1399003 (<https://api.semanticscholar.org/CorpusID:1399003>).
32. Sinclair J (March 2008). "Human cytomegalovirus: Latency and reactivation in the myeloid lineage". *Journal of Clinical Virology*. **41** (3): 180–85. doi:10.1016/j.jcv.2007.11.014 (<https://doi.org/10.1016%2Fj.jcv.2007.11.014>). PMID 18164651 (<https://pubmed.ncbi.nlm.nih.gov/18164651>).
33. Jordan MC, Jordan GW, Stevens JG, Miller G (June 1984). "Latent herpesviruses of humans". *Annals of Internal Medicine*. **100** (6): 866–80. doi:10.7326/0003-4819-100-6-866 (<https://doi.org/10.7326%2F0003-4819-100-6-866>). PMID 6326635 (<https://pubmed.ncbi.nlm.nih.gov/6326635>).
34. Sissons JG, Bain M, Wills MR (February 2002). "Latency and reactivation of human cytomegalovirus". *The Journal of Infection*. **44** (2): 73–77. doi:10.1053/jinf.2001.0948 (<https://doi.org/10.1053%2Fjinf.2001.0948>). PMID 12076064 (<https://pubmed.ncbi.nlm.nih.gov/12076064>).
35. Crawford DH (2011). *Viruses: A Very Short Introduction* (<https://archive.org/details/virusesveryshort0000craw/page/16>). Oxford University Press, US. pp. 16 (<https://archive.org/details/virusesvveryshort0000craw/page/16>). ISBN 978-0-19-957485-8.
36. Shors p. 643
37. Shors p. 631
38. Dimmock p. 272
39. Baggesen DL, Sørensen G, Nielsen EM, Wegener HC (January 2010). "Phage typing of *Salmonella Typhimurium* – is it still a useful tool for surveillance and outbreak investigation?" (<http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19471>). *Euro Surveillance*. **15** (4): 19471. PMID 20122382 (<https://pubmed.ncbi.nlm.nih.gov/20122382>). Retrieved 19 December 2014.
40. Lwoff A, Horne RW, Tournier P (June 1962). "[A virus system]". *Comptes Rendus Hebdomadaires des Séances de l'Academie des Sciences* (in French). **254**: 4225–27. PMID 14467544 (<https://pubmed.ncbi.nlm.nih.gov/14467544>).
41. Lwoff A, Horne R, Tournier P (1962). "A system of viruses". *Cold Spring Harbor Symposia on Quantitative Biology*. **27**: 51–55. doi:10.1101/sqb.1962.027.001.008 (<https://doi.org/10.1101%2Fsqb.1962.027.001.008>). PMID 13931895 (<https://pubmed.ncbi.nlm.nih.gov/13931895>).
42. Fauquet CM, Fargette D (August 2005). "International Committee on Taxonomy of Viruses and the 3,142 unassigned species" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1208960>). *Virology Journal*. **2**: 64. doi:10.1186/1743-422X-2-64 (<https://doi.org/10.1186%2F1743-422X-2-64>). PMC 1208960 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1208960>). PMID 16105179 (<https://pubmed.ncbi.nlm.nih.gov/16105179>).

43. Delwart EL (2007). "Viral metagenomics" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7169062>). *Reviews in Medical Virology*. **17** (2): 115–31. doi:[10.1002/rmv.532](https://doi.org/10.1002/rmv.532) (<https://doi.org/10.1002/rmv.532>). PMC 7169062 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7169062>). PMID 17295196 (<https://pubmed.ncbi.nlm.nih.gov/17295196>).
44. Baltimore D (1974). "The strategy of RNA viruses". *Harvey Lectures*. 70 Series. 70 Series: 57–74. PMID 4377923 (<https://pubmed.ncbi.nlm.nih.gov/4377923>).
45. van Regenmortel MH, Mahy BW (January 2004). "Emerging issues in virus taxonomy" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3322749>). *Emerging Infectious Diseases*. **10** (1): 8–13. doi:[10.3201/eid1001.030279](https://doi.org/10.3201/eid1001.030279) (<https://doi.org/10.3201/eid1001.030279>). PMC 3322749 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3322749>). PMID 15078590 (<https://pubmed.ncbi.nlm.nih.gov/15078590>).
46. Mayo MA (1999). "Developments in plant virus taxonomy since the publication of the 6th ICTV Report. International Committee on Taxonomy of Viruses". *Archives of Virology*. **144** (8): 1659–66. doi:[10.1007/s007050050620](https://doi.org/10.1007/s007050050620) (<https://doi.org/10.1007/s007050050620>). PMID 10486120 (<https://pubmed.ncbi.nlm.nih.gov/10486120>). S2CID 33422303 (<https://api.semanticscholar.org/CorpusID:33422303>).
47. de Villiers EM, Fauquet C, Broker TR, Bernard HU, zur Hausen H (June 2004). "Classification of papillomaviruses". *Virology*. **324** (1): 17–27. doi:[10.1016/j.virol.2004.03.033](https://doi.org/10.1016/j.virol.2004.03.033) (<https://doi.org/10.1016/j.virol.2004.03.033>). PMID 15183049 (<https://pubmed.ncbi.nlm.nih.gov/15183049>).
48. Parker MT (September 2016). "An Ecological Framework of the Human Virome Provides Classification of Current Knowledge and Identifies Areas of Forthcoming Discovery" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5045143>). *The Yale Journal of Biology and Medicine*. **89** (3): 339–51. PMC 5045143 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5045143>). PMID 27698618 (<https://pubmed.ncbi.nlm.nih.gov/27698618>).
49. Mainly Chapter 33 (Disease summaries), pp. 367–92 in: Fisher B, Harvey RP, Champe PC (2007). *Lippincott's Illustrated Reviews: Microbiology*. Lippincott's Illustrated Reviews Series. Hagerstwon, MD: Lippincott Williams & Wilkins. pp. 367–92. ISBN 978-0-7817-8215-9.
50. Komaroff AL (December 2006). "Is human herpesvirus-6 a trigger for chronic fatigue syndrome?". *Journal of Clinical Virology*. **37** (Suppl 1): S39–46. doi:[10.1016/S1386-6532\(06\)70010-5](https://doi.org/10.1016/S1386-6532(06)70010-5) ([https://doi.org/10.1016/S1386-6532\(06\)70010-5](https://doi.org/10.1016/S1386-6532(06)70010-5)). PMID 17276367 (<https://pubmed.ncbi.nlm.nih.gov/17276367>).
51. Chen CH, Chiu YL, Wei FC, Koong FJ, Liu HC, Shaw CK, et al. (January 1999). "High seroprevalence of Borna virus infection in schizophrenic patients, family members and mental health workers in Taiwan". *Molecular Psychiatry*. **4** (1): 33–38. doi:[10.1038/sj.mp.4000484](https://doi.org/10.1038/sj.mp.4000484) (<https://doi.org/10.1038/sj.mp.4000484>). PMID 10089006 (<https://pubmed.ncbi.nlm.nih.gov/10089006>). S2CID 19830976 (<https://api.semanticscholar.org/CorpusID:19830976>).
52. Margolis TP, Elfman FL, Leib D, Pakpour N, Apakupakul K, Imai Y, Voytek C (October 2007). "Spontaneous reactivation of herpes simplex virus type 1 in latently infected murine sensory ganglia" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2045564>). *Journal of Virology*. **81** (20): 11069–74. doi:[10.1128/JVI.00243-07](https://doi.org/10.1128/JVI.00243-07) (<https://doi.org/10.1128/JVI.00243-07>). PMC 2045564 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2045564>). PMID 17686862 (<https://pubmed.ncbi.nlm.nih.gov/17686862>).
53. Whitley RJ, Roizman B (May 2001). "Herpes simplex virus infections". *Lancet*. **357** (9267): 1513–18. doi:[10.1016/S0140-6736\(00\)04638-9](https://doi.org/10.1016/S0140-6736(00)04638-9) ([https://doi.org/10.1016/S0140-6736\(00\)04638-9](https://doi.org/10.1016/S0140-6736(00)04638-9)). PMID 11377626 (<https://pubmed.ncbi.nlm.nih.gov/11377626>).
54. Barton ES, White DW, Cathelyn JS, Brett-McClellan KA, Engle M, Diamond MS, et al. (May 2007). "Herpesvirus latency confers symbiotic protection from bacterial infection". *Nature*. **447** (7142): 326–29. Bibcode:2007Natur.447..326B (<https://ui.adsabs.harvard.edu/abs/2007Natur.447..326B>). doi:[10.1038/nature05762](https://doi.org/10.1038/nature05762) (<https://doi.org/10.1038/nature05762>). PMID 17507983 (<https://pubmed.ncbi.nlm.nih.gov/17507983>).

55. Bertoletti A, Gehring A (October 2007). "Immune response and tolerance during chronic hepatitis B virus infection". *Hepatology Research*. **37** (Suppl 3): S331–38. doi:10.1111/j.1872-034X.2007.00221.x (<https://doi.org/10.1111%2Fj.1872-034X.2007.00221.x>). PMID 17931183 (<https://pubmed.ncbi.nlm.nih.gov/17931183>).
56. Rodrigues C, Deshmukh M, Jacob T, Nukala R, Menon S, Mehta A (2001). "Significance of HBV DNA by PCR over serological markers of HBV in acute and chronic patients". *Indian Journal of Medical Microbiology*. **19** (3): 141–44. PMID 17664817 (<https://pubmed.ncbi.nlm.nih.gov/17664817>).
57. Nguyen VT, McLaws ML, Dore GJ (December 2007). "Highly endemic hepatitis B infection in rural Vietnam". *Journal of Gastroenterology and Hepatology*. **22** (12): 2093–100. doi:10.1111/j.1440-1746.2007.05010.x (<https://doi.org/10.1111%2Fj.1440-1746.2007.05010.x>). PMID 17645465 (<https://pubmed.ncbi.nlm.nih.gov/17645465>).
58. Fowler MG, Lampe MA, Jamieson DJ, Kourtis AP, Rogers MF (September 2007). "Reducing the risk of mother-to-child human immunodeficiency virus transmission: past successes, current progress and challenges, and future directions". *American Journal of Obstetrics and Gynecology*. **197** (3 Suppl): S3–9. doi:10.1016/j.ajog.2007.06.048 (<https://doi.org/10.1016%2Fj.ajog.2007.06.048>). PMID 17825648 (<https://pubmed.ncbi.nlm.nih.gov/17825648>).
59. Sauerbrei A, Wutzler P (December 2000). "The congenital varicella syndrome". *Journal of Perinatology*. **20** (8 Pt 1): 548–54. doi:10.1038/sj.jp.7200457 (<https://doi.org/10.1038%2Fsj.jp.7200457>). PMID 11190597 (<https://pubmed.ncbi.nlm.nih.gov/11190597>). S2CID 7973561 (<http://api.semanticscholar.org/CorpusID:7973561>).
60. Garnett GP (February 2005). "Role of herd immunity in determining the effect of vaccines against sexually transmitted disease". *The Journal of Infectious Diseases*. **191** (Suppl 1): S97–106. doi:10.1086/425271 (<https://doi.org/10.1086%2F425271>). PMID 15627236 (<https://pubmed.ncbi.nlm.nih.gov/15627236>).
61. Platonov AE (2006). "[The influence of weather conditions on the epidemiology of vector-borne diseases by the example of West Nile fever in Russia]". *Vestnik Rossiiskoi Akademii Meditsinskikh Nauk* (in Russian) (2): 25–29. PMID 16544901 (<https://pubmed.ncbi.nlm.nih.gov/16544901>).
62. Shors p. 264
63. Shors pp. 894
64. Jewell CP, Keeling MJ, Roberts GO (December 2009). "Predicting undetected infections during the 2007 foot-and-mouth disease outbreak" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2817150>). *Journal of the Royal Society, Interface*. **6** (41): 1145–51. doi:10.1098/rsif.2008.0433 (<https://doi.org/10.1098%2Frsif.2008.0433>). PMC 2817150 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2817150>). PMID 19091686 (<https://pubmed.ncbi.nlm.nih.gov/19091686>).
65. Shors p. 170
66. Shors pp. 170–72
67. Shors p. 272
68. Shors pp. 891
69. Collier pp. 409–15
70. Patterson KD, Pyle GF (1991). "The geography and mortality of the 1918 influenza pandemic". *Bulletin of the History of Medicine*. **65** (1): 4–21. PMID 2021692 (<https://pubmed.ncbi.nlm.nih.gov/2021692>).
71. Johnson NP, Mueller J (2002). "Updating the accounts: global mortality of the 1918-1920 "Spanish" influenza pandemic". *Bulletin of the History of Medicine*. **76** (1): 105–15. doi:10.1353/bhm.2002.0022 (<https://doi.org/10.1353%2Fbhm.2002.0022>). PMID 11875246 (<https://pubmed.ncbi.nlm.nih.gov/11875246>).

72. Eisinger RW, Fauci AS (March 2018). "1" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5823353>). *Emerging Infectious Diseases*. **24** (3): 413–16. doi:10.3201/eid2403.171797 (<https://doi.org/10.3201%2Feid2403.171797>). PMC 5823353 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5823353>). PMID 29460740 (<https://pubmed.ncbi.nlm.nih.gov/29460740>).
73. Qin Y, Zhao MJ, Tan YY, Li XQ, Zheng JD, Peng ZB, Feng LZ (August 2018). "[History of influenza pandemics in China during the past century]". *Zhonghua Liu Xing Bing Xue Za Zhi = Zhonghua Liuxingbingxue Zazhi* (in Chinese). **39** (8): 1028–31. doi:10.3760/cma.j.issn.0254-6450.2018.08.003 (<https://doi.org/10.3760%2Fcma.j.issn.0254-6450.2018.08.003>). PMID 30180422 (<https://pubmed.ncbi.nlm.nih.gov/30180422>).
74. Gao F, Bailes E, Robertson DL, Chen Y, Rodenburg CM, Michael SF, et al. (February 1999). "Origin of HIV-1 in the chimpanzee Pan troglodytes troglodytes". *Nature*. **397** (6718): 436–41. Bibcode:1999Natur.397..436G (<https://ui.adsabs.harvard.edu/abs/1999Natur.397..436G>). doi:10.1038/17130 (<https://doi.org/10.1038%2F17130>). PMID 9989410 (<https://pubmed.ncbi.nlm.nih.gov/9989410>).
75. "Fact Sheet" ([https://www.unaids.org/sites/default/files/media\\_asset/2019-UNAIDS-data\\_en.pdf](https://www.unaids.org/sites/default/files/media_asset/2019-UNAIDS-data_en.pdf)) (PDF). UNAIDS.org. 2018. Retrieved 12 December 2019.
76. "UN AIDS DATA2019" (<https://www.unaids.org/en/resources/fact-sheet>). UNAIDS.org. 2019. Retrieved 5 December 2019.
77. Mawar N, Saha S, Pandit A, Mahajan U (December 2005). "The third phase of HIV pandemic: social consequences of HIV/AIDS stigma & discrimination & future needs" (<https://web.archive.org/web/20160304023223/http://www.icmr.nic.in/ijmr/2005/december/1201.pdf>) (PDF). *The Indian Journal of Medical Research*. **122** (6): 471–84. PMID 16517997 (<https://pubmed.ncbi.nlm.nih.gov/16517997>). Archived from the original (<http://www.icmr.nic.in/ijmr/2005/december/1201.pdf>) (PDF) on 4 March 2016. Retrieved 19 December 2014.
78. "Status of the global HIV epidemic" ([https://web.archive.org/web/20151122231422/http://data.unaids.org/pub/GlobalReport/2008/jc1510\\_2008\\_global\\_report\\_pp29\\_62\\_en.pdf](https://web.archive.org/web/20151122231422/http://data.unaids.org/pub/GlobalReport/2008/jc1510_2008_global_report_pp29_62_en.pdf)) (PDF). UNAIDS. 2008. Archived from the original ([http://data.unaids.org/pub/GlobalReport/2008/jc1510\\_2008\\_global\\_report\\_pp29\\_62\\_en.pdf](http://data.unaids.org/pub/GlobalReport/2008/jc1510_2008_global_report_pp29_62_en.pdf)) (PDF) on 22 November 2015. Retrieved 19 December 2014.
79. Towner JS, Khristova ML, Sealy TK, Vincent MJ, Erickson BR, Bawiec DA, et al. (July 2006). "Marburgvirus genomics and association with a large hemorrhagic fever outbreak in Angola" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1488971>). *Journal of Virology*. **80** (13): 6497–516. doi:10.1128/JVI.00069-06 (<https://doi.org/10.1128%2FJVI.00069-06>). PMC 1488971 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1488971>). PMID 16775337 (<https://pubmed.ncbi.nlm.nih.gov/16775337>).
80. "World Health Organisation report, 24 September 2014" ([http://apps.who.int/iris/bitstream/10665/134771/1/roadmapsitrep\\_24Sept2014\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/134771/1/roadmapsitrep_24Sept2014_eng.pdf?ua=1)) (PDF).
81. "Virology Journal" (<https://virologyj.biomedcentral.com/articles/sections/emerging-viruses>). *Virology Journal*.
82. Weiss SR, Leibowitz JL (2011). *Coronavirus pathogenesis*. Advances in Virus Research. **81**. pp. 85–164. doi:10.1016/B978-0-12-385885-6.00009-2 (<https://doi.org/10.1016%2FB978-0-12-385885-6.00009-2>). ISBN 978-0-12-385885-6. PMC 7149603 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7149603>). PMID 22094080 (<https://pubmed.ncbi.nlm.nih.gov/22094080>).
83. Wong AT, Chen H, Liu SH, Hsu EK, Luk KS, Lai CK, et al. (May 2017). "From SARS to Avian Influenza Preparedness in Hong Kong". *Clinical Infectious Diseases*. **64** (suppl\_2): S98–S104. doi:10.1093/cid/cix123 (<https://doi.org/10.1093%2Fcid%2Fcix123>). PMID 28475794 (<https://pubmed.ncbi.nlm.nih.gov/28475794>).

84. Ashour HM, Elkhattib WF, Rahman MM, Elshabrawy HA (March 2020). "Insights into the Recent 2019 Novel Coronavirus (SARS-CoV-2) in Light of Past Human Coronavirus Outbreaks" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7157630>). *Pathogens*. **9** (3): 186. doi:10.3390/pathogens9030186 (<https://doi.org/10.3390%2Fpathogens9030186>). PMC 7157630 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7157630>). PMID 32143502 (<https://pubmed.ncbi.nlm.nih.gov/32143502>).
85. Deng SQ, Peng HJ (February 2020). "Characteristics of and Public Health Responses to the Coronavirus Disease 2019 Outbreak in China" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7074453>). *Journal of Clinical Medicine*. **9** (2): 575. doi:10.3390/jcm9020575 (<https://doi.org/10.3390%2Fjcm9020575>). PMC 7074453 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7074453>). PMID 32093211 (<https://pubmed.ncbi.nlm.nih.gov/32093211>).
86. Han Q, Lin Q, Jin S, You L (April 2020). "Coronavirus 2019-nCoV: A brief perspective from the front line" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102581>). *The Journal of Infection*. **80** (4): 373–77. doi:10.1016/j.jinf.2020.02.010 (<https://doi.org/10.1016%2Fj.jinf.2020.02.010>). PMC 7102581 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102581>). PMID 32109444 (<https://pubmed.ncbi.nlm.nih.gov/32109444>).
87. Londoño E, Ortiz A (16 March 2020). "Coronavirus Travel Restrictions, Across the Globe" (<https://www.nytimes.com/article/coronavirus-travel-restrictions.html>) – via NYTimes.com.
88. "US takes more big pandemic response steps; Europe COVID-19 cases soar" (<http://www.cidrap.umn.edu/news-perspective/2020/03/us-takes-more-big-pandemic-response-steps-europe-covid-19-cases-soar>). CIDRAP.
89. Einstein MH, Schiller JT, Viscidi RP, Strickler HD, Coursaget P, Tan T, et al. (June 2009). "Clinician's guide to human papillomavirus immunology: knowns and unknowns". *The Lancet. Infectious Diseases*. **9** (6): 347–56. doi:10.1016/S1473-3099(09)70108-2 (<https://doi.org/10.1016%2FS1473-3099%2809%2970108-2>). PMID 19467474 (<https://pubmed.ncbi.nlm.nih.gov/19467474>).
90. Shuda M, Feng H, Kwun HJ, Rosen ST, Gjoerup O, Moore PS, Chang Y (October 2008). "T antigen mutations are a human tumor-specific signature for Merkel cell polyomavirus" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2551627>). *Proceedings of the National Academy of Sciences of the United States of America*. **105** (42): 16272–77. Bibcode:2008PNAS..10516272S (<https://ui.adsabs.harvard.edu/abs/2008PNAS..10516272S>). doi:10.1073/pnas.0806526105 (<https://doi.org/10.1073%2Fpnas.0806526105>). PMC 2551627 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2551627>). PMID 18812503 (<https://pubmed.ncbi.nlm.nih.gov/18812503>).
91. Pulitzer MP, Amin BD, Busam KJ (May 2009). "Merkel cell carcinoma: review". *Advances in Anatomic Pathology*. **16** (3): 135–44. doi:10.1097/PAP.0b013e3181a12f5a (<https://doi.org/10.1097%2FPAP.0b013e3181a12f5a>). PMID 19395876 (<https://pubmed.ncbi.nlm.nih.gov/19395876>).
92. Koike K (June 2007). "Hepatitis C virus contributes to hepatocarcinogenesis by modulating metabolic and intracellular signaling pathways". *Journal of Gastroenterology and Hepatology*. **22** (Suppl 1): S108–11. doi:10.1111/j.1440-1746.2006.04669.x (<https://doi.org/10.1111%2Fj.1440-1746.2006.04669.x>). PMID 17567457 (<https://pubmed.ncbi.nlm.nih.gov/17567457>).
93. Hu J, Ludgate L (2007). "HIV-HBV and HIV-HCV coinfection and liver cancer development". *Cancer Treatment and Research*. **133**: 241–52. doi:10.1007/978-0-387-46816-7\_9 ([https://doi.org/10.1007%2F978-0-387-46816-7\\_9](https://doi.org/10.1007%2F978-0-387-46816-7_9)). ISBN 978-0-387-46804-4. PMID 17672044 (<https://pubmed.ncbi.nlm.nih.gov/17672044>).
94. Bellon M, Nicot C (2007). "Telomerase: a crucial player in HTLV-I-induced human T-cell leukemia". *Cancer Genomics & Proteomics*. **4** (1): 21–25. PMID 17726237 (<https://pubmed.ncbi.nlm.nih.gov/17726237>).
95. Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S (September 2007). "Human papillomavirus and cervical cancer". *Lancet*. **370** (9590): 890–907. doi:10.1016/S0140-6736(07)61416-0 (<https://doi.org/10.1016%2FS0140-6736%2807%2961416-0>). PMID 17826171 (<https://pubmed.ncbi.nlm.nih.gov/17826171>).

96. Klein E, Kis LL, Klein G (February 2007). "Epstein-Barr virus infection in humans: from harmless to life endangering virus-lymphocyte interactions". *Oncogene*. **26** (9): 1297–305. doi:10.1038/sj.onc.1210240 (<https://doi.org/10.1038%2Fsj.onc.1210240>). PMID 17322915 (<https://pubmed.ncbi.nlm.nih.gov/17322915>).
97. Zur Hausen H (July 2008). "Novel human polyomaviruses – re-emergence of a well known virus family as possible human carcinogens". *International Journal of Cancer*. **123** (2): 247–50. doi:10.1002/ijc.23620 (<https://doi.org/10.1002%2Fijc.23620>). PMID 18449881 (<https://pubmed.ncbi.nlm.nih.gov/18449881>).
98. Alberta B, Johnson A, Lewis J, Raff M, Roberts K, Walters P (2002). *Molecular Biology of the Cell* (<https://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowTOC&rid=mboc4.TOC&depth=2>) (Fourth ed.). New York and London: Garland Science. ISBN 0-8153-3218-1.
99. Ding SW, Voinnet O (August 2007). "Antiviral immunity directed by small RNAs" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2703654>). *Cell*. **130** (3): 413–26. doi:10.1016/j.cell.2007.07.039 (<https://doi.org/10.1016%2Fj.cell.2007.07.039>). PMC 2703654 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2703654>). PMID 17693253 (<https://pubmed.ncbi.nlm.nih.gov/17693253>).
00. Patton JT, Vasquez-Del Carpio R, Spencer E (2004). "Replication and transcription of the rotavirus genome". *Current Pharmaceutical Design*. **10** (30): 3769–77. doi:10.2174/1381612043382620 (<https://doi.org/10.2174%2F1381612043382620>). PMID 15579070 (<https://pubmed.ncbi.nlm.nih.gov/15579070>).
01. Jayaram H, Estes MK, Prasad BV (April 2004). "Emerging themes in rotavirus cell entry, genome organization, transcription and replication". *Virus Research*. **101** (1): 67–81. doi:10.1016/j.virusres.2003.12.007 (<https://doi.org/10.1016%2Fj.virusres.2003.12.007>). PMID 15010218 (<https://pubmed.ncbi.nlm.nih.gov/15010218>).
02. Greer S, Alexander GJ (December 1995). "Viral serology and detection". *Bailliere's Clinical Gastroenterology*. **9** (4): 689–721. doi:10.1016/0950-3528(95)90057-8 (<https://doi.org/10.1016%2F0950-3528%2895%2990057-8>). PMID 8903801 (<https://pubmed.ncbi.nlm.nih.gov/8903801>).
03. Matter L, Kogelschatz K, Germann D (April 1997). "Serum levels of rubella virus antibodies indicating immunity: response to vaccination of subjects with low or undetectable antibody concentrations". *The Journal of Infectious Diseases*. **175** (4): 749–55. doi:10.1086/513967 (<https://doi.org/10.1086%2F513967>). PMID 9086126 (<https://pubmed.ncbi.nlm.nih.gov/9086126>).
04. Mallery DL, McEwan WA, Bidgood SR, Towers GJ, Johnson CM, James LC (November 2010). "Antibodies mediate intracellular immunity through tripartite motif-containing 21 (TRIM21)" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2993423>). *Proceedings of the National Academy of Sciences of the United States of America*. **107** (46): 19985–90. Bibcode:2010PNAS..10719985M (<https://ui.adsabs.harvard.edu/abs/2010PNAS..10719985M>). doi:10.1073/pnas.1014074107 (<https://doi.org/10.1073%2Fpnas.1014074107>). PMC 2993423 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2993423>). PMID 21045130 (<https://pubmed.ncbi.nlm.nih.gov/21045130>).
05. Cascalho M, Platt JL (2007). "Novel functions of B cells". *Critical Reviews in Immunology*. **27** (2): 141–51. doi:10.1615/critrevimmunol.v27.i2.20 (<https://doi.org/10.1615%2Fcritrevimmunol.v27.i2.20>). PMID 17725500 (<https://pubmed.ncbi.nlm.nih.gov/17725500>).
06. Le Page C, Génin P, Baines MG, Hiscott J (2000). "Interferon activation and innate immunity". *Reviews in Immunogenetics*. **2** (3): 374–86. PMID 11256746 (<https://pubmed.ncbi.nlm.nih.gov/11256746>).
07. Hilleman MR (October 2004). "Strategies and mechanisms for host and pathogen survival in acute and persistent viral infections" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC521982>). *Proceedings of the National Academy of Sciences of the United States of America*. **101** (Suppl 2): 14560–66. Bibcode:2004PNAS..10114560H (<https://ui.adsabs.harvard.edu/abs/2004PNA..10114560H>). doi:10.1073/pnas.0404758101 (<https://doi.org/10.1073%2Fpnas.0404758101>). PMC 521982 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC521982>). PMID 15297608 (<https://pubmed.ncbi.nlm.nih.gov/15297608>).

08. Asaria P, MacMahon E (October 2006). "Measles in the United Kingdom: can we eradicate it by 2010?" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1626346>). *BMJ*. **333** (7574): 890–95. doi:[10.1136/bmj.38989.445845.7C](https://doi.org/10.1136/bmj.38989.445845.7C) (<https://doi.org/10.1136%2Fbmj.38989.445845.7C>). PMC [1626346](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1626346) (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1626346>). PMID [17068034](https://pubmed.ncbi.nlm.nih.gov/17068034) ([http://pubmed.ncbi.nlm.nih.gov/17068034](https://pubmed.ncbi.nlm.nih.gov/17068034)).
09. Lane JM (2006). "Mass vaccination and surveillance/containment in the eradication of smallpox" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7120753>). *Current Topics in Microbiology and Immunology*. **304**: 17–29. doi:[10.1007/3-540-36583-4\\_2](https://doi.org/10.1007/3-540-36583-4_2) ([https://doi.org/10.1007%2F3-540-36583-4\\_2](https://doi.org/10.1007%2F3-540-36583-4_2)). ISBN [978-3-540-29382-8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7120753). PMC [7120753](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7120753) (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7120753>). PMID [16989262](https://pubmed.ncbi.nlm.nih.gov/16989262) (<https://pubmed.ncbi.nlm.nih.gov/16989262>).
10. Arvin AM, Greenberg HB (January 2006). "New viral vaccines". *Virology*. **344** (1): 240–49. doi:[10.1016/j.virol.2005.09.057](https://doi.org/10.1016/j.virol.2005.09.057) (<https://doi.org/10.1016%2Fj.virol.2005.09.057>). PMID [16364754](https://pubmed.ncbi.nlm.nih.gov/16364754) (<https://pubmed.ncbi.nlm.nih.gov/16364754>).
11. Pastoret PP, Schudel AA, Lombard M (August 2007). "Conclusions--future trends in veterinary vaccinology". *Revue Scientifique et Technique*. **26** (2): 489–94, 495–501, 503–09. doi:[10.20506/rst.26.2.1759](https://doi.org/10.20506/rst.26.2.1759) (<https://doi.org/10.20506%2Frst.26.2.1759>). PMID [17892169](https://pubmed.ncbi.nlm.nih.gov/17892169) ([http://pubmed.ncbi.nlm.nih.gov/17892169](https://pubmed.ncbi.nlm.nih.gov/17892169)).
12. Palese P (January 2006). "Making better influenza virus vaccines?" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291403>). *Emerging Infectious Diseases*. **12** (1): 61–65. doi:[10.3201/eid1201.051043](https://doi.org/10.3201/eid1201.051043) (<https://doi.org/10.3201%2Feid1201.051043>). PMC [3291403](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291403) (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291403>). PMID [16494719](https://pubmed.ncbi.nlm.nih.gov/16494719) (<https://pubmed.ncbi.nlm.nih.gov/16494719>).
13. Thomssen R (1975). "Live attenuated versus killed virus vaccines". *Monographs in Allergy*. **9**: 155–76. PMID [1090805](https://pubmed.ncbi.nlm.nih.gov/1090805) (<https://pubmed.ncbi.nlm.nih.gov/1090805>).
14. McLean AA (1986). "Development of vaccines against hepatitis A and hepatitis B". *Reviews of Infectious Diseases*. **8** (4): 591–98. doi:[10.1093/clinids/8.4.591](https://doi.org/10.1093/clinids/8.4.591) (<https://doi.org/10.1093%2Fclinids%2F8.4.591>). PMID [3018891](https://pubmed.ncbi.nlm.nih.gov/3018891) (<https://pubmed.ncbi.nlm.nih.gov/3018891>).
15. Casswall TH, Fischler B (October 2005). "Vaccination of the immunocompromised child". *Expert Review of Vaccines*. **4** (5): 725–38. doi:[10.1586/14760584.4.5.725](https://doi.org/10.1586/14760584.4.5.725) (<https://doi.org/10.1586%2F14760584.4.5.725>). PMID [16221073](https://pubmed.ncbi.nlm.nih.gov/16221073) (<https://pubmed.ncbi.nlm.nih.gov/16221073>). S2CID [40821818](https://api.semanticscholar.org/CorpusID:40821818) (<https://api.semanticscholar.org/CorpusID:40821818>).
16. Barnett ED, Wilder-Smith A, Wilson ME (July 2008). "Yellow fever vaccines and international travelers". *Expert Review of Vaccines*. **7** (5): 579–87. doi:[10.1586/14760584.7.5.579](https://doi.org/10.1586/14760584.7.5.579) (<https://doi.org/10.1586%2F14760584.7.5.579>). PMID [18564013](https://pubmed.ncbi.nlm.nih.gov/18564013) (<https://pubmed.ncbi.nlm.nih.gov/18564013>). S2CID [19352868](https://api.semanticscholar.org/CorpusID:19352868) (<https://api.semanticscholar.org/CorpusID:19352868>).
17. Magden J, Kääriäinen L, Ahola T (March 2005). "Inhibitors of virus replication: recent developments and prospects" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7082807>). *Applied Microbiology and Biotechnology*. **66** (6): 612–21. doi:[10.1007/s00253-004-1783-3](https://doi.org/10.1007/s00253-004-1783-3) (<https://doi.org/10.1007%2Fs00253-004-1783-3>). PMC [7082807](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7082807) (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7082807>). PMID [15592828](https://pubmed.ncbi.nlm.nih.gov/15592828) (<https://pubmed.ncbi.nlm.nih.gov/15592828>).
18. Mindel A, Sutherland S (September 1983). "Genital herpes - the disease and its treatment including intravenous acyclovir". *The Journal of Antimicrobial Chemotherapy*. **12** (Suppl B): 51–59. doi:[10.1093/jac/12.suppl\\_b.51](https://doi.org/10.1093/jac/12.suppl_b.51) ([https://doi.org/10.1093%2Fjac%2F12.suppl\\_b.51](https://doi.org/10.1093%2Fjac%2F12.suppl_b.51)). PMID [6355051](https://pubmed.ncbi.nlm.nih.gov/6355051) (<https://pubmed.ncbi.nlm.nih.gov/6355051>).
19. Palmisano L, Vella S (2011). "A brief history of antiretroviral therapy of HIV infection: success and challenges". *Annali dell'Istituto Superiore di Sanità*. **47** (1): 44–48. doi:[10.4415/ANN\\_11\\_01\\_10](https://doi.org/10.4415/ANN_11_01_10) ([https://doi.org/10.4415%2FANN\\_11\\_01\\_10](https://doi.org/10.4415%2FANN_11_01_10)). PMID [21430338](https://pubmed.ncbi.nlm.nih.gov/21430338) (<https://pubmed.ncbi.nlm.nih.gov/21430338>).

20. Witthöft T, Möller B, Wiedmann KH, Mauss S, Link R, Lohmeyer J, et al. (November 2007). "Safety, tolerability and efficacy of peginterferon alpha-2a and ribavirin in chronic hepatitis C in clinical practice: The German Open Safety Trial" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2156112>). *Journal of Viral Hepatitis*. **14** (11): 788–96. doi:[10.1111/j.1365-2893.2007.00871.x](https://doi.org/10.1111/j.1365-2893.2007.00871.x) (<https://doi.org/10.1111%2Fj.1365-2893.2007.00871.x>). PMC 2156112 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2156112>). PMID 17927615 (<https://pubmed.ncbi.nlm.nih.gov/17927615>).
21. Rudin D, Shah SM, Kiss A, Wetz RV, Sottile VM (November 2007). "Interferon and lamivudine vs. interferon for hepatitis B e antigen-positive hepatitis B treatment: meta-analysis of randomized controlled trials" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2156150>). *Liver International*. **27** (9): 1185–93. doi:[10.1111/j.1478-3231.2007.01580.x](https://doi.org/10.1111/j.1478-3231.2007.01580.x) (<https://doi.org/10.1111%2Fj.1478-3231.2007.01580.x>). PMC 2156150 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2156150>). PMID 17919229 (<https://pubmed.ncbi.nlm.nih.gov/17919229>).
22. Dimmock p. 3
23. Goris N, Vandenbussche F, De Clercq K (April 2008). "Potential of antiviral therapy and prophylaxis for controlling RNA viral infections of livestock". *Antiviral Research*. **78** (1): 170–78. doi:[10.1016/j.antiviral.2007.10.003](https://doi.org/10.1016/j.antiviral.2007.10.003) (<https://doi.org/10.1016%2Fj.antiviral.2007.10.003>). PMID 18035428 (<https://pubmed.ncbi.nlm.nih.gov/18035428>).
24. Carmichael LE (2005). "An annotated historical account of canine parvovirus". *Journal of Veterinary Medicine. B, Infectious Diseases and Veterinary Public Health*. **52** (7–8): 303–11. doi:[10.1111/j.1439-0450.2005.00868.x](https://doi.org/10.1111/j.1439-0450.2005.00868.x) (<https://doi.org/10.1111%2Fj.1439-0450.2005.00868.x>). PMID 16316389 (<https://pubmed.ncbi.nlm.nih.gov/16316389>).
25. Chen Y, Zhao Y, Hammond J, Hsu HT, Evans J, Feldlaufer M (October–November 2004). "Multiple virus infections in the honey bee and genome divergence of honey bee viruses" (<http://digitalcommons.unl.edu/cgi/viewcontent.cgi?article=1395&context=usdaarsfacpub>). *Journal of Invertebrate Pathology*. **87** (2–3): 84–93. doi:[10.1016/j.jip.2004.07.005](https://doi.org/10.1016/j.jip.2004.07.005) (<https://doi.org/10.1016%2Fj.jip.2004.07.005>). PMID 15579317 (<https://pubmed.ncbi.nlm.nih.gov/15579317>).
26. Shors p. 802
27. Shors pp. 799–807
28. Zaheer K, Akhtar MH (2016). "Potato Production, Usage, and Nutrition – A Review". *Critical Reviews in Food Science and Nutrition*. **56** (5): 711–21. doi:[10.1080/10408398.2012.724479](https://doi.org/10.1080/10408398.2012.724479) (<https://doi.org/10.1080%2F10408398.2012.724479>). PMID 24925679 (<https://pubmed.ncbi.nlm.nih.gov/24925679>).
29. Fuentes S, Jones RA, Matsuoka H, Ohshima K, Kreuze J, Gibbs AJ (July 2019). "Potato virus Y; the Andean connection" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6755682>). *Virus Evolution*. **5** (2): vez037. doi:[10.1093/ve/vez037](https://doi.org/10.1093/ve/vez037) (<https://doi.org/10.1093%2Fve%2Fvez037>). PMC 6755682 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6755682>). PMID 31559020 (<https://pubmed.ncbi.nlm.nih.gov/31559020>).
30. Dinesh-Kumar SP, Tham WH, Baker BJ (December 2000). "Structure-function analysis of the tobacco mosaic virus resistance gene N" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC18997>). *Proceedings of the National Academy of Sciences of the United States of America*. **97** (26): 14789–94. Bibcode:2000PNAS...9714789D (<https://ui.adsabs.harvard.edu/abs/2000PNAS...9714789D>). doi:[10.1073/pnas.97.26.14789](https://doi.org/10.1073/pnas.97.26.14789) (<https://doi.org/10.1073%2Fpnas.97.26.14789>). PMC 18997 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC18997>). PMID 11121079 (<https://pubmed.ncbi.nlm.nih.gov/11121079>).
31. Shors pp. 809
32. Soosaar JL, Burch-Smith TM, Dinesh-Kumar SP (October 2005). "Mechanisms of plant resistance to viruses". *Nature Reviews Microbiology*. **3** (10): 789–98. doi:[10.1038/nrmicro1239](https://doi.org/10.1038/nrmicro1239) (<https://doi.org/10.1038%2Fnrmicro1239>). PMID 16132037 (<https://pubmed.ncbi.nlm.nih.gov/16132037>).

33. Lomonosoff GP (2011). "Virus Particles and the Uses of Such Particles in Bio- and Nanotechnology". *Recent Advances in Plant Virology*. Caister Academic Press. ISBN 978-1-904455-75-2.
34. Wommack KE, Colwell RR (March 2000). "Viriplankton: viruses in aquatic ecosystems" (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC98987>). *Microbiology and Molecular Biology Reviews*. **64** (1): 69–114. doi:10.1128/MMBR.64.1.69-114.2000 (<https://doi.org/10.1128%2FMMBR.64.1.69-114.2000>). PMC 98987 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC98987>). PMID 10704475 (<https://pubmed.ncbi.nlm.nih.gov/10704475>).
35. Bergh O, Børshem KY, Bratbak G, Heldal M (August 1989). "High abundance of viruses found in aquatic environments". *Nature*. **340** (6233): 467–68. Bibcode:1989Natur.340..467B (<https://ui.adsabs.harvard.edu/abs/1989Natur.340..467B>). doi:10.1038/340467a0 (<https://doi.org/10.1038%2F340467a0>). PMID 2755508 (<https://pubmed.ncbi.nlm.nih.gov/2755508>).
36. Shors pp. 834–35
37. Bickle TA, Krüger DH (June 1993). "Biology of DNA restriction" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC372918>). *Microbiological Reviews*. **57** (2): 434–50. doi:10.1128/MMBR.57.2.434-450.1993 (<https://doi.org/10.1128%2FMMBR.57.2.434-450.1993>). PMC 372918 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC372918>). PMID 8336674 (<https://pubmed.ncbi.nlm.nih.gov/8336674>).
38. Barrangou R, Fremaux C, Deveau H, Richards M, Boyaval P, Moineau S, et al. (March 2007). "CRISPR provides acquired resistance against viruses in prokaryotes". *Science*. **315** (5819): 1709–12. Bibcode:2007Sci...315.1709B (<https://ui.adsabs.harvard.edu/abs/2007Sci...315.1709B>). doi:10.1126/science.1138140 (<https://doi.org/10.1126%2Fscience.1138140>). hdl:20.500.11794/38902 (<https://hdl.handle.net/20.500.11794%2F38902>). PMID 17379808 (<https://pubmed.ncbi.nlm.nih.gov/17379808>).
39. Brouns SJ, Jore MM, Lundgren M, Westra ER, Slijkhuis RJ, Snijders AP, et al. (August 2008). "Small CRISPR RNAs guide antiviral defense in prokaryotes" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5898235>). *Science*. **321** (5891): 960–64. Bibcode:2008Sci...321..960B (<https://ui.adsabs.harvard.edu/abs/2008Sci...321..960B>). doi:10.1126/science.1159689 (<https://doi.org/10.1126%2Fscience.1159689>). PMC 5898235 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5898235>). PMID 18703739 (<https://pubmed.ncbi.nlm.nih.gov/18703739>).
40. Mojica FJ, Rodriguez-Valera F (September 2016). "The discovery of CRISPR in archaea and bacteria". *The FEBS Journal*. **283** (17): 3162–69. doi:10.1111/febs.13766 (<https://doi.org/10.1111%2Ffebs.13766>). hdl:10045/57676 (<https://hdl.handle.net/10045%2F57676>). PMID 27234458 (<https://pubmed.ncbi.nlm.nih.gov/27234458>).
41. Prangishvili D, Garrett RA (April 2004). "Exceptionally diverse morphotypes and genomes of crenarchaeal hyperthermophilic viruses" (<https://curis.ku.dk/ws/files/51497971/0320204.pdf>) (PDF). *Biochemical Society Transactions*. **32** (Pt 2): 204–08. doi:10.1042/BST0320204 (<https://doi.org/10.1042%2FBST0320204>). PMID 15046572 (<https://pubmed.ncbi.nlm.nih.gov/15046572>).
42. Mojica FJ, Díez-Villaseñor C, García-Martínez J, Soria E (February 2005). "Intervening sequences of regularly spaced prokaryotic repeats derive from foreign genetic elements". *Journal of Molecular Evolution*. **60** (2): 174–82. Bibcode:2005JMolE..60..174M (<https://ui.adsabs.harvard.edu/abs/2005JMolE..60..174M>). doi:10.1007/s00239-004-0046-3 (<https://doi.org/10.1007%2Fs00239-004-0046-3>). PMID 15791728 (<https://pubmed.ncbi.nlm.nih.gov/15791728>).
43. Makarova KS, Grishin NV, Shabalina SA, Wolf YI, Koonin EV (March 2006). "A putative RNA-interference-based immune system in prokaryotes: computational analysis of the predicted enzymatic machinery, functional analogies with eukaryotic RNAi, and hypothetical mechanisms of action" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1462988>). *Biology Direct*. **1**: 7. doi:10.1186/1745-6150-1-7 (<https://doi.org/10.1186%2F1745-6150-1-7>). PMC 1462988 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1462988>). PMID 16545108 (<https://pubmed.ncbi.nlm.nih.gov/16545108>).

44. van der Oost J, Westra ER, Jackson RN, Wiedenheft B (July 2014). "Unravelling the structural and mechanistic basis of CRISPR-Cas systems" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4225775>). *Nature Reviews. Microbiology.* **12** (7): 479–92. doi:10.1038/nrmicro3279 (<https://doi.org/10.1038%2Fnrnmicro3279>). PMC 4225775 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4225775>). PMID 24909109 (<https://pubmed.ncbi.nlm.nih.gov/24909109>).
45. Dávila-Ramos S, Castelán-Sánchez HG, Martínez-Ávila L, Sánchez-Carbente MD, Peralta R, Hernández-Mendoza A, et al. (2019). "A Review on Viral Metagenomics in Extreme Environments" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6842933>). *Frontiers in Microbiology.* **10**: 2403. doi:10.3389/fmicb.2019.02403 (<https://doi.org/10.3389%2Ffmicb.2019.02403>). PMC 6842933 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6842933>). PMID 31749771 (<https://pubmed.ncbi.nlm.nih.gov/31749771>).
46. Zhang QY, Gui JF (December 2018). "Diversity, evolutionary contribution and ecological roles of aquatic viruses". *Science China. Life Sciences.* **61** (12): 1486–1502. doi:10.1007/s11427-018-9414-7 (<https://doi.org/10.1007%2Fs11427-018-9414-7>). PMID 30443861 (<https://pubmed.ncbi.nlm.nih.gov/30443861>). S2CID 53564176 (<https://api.semanticscholar.org/CorpusID:53564176>).
47. Weitz JS, Wilhelm SW (2013). "An ocean of viruses" (<https://www.the-scientist.com/?articles.view/articleNo/36120/title/An-Ocean-of-Viruses/>). *The Scientist.* **27** (7): 35–39.
48. Suttle CA (September 2005). "Viruses in the sea". *Nature.* **437** (7057): 356–61. Bibcode:2005Natur.437..356S (<https://ui.adsabs.harvard.edu/abs/2005Natur.437..356S>). doi:10.1038/nature04160 (<https://doi.org/10.1038%2Fnature04160>). PMID 16163346 (<https://pubmed.ncbi.nlm.nih.gov/16163346>).
49. Wilhelm SW, Suttle CA (1999). "Viruses and nutrient cycles in the sea: viruses play critical roles in the structure and function of aquatic food webs". *BioScience.* **49** (10): 781–88. doi:10.2307/1313569 (<https://doi.org/10.2307%2F1313569>). JSTOR 1313569 (<https://www.jstor.org/stable/1313569>).
50. Shelford EJ, Suttle CA (2018). "Virus-mediated transfer of nitrogen from heterotrophic bacteria to phytoplankton" (<https://www.biogeosciences.net/15/809/2018/bg-15-809-2018.html>). *Biogeosciences.* **15** (3): 809–15. Bibcode:2018BGeo...15..809S (<https://ui.adsabs.harvard.edu/abs/2018BGeo...15..809S>). doi:10.5194/bg-15-809-2018 (<https://doi.org/10.5194%2Fbg-15-809-2018>).
51. Suttle CA (October 2007). "Marine viruses – major players in the global ecosystem". *Nature Reviews. Microbiology.* **5** (10): 801–12. doi:10.1038/nrmicro1750 (<https://doi.org/10.1038%2Fnrmicro1750>). PMID 17853907 (<https://pubmed.ncbi.nlm.nih.gov/17853907>).
52. Wigington CH, Sonderegger D, Brussaard CP, Buchan A, Finke JF, Fuhrman JA, et al. (January 2016). "Re-examination of the relationship between marine virus and microbial cell abundances" (<http://www.vliz.be/imisdocs/publications/23/301523.pdf>) (PDF). *Nature Microbiology.* **1** (15024): 15024. doi:10.1038/nmicrobiol.2015.24 (<https://doi.org/10.1038%2Fnmicrobiol.2015.24>). PMID 27572161 (<https://pubmed.ncbi.nlm.nih.gov/27572161>). S2CID 52829633 (<https://api.semanticscholar.org/CorpusID:52829633>).
53. Brussaard CP (2004). "Viral control of phytoplankton populations – a review". *The Journal of Eukaryotic Microbiology.* **51** (2): 125–38. doi:10.1111/j.1550-7408.2004.tb00537.x (<https://doi.org/10.1111%2Fj.1550-7408.2004.tb00537.x>). PMID 15134247 (<https://pubmed.ncbi.nlm.nih.gov/15134247>).
54. Robbins J (13 April 2018). "Trillions Upon Trillions of Viruses Fall From the Sky Each Day" (<https://www.nytimes.com/2018/04/13/science/virosphere-evolution.html>). *The New York Times.* Retrieved 14 April 2018.
55. Reche I, D'Orta G, Mladenov N, Winget DM, Suttle CA (April 2018). "Deposition rates of viruses and bacteria above the atmospheric boundary layer" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5864199>). *The ISME Journal.* **12** (4): 1154–62. doi:10.1038/s41396-017-0042-4 (<https://doi.org/10.1038%2Fs41396-017-0042-4>). PMC 5864199 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5864199>). PMID 29379178 (<https://pubmed.ncbi.nlm.nih.gov/29379178>).

56. Hall AJ, Jepson PD, Goodman SJ, Harkonen T (2006). "Phocine distemper virus in the North and European Seas – data and models, nature and nurture". *Biological Conservation*. **131** (2): 221–29. doi:[10.1016/j.biocon.2006.04.008](https://doi.org/10.1016/j.biocon.2006.04.008) (<https://doi.org/10.1016%2Fj.biocon.2006.04.008>).
57. Forterre P, Philippe H (June 1999). "The last universal common ancestor (LUCA), simple or complex?". *The Biological Bulletin*. **196** (3): 373–75, discussion 375–77. doi:[10.2307/1542973](https://doi.org/10.2307/1542973) (<https://doi.org/10.2307%2F1542973>). JSTOR 1542973 (<https://www.jstor.org/stable/1542973>). PMID 11536914 (<https://pubmed.ncbi.nlm.nih.gov/11536914>).
58. Collier p. 8
59. Lodish H, Berk A, Zipursky SL, Matsudaira P, Baltimore D, Darnell J (2000). "Viruses: Structure, Function, and Uses" (<https://www.ncbi.nlm.nih.gov/books/bv.fcgi?highlight=Viruses&rid=mcb.section.1408#1422>). *Molecular Cell Biology* (4th ed.). New York: W. H. Freeman.
60. Matsuzaki S, Rashel M, Uchiyama J, Sakurai S, Ujihara T, Kuroda M, et al. (October 2005). "Bacteriophage therapy: a revitalized therapy against bacterial infectious diseases". *Journal of Infection and Chemotherapy*. **11** (5): 211–19. doi:[10.1007/s10156-005-0408-9](https://doi.org/10.1007/s10156-005-0408-9) (<https://doi.org/10.1007%2Fs10156-005-0408-9>). PMID 16258815 (<https://pubmed.ncbi.nlm.nih.gov/16258815>).
61. Gleba YY, Giritch A (2011). "Plant Viral Vectors for Protein Expression". *Recent Advances in Plant Virology*. Caister Academic Press. ISBN 978-1-904455-75-2.
62. Jefferson A, Cadet VE, Hielscher A (September 2015). "The mechanisms of genetically modified vaccinia viruses for the treatment of cancer". *Critical Reviews in Oncology/Hematology*. **95** (3): 407–16. doi:[10.1016/j.critrevonc.2015.04.001](https://doi.org/10.1016/j.critrevonc.2015.04.001) (<https://doi.org/10.1016%2Fj.critrevonc.2015.04.001>). PMID 25900073 (<https://pubmed.ncbi.nlm.nih.gov/25900073>).
63. Karimkhani C, Gonzalez R, Dellavalle RP (August 2014). "A review of novel therapies for melanoma". *American Journal of Clinical Dermatology*. **15** (4): 323–37. doi:[10.1007/s40257-014-0083-7](https://doi.org/10.1007/s40257-014-0083-7) (<https://doi.org/10.1007%2Fs40257-014-0083-7>). PMID 24928310 (<https://pubmed.ncbi.nlm.nih.gov/24928310>). S2CID 38864550 (<https://api.semanticscholar.org/CorpusID:38864550>).
64. "FDA approves Amgen's injected immunotherapy for melanoma" (<https://www.reuters.com/article/us-amgen-fda-idUSKCN0SL2YH20151027>). Reuters. 27 October 2015. Retrieved 24 January 2020.
65. Burke J, Nieva J, Borad MJ, Breitbach CJ (August 2015). "Oncolytic viruses: perspectives on clinical development". *Current Opinion in Virology*. **13**: 55–60. doi:[10.1016/j.coviro.2015.03.020](https://doi.org/10.1016/j.coviro.2015.03.020) (<https://doi.org/10.1016%2Fj.coviro.2015.03.020>). PMID 25989094 (<https://pubmed.ncbi.nlm.nih.gov/25989094>).
66. Fischlechner M, Donath E (2007). "Viruses as building blocks for materials and devices". *Angewandte Chemie*. **46** (18): 3184–93. doi:[10.1002/anie.200603445](https://doi.org/10.1002/anie.200603445) (<https://doi.org/10.1002%2Fanie.200603445>). PMID 17348058 (<https://pubmed.ncbi.nlm.nih.gov/17348058>).
67. Soto CM, Blum AS, Vora GJ, Lebedev N, Meador CE, Won AP, et al. (April 2006). "Fluorescent signal amplification of carbocyanine dyes using engineered viral nanoparticles". *Journal of the American Chemical Society*. **128** (15): 5184–89. doi:[10.1021/ja058574x](https://doi.org/10.1021/ja058574x) (<https://doi.org/10.1021%2Fja058574x>). PMID 16608355 (<https://pubmed.ncbi.nlm.nih.gov/16608355>).
68. Blum AS, Soto CM, Wilson CD, Brower TL, Pollack SK, Schull TL, et al. (July 2005). "An engineered virus as a scaffold for three-dimensional self-assembly on the nanoscale". *Small*. **1** (7): 702–06. doi:[10.1002/smll.200500021](https://doi.org/10.1002/smll.200500021) (<https://doi.org/10.1002%2Fsmll.200500021>). PMID 17193509 (<https://pubmed.ncbi.nlm.nih.gov/17193509>).
69. Cello J, Paul AV, Wimmer E (August 2002). "Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template". *Science*. **297** (5583): 1016–18. Bibcode:2002Sci...297.1016C (<https://ui.adsabs.harvard.edu/abs/2002Sci...297.1016C>). doi:[10.1126/science.1072266](https://doi.org/10.1126/science.1072266) (<https://doi.org/10.1126%2Fscience.1072266>). PMID 12114528 (<https://pubmed.ncbi.nlm.nih.gov/12114528>). S2CID 5810309 (<https://api.semanticscholar.org/CorpusID:5810309>).

70. Coleman JR, Papamichail D, Skiena S, Futcher B, Wimmer E, Mueller S (June 2008). "Virus attenuation by genome-scale changes in codon pair bias" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754401>). *Science*. **320** (5884): 1784–87. Bibcode:2008Sci...320.1784C (<https://ui.adsabs.harvard.edu/abs/2008Sci...320.1784C>). doi:10.1126/science.1155761 (<https://doi.org/10.1126%2Fscience.1155761>). PMC 2754401 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754401>). PMID 18583614 (<https://pubmed.ncbi.nlm.nih.gov/18583614>).
71. "NIH viral genome database" (<https://www.ncbi.nlm.nih.gov/genomes/GenomesGroup.cgi?taxid=10239>). Ncbi.nlm.nih.gov. Retrieved 15 November 2017.
72. Zilinskas RA (August 2017). "A brief history of biological weapons programmes and the use of animal pathogens as biological warfare agents". *Revue Scientifique et Technique (International Office of Epizootics)*. **36** (2): 415–422. doi:10.20506/rst.36.2.2662 (<https://doi.org/10.20506%2Frst.36.2.2662>). PMID 30152475 (<https://pubmed.ncbi.nlm.nih.gov/30152475>).
73. Artenstein AW, Grabenstein JD (October 2008). "Smallpox vaccines for biodefense: need and feasibility". *Expert Review of Vaccines*. **7** (8): 1225–37. doi:10.1586/14760584.7.8.1225 (<http://doi.org/10.1586%2F14760584.7.8.1225>). PMID 18844596 (<https://pubmed.ncbi.nlm.nih.gov/18844596>). S2CID 33855724 (<https://api.semanticscholar.org/CorpusID:33855724>).

## Bibliography

- Collier L, Balows A, Sussman M (1998). Mahy, B, Collier LA (eds.). *Topley and Wilson's Microbiology and Microbial Infections*. Virology. **1** (Ninth ed.). ISBN 0-340-66316-2.
- Dimmock NJ, Easton AJ, Leppard K (2007). *Introduction to Modern Virology* (Sixth ed.). Blackwell Publishing. ISBN 978-1-4051-3645-7.
- Knipe DM, Howley PM, Griffin DE, Lamb RA, Martin MA, Roizman B, Straus SE (2007). *Fields Virology*. Lippincott Williams & Wilkins. ISBN 978-0-7817-6060-7.
- Shors T (2017). *Understanding Viruses*. Jones and Bartlett Publishers. ISBN 978-1-284-02592-7.

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- [ViralZone](http://viralzone.expasy.org/) (<http://viralzone.expasy.org/>) A Swiss Institute of Bioinformatics resource for all viral families, providing general molecular and epidemiological information

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