21 | VIRUSES

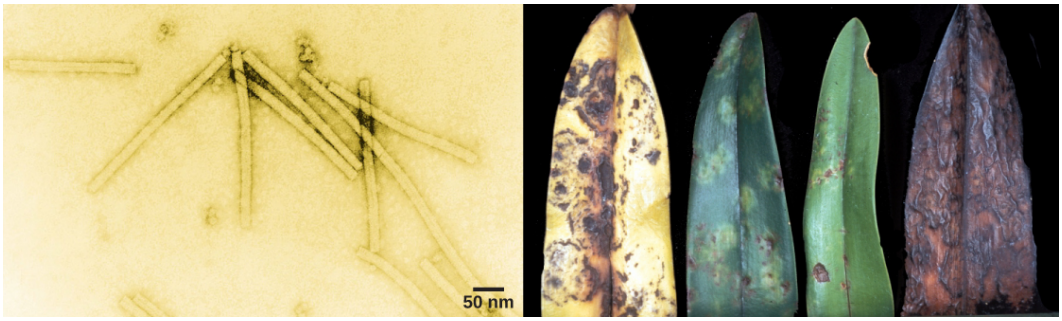


Figure 21.1 The tobacco mosaic virus, seen here by transmission electron microscopy (left), was the first virus to be discovered. The virus causes disease in tobacco and other plants, such as the orchid (right). (credit a: USDA ARS; credit b: modification of work by USDA Forest Service, Department of Plant Pathology Archive North Carolina State University; scale-bar data from Matt Russell)

Chapter Outline

Introduction

Viruses are noncellular parasitic entities that cannot be classified within any kingdom. They can infect organisms as diverse as bacteria, plants, and animals. In fact, viruses exist in a sort of netherworld between a living organism and a nonliving entity. Living things grow, metabolize, and reproduce. In contrast, viruses are not cellular, do not have a metabolism or grow, and cannot divide by cell division. Viruses *can* copy, or replicate themselves; however, they are entirely dependent on resources derived from their host cells to produce progeny viruses—which are assembled in their mature form. No one knows exactly when or how viruses evolved or from what ancestral source because viruses have not left a fossil record. Some virologists contend that modern viruses are a mosaic of bits and pieces of nucleic acids picked up from various sources along their respective evolutionary paths.

21.1 | Viral Evolution, Morphology, and Classification

By the end of this section, you will be able to do the following:

- Describe how viruses were first discovered and how they are detected
- Discuss three hypotheses about how viruses evolved
- Describe the general structure of a virus
- Recognize the basic shapes of viruses
- Understand past and emerging classification systems for viruses
- Describe the basis for the Baltimore classification system

Viruses are diverse entities: They vary in structure, methods of replication, and the hosts they infect. Nearly all forms of life—from prokaryotic bacteria and archaeans, to eukaryotes such as plants, animals, and fungi—have viruses that infect them. While most biological diversity can be understood through evolutionary history (such as

how species have adapted to changing environmental conditions and how different species are related to one another through common descent), much about virus origins and evolution remains unknown.

Discovery and Detection

Viruses were first discovered after the development of a porcelain filter—the Chamberland-Pasteur filter—that could remove all bacteria visible in the microscope from any liquid sample. In 1886, Adolph Meyer demonstrated that a disease of tobacco plants— **tobacco mosaic disease**—could be transferred from a diseased plant to a healthy one via liquid plant extracts. In 1892, Dmitri Ivanowski showed that this disease could be transmitted in this way even after the Chamberland-Pasteur filter had removed all viable bacteria from the extract. Still, it was many years before it was proved that these "filterable" infectious agents were not simply very small bacteria but were a new type of very small, disease-causing particle.

Most **virions**, or single virus particles, are very small, about 20 to 250 nanometers in diameter. However, some recently discovered viruses from amoebae range up to 1000 nm in diameter. With the exception of large virions, like the poxvirus and other large DNA viruses, viruses cannot be seen with a light microscope. It was not until the development of the electron microscope in the late 1930s that scientists got their first good view of the structure of the tobacco mosaic virus (TMV) (**Figure 21.1**), discussed above, and other viruses (**Figure 21.2**). The surface structure of virions can be observed by both scanning and transmission electron microscopy, whereas the internal structures of the virus can only be observed in images from a transmission electron microscope. The use of electron microscopy and other technologies has allowed for the discovery of many viruses of all types of living organisms.

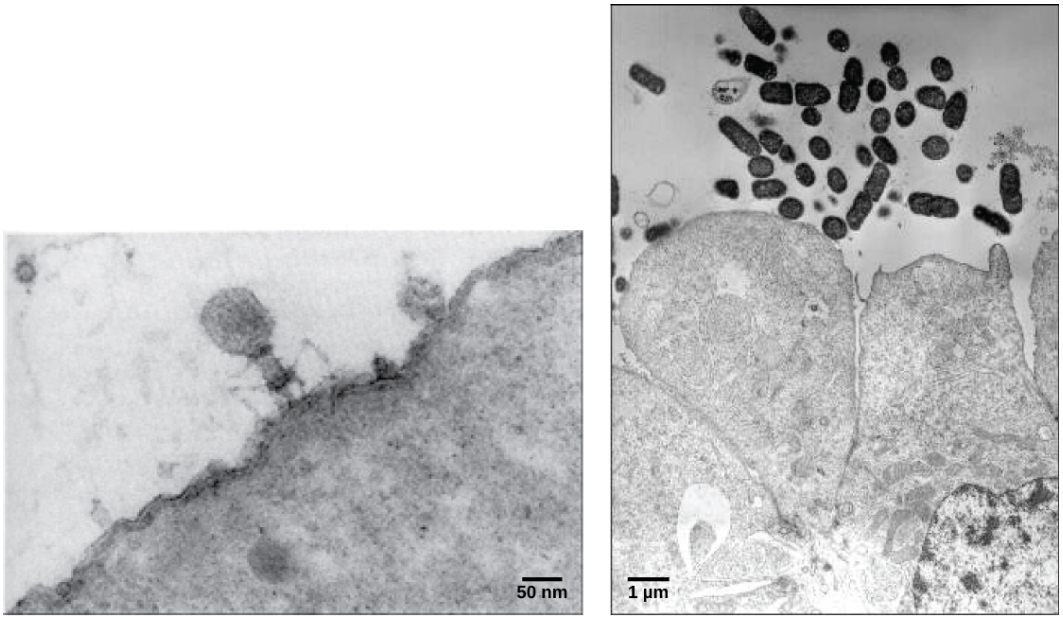


Figure 21.2 Most virus particles are visible only by electron microscopy. In these transmission electron micrographs, (a) a virus is as dwarfed by the bacterial cell it infects, as (b) these *E. coli* cells are dwarfed by cultured colon cells. (credit a: modification of work by U.S. Dept. of Energy, Office of Science, LBL, PBD; credit b: modification of work by J.P. Nataro and S. Sears, unpub. data, CDC; scale-bar data from Matt Russell)

Evolution of Viruses

Although biologists have a significant amount of knowledge about how present-day viruses mutate and adapt, much less is known about how viruses originated in the first place. When exploring the evolutionary history of most organisms, scientists can look at fossil records and similar historic evidence. However, viruses do not fossilize, as far as we know, so researchers must extrapolate from investigations of how today's viruses evolve and by using biochemical and genetic information to create speculative virus histories.

Most scholars agree that viruses don't have a single common ancestor, nor is there a single reasonable hypothesis about virus origins. There are current evolutionary scenarios that may explain the origin of viruses. One such hypothesis, the "devolution" or the *regressive hypothesis*, suggests that viruses evolved from free-living cells, or from intracellular prokaryotic parasites. However, many components of how this process might

have occurred remain a mystery. A second hypothesis, the escapist or the *progressive hypothesis*, suggests that viruses originated from RNA and DNA molecules that escaped from a host cell. A third hypothesis, the *self-replicating hypothesis,* suggests that viruses may have originated from self-replicating entities similar to transposons or other mobile genetic elements. In all cases, viruses are probably continuing to evolve along with the cells on which they rely on as hosts.

As technology advances, scientists may develop and refine additional hypotheses to explain the origins of viruses. The emerging field called virus molecular systematics attempts to do just that through comparisons of sequenced genetic material. These researchers hope one day to better understand the origin of viruses—a discovery that could lead to advances in the treatments for the ailments they produce.

Viral Morphology

Viruses are **noncellular**, meaning they are biological entities that do not have a cellular structure. They therefore lack most of the components of cells, such as organelles, ribosomes, and the plasma membrane. A virion consists of a nucleic acid core, an outer protein coating or **capsid**, and sometimes an outer **envelope** made of protein and phospholipid membranes derived from the host cell. Viruses may also contain additional proteins, such as enzymes, within the capsid or attached to the viral genome. The most obvious difference between members of different viral families is the variation in their morphology, which is quite diverse. An interesting feature of viral complexity is that the complexity of the host does not necessarily correlate with the complexity of the virion. In fact, some of the most complex virion structures are found in the **bacteriophages**—viruses that infect the simplest living organisms, bacteria.

Morphology

Viruses come in many shapes and sizes, but these features are consistent for each viral family. As we have seen, all virions have a nucleic acid genome covered by a protective capsid. The proteins of the capsid are encoded in the viral genome, and are called ***capsomeres***. Some viral capsids are simple helices or polyhedral "spheres," whereas others are quite complex in structure (Figure 21.3).

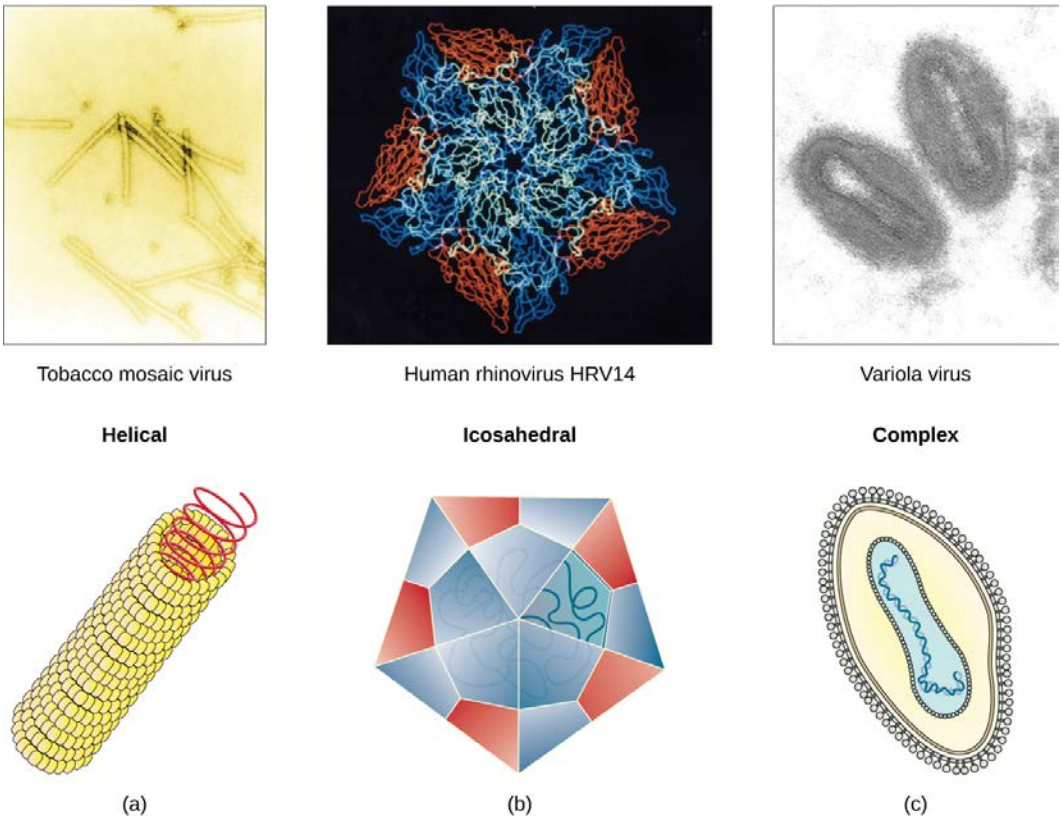


Figure 21.3 Viral capsids can be (a) helical, (b) polyhedral, or (c) have a complex shape. (credit a "micrograph": modification of work by USDA ARS; credit b "micrograph": modification of work by U.S. Department of Energy)

In general, the capsids of viruses are classified into four groups: helical, icosahedral, enveloped, and head-and-tail. *Helical capsids* are long and cylindrical. Many plant viruses are helical, including TMV. *Icosahedral viruses*

have shapes that are roughly spherical, such as those of poliovirus or herpesviruses. *Enveloped viruses* have membranes derived from the host cell that surrounds the capsids. Animal viruses, such as HIV, are frequently enveloped. *Head-and-tail viruses* infect bacteria and have a head that is similar to icosahedral viruses and a tail shaped like helical viruses.

Many viruses use some sort of *glycoprotein* to attach to their host cells via molecules on the cell called ***viral receptors***. For these viruses, attachment is required for later penetration of the cell membrane; only after penetration takes place can the virus complete its replication inside the cell. The receptors that viruses use are molecules that are normally found on cell surfaces and have their own physiological functions. It appears that viruses have simply evolved to make use of these molecules for their own replication. For example, HIV uses the CD4 molecule on T lymphocytes as one of its receptors (**Figure 21.4**). CD4 is a type of molecule called a *cell adhesion molecule*, which functions to keep different types of immune cells in close proximity to each other during the generation of a T lymphocyte immune response.

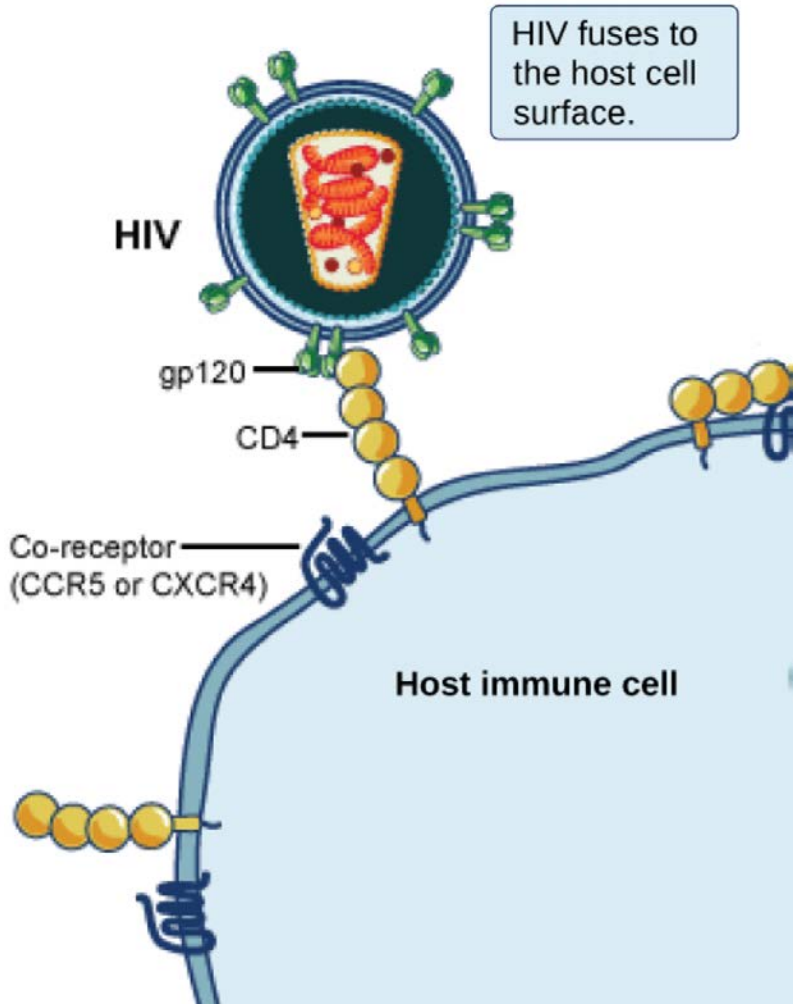


Figure 21.4 A virus and its host receptor protein. The HIV virus binds the CD4 receptor on the surface of human cells. CD4 receptors help white blood cells to communicate with other cells of the immune system when producing an immune response. (credit: modification of work by NIAID, NIH)

One of the most complex virions known, the T4 bacteriophage (which infects the *Escherichia coli*) bacterium, has a tail structure that the virus uses to attach to host cells and a head structure that houses its DNA.

Adenovirus, a non-enveloped animal virus that causes respiratory illnesses in humans, uses glycoprotein spikes protruding from its capsomeres to attach to host cells. Non-enveloped viruses also include those that cause polio (poliovirus), plantar warts (papillomavirus), and hepatitis A (hepatitis A virus).

Enveloped virions, such as the influenza virus, consist of nucleic acid (RNA in the case of influenza) and capsid proteins surrounded by a phospholipid bilayer envelope that contains virus-encoded proteins. Glycoproteins

embedded in the viral envelope are used to attach to host cells. Other envelope proteins are the **matrix proteins** that stabilize the envelope and often play a role in the assembly of progeny virions. Chicken pox, HIV, and mumps are other examples of diseases caused by viruses with envelopes. Because of the fragility of the envelope, non-enveloped viruses are more resistant to changes in temperature, pH, and some disinfectants than enveloped viruses.

Overall, the shape of the virion and the presence or absence of an envelope tell us little about what disease the virus may cause or what species it might infect, but they are still useful means to begin viral classification (**Figure 21.5**).

visual CONNECTION

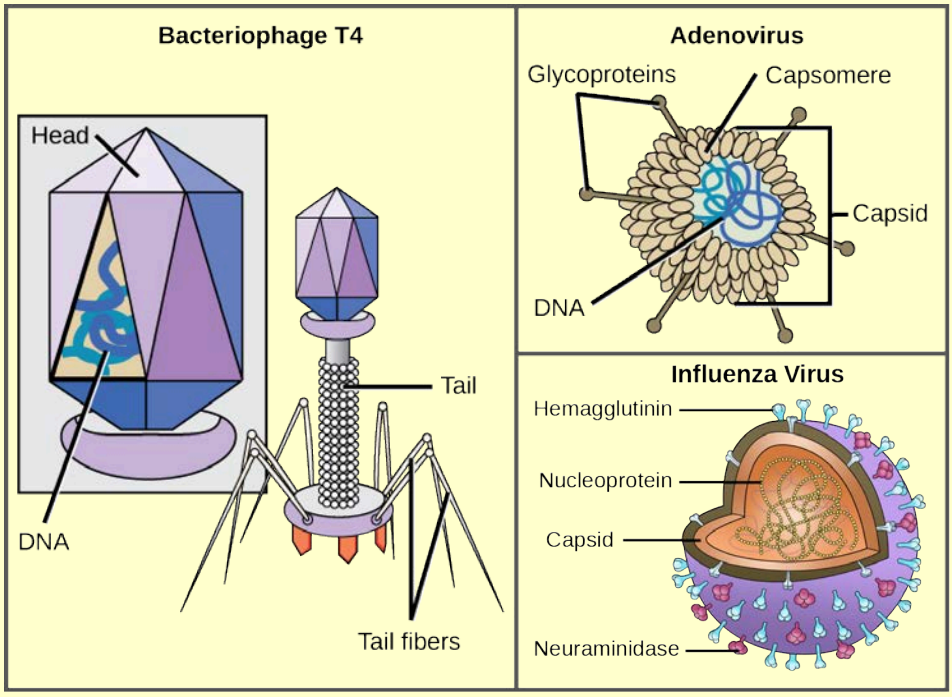


Figure 21.5 Complex Viruses. Viruses can be either complex or relatively simple in shape. This figure shows three relatively complex virions: the bacteriophage T4, with its DNA-containing head group and tail fibers that attach to host cells; adenovirus, which uses spikes from its capsid to bind to host cells; and the influenza virus, which uses glycoproteins embedded in its envelope to bind to host cells. The influenza virus also has matrix proteins, internal to the envelope, which help stabilize the virion's shape. (credit "bacteriophage, adenovirus": modification of work by NCBI, NIH; credit "influenza virus": modification of work by Dan Higgins, Centers for Disease Control and Prevention)

Which of the following statements about virus structure is true?

a. All viruses are encased in a viral membrane.
b. The capsomere is made up of small protein subunits called capsids.
c. DNA is the genetic material in all viruses.
d. Glycoproteins help the virus attach to the host cell.

Types of Nucleic Acid

Unlike nearly all living organisms that use DNA as their genetic material, viruses may use either DNA or RNA. The **virus core** contains the genome—the total genetic content of the virus. Viral genomes tend to be small, containing only those genes that encode proteins which the virus cannot get from the host cell. This genetic material may be single- or double-stranded. It may also be linear or circular. While most viruses contain a single nucleic acid, others have genomes divided into several segments. The RNA genome of the influenza virus is

segmented, which contributes to its variability and continuous evolution, and explains why it is difficult to develop a vaccine against it.

In DNA viruses, the viral DNA directs the host cell's replication proteins to synthesize new copies of the viral genome and to transcribe and translate that genome into viral proteins. Human diseases caused by DNA viruses include chickenpox, hepatitis B, and adenoviruses. Sexually transmitted DNA viruses include the herpes virus and the human papilloma virus (HPV), which has been associated with cervical cancer and genital warts.

RNA viruses contain only RNA as their genetic material. To replicate their genomes in the host cell, the RNA viruses must encode their own enzymes that can replicate RNA into RNA or, in the retroviruses, into DNA. These *RNA polymerase enzymes* are more likely to make copying errors than DNA polymerases, and therefore often make mistakes during transcription. For this reason, mutations in RNA viruses occur more frequently than in DNA viruses. This causes them to change and adapt more rapidly to their host. Human diseases caused by RNA viruses include influenza, hepatitis C, measles, and rabies. The HIV virus, which is sexually transmitted, is an RNA retrovirus.

The Challenge of Virus Classification

Because most viruses probably evolved from different ancestors, the systematic methods that scientists have used to classify prokaryotic and eukaryotic cells are not very useful. If viruses represent "remnants" of different organisms, then even genomic or protein analysis is not useful. Why?, *Because viruses have no common genomic sequence that they all share*. For example, the 16S rRNA sequence so useful for constructing prokaryote phylogenies is of no use for a creature with no ribosomes! Biologists have used several classification systems in the past. Viruses were initially grouped by shared morphology. Later, groups of viruses were classified by the type of nucleic acid they contained, DNA or RNA, and whether their nucleic acid was single- or double-stranded. However, these earlier classification methods grouped viruses differently, because they were based on different sets of characters of the virus. The most commonly used classification method today is called the Baltimore classification scheme, and is based on how messenger RNA (mRNA) is generated in each particular type of virus.

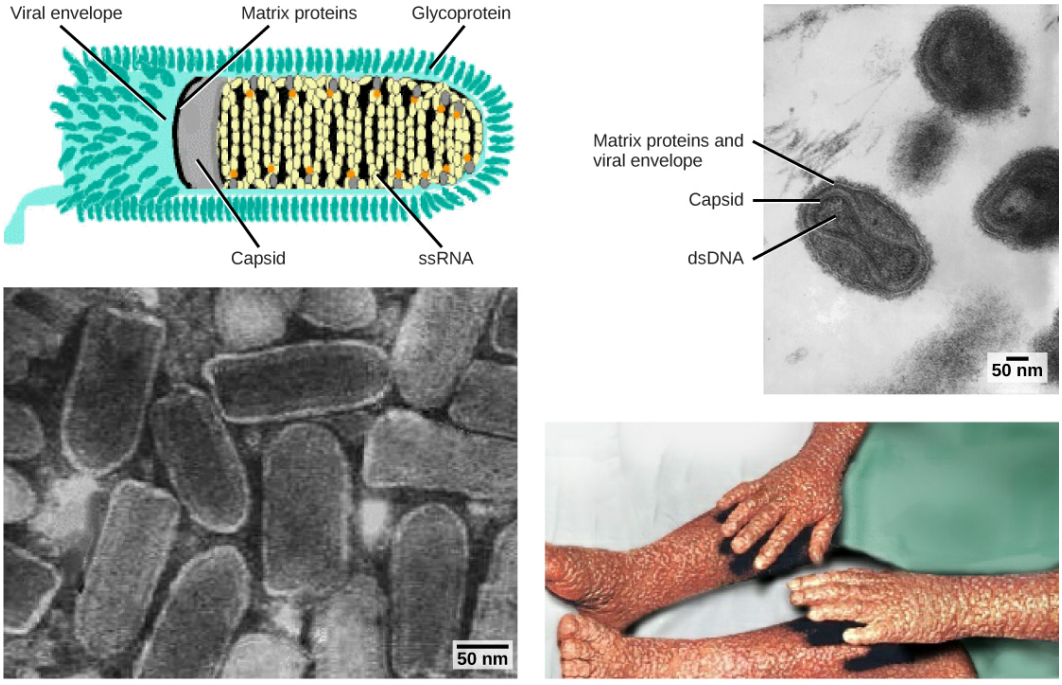
Past Systems of Classification

Viruses contain only a few elements by which they can be classified: the viral genome, the type of capsid, and the envelope structure for the enveloped viruses. All of these elements have been used in the past for viral classification (**Table 21.1** and **Figure 21.6**). Viral genomes may vary in the type of genetic material (DNA or RNA) and its organization (single- or double-stranded, linear or circular, and segmented or non-segmented). In some viruses, additional proteins needed for replication are associated directly with the genome or contained within the viral capsid.

Virus Classification by Genome Structure

Genome Structure	Examples
RNA	Rabies virus, retroviruses
DNA	Herpesviruses, smallpox virus
Single-stranded	Rabies virus, retroviruses
Double-stranded	Herpesviruses, smallpox virus
Linear	Rabies virus, retroviruses, herpesviruses, smallpox virus
Circular	Papillomaviruses, many bacteriophages
Non-segmented: genome consists of a single segment of genetic material	Parainfluenza viruses
Segmented: genome is divided into multiple segments	Influenza viruses

Table 21.1



(a) Rabies virus (b) Variola virus

Figure 21.6 Viruses can be classified according to their core genetic material and capsid design. (a) Rabies virus has a single-stranded RNA (ssRNA) core and an enveloped helical capsid, whereas (b) variola virus, the causative agent of smallpox, has a double-stranded DNA (dsDNA) core and a complex capsid. Rabies transmission occurs when saliva from an infected mammal enters a wound. The virus travels through neurons in the peripheral nervous system to the central nervous system, where it impairs brain function, and then travels to other tissues. The virus can infect any mammal, and most die within weeks of infection. Smallpox is a human virus transmitted by inhalation of the variola virus, localized in the skin, mouth, and throat, which causes a characteristic rash. Before its eradication in 1979, infection resulted in a 30 to 35 percent mortality rate. (credit “rabies diagram”: modification of work by CDC; “rabies micrograph”: modification of work by Dr. Fred Murphy, CDC; credit “small pox micrograph”: modification of work by Dr. Fred Murphy, Sylvia Whitfield, CDC; credit “smallpox photo”: modification of work by CDC; scale-bar data from Matt Russell)

Viruses can also be classified by the design of their capsids (**Table 21.2** and **Figure 21.7**). Capsids are classified as naked icosahedral, enveloped icosahedral, enveloped helical, naked helical, and complex. The type of genetic material (DNA or RNA) and its structure (single- or double-stranded, linear or circular, and segmented or non-segmented) are used to classify the virus core structures (**Table 21.2**).

Virus Classification by Capsid Structure

Capsid Classification	Examples
Naked icosahedral	Hepatitis A virus, polioviruses
Enveloped icosahedral	Epstein-Barr virus, herpes simplex virus, rubella virus, yellow fever virus, HIV-1
Enveloped helical	Influenza viruses, mumps virus, measles virus, rabies virus
Naked helical	Tobacco mosaic virus
Complex with many proteins; some have combinations of icosahedral and helical capsid structures	Herpesviruses, smallpox virus, hepatitis B virus, T4 bacteriophage

Table 21.2

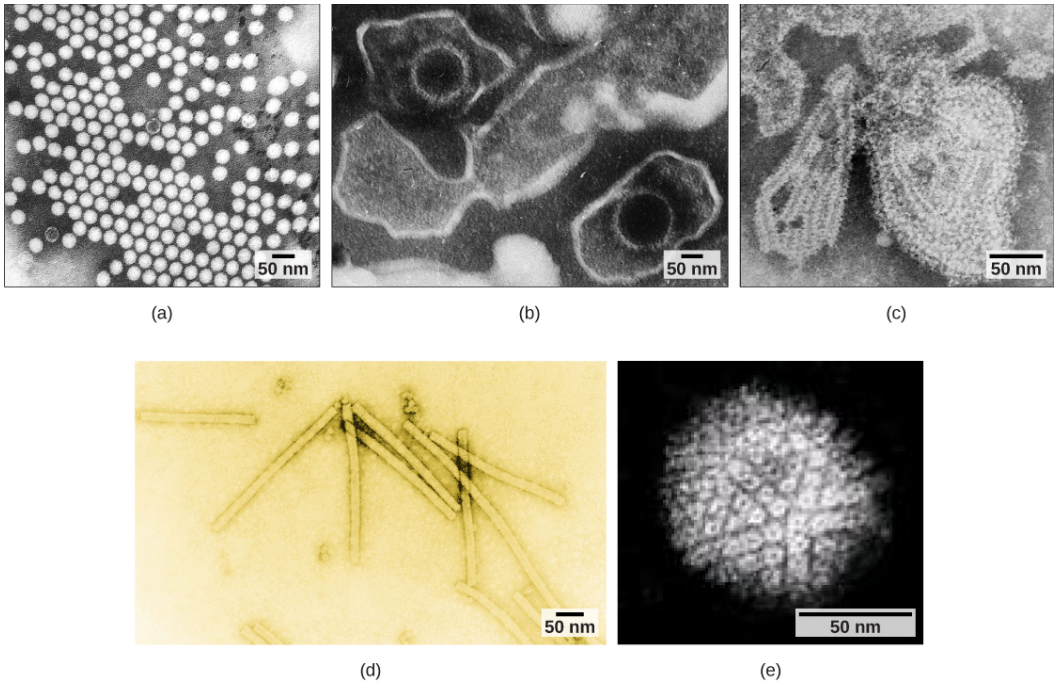


Figure 21.7 Transmission electron micrographs of various viruses show their capsid structures. The capsid of the (a) polio virus is naked icosahedral; (b) the Epstein-Barr virus capsid is enveloped icosahedral; (c) the mumps virus capsid is an enveloped helix; (d) the tobacco mosaic virus capsid is naked helical; and (e) the herpesvirus capsid is complex. (credit a: modification of work by Dr. Fred Murphy, Sylvia Whitfield; credit b: modification of work by Liza Gross; credit c: modification of work by Dr. F. A. Murphy, CDC; credit d: modification of work by USDA ARS; credit e: modification of work by Linda Stannard, Department of Medical Microbiology, University of Cape Town, South Africa, NASA; scale-bar data from Matt Russell)

Baltimore Classification

The most commonly and currently used system of virus classification was first developed by Nobel Prize-winning biologist David Baltimore in the early 1970s. In addition to the differences in morphology and genetics mentioned above, the Baltimore classification scheme groups viruses according to how the mRNA is produced during the replicative cycle of the virus.

Group I viruses contain double-stranded DNA (dsDNA) as their genome. Their mRNA is produced by transcription in much the same way as with cellular DNA, using the enzymes of the host cell.

Group II viruses have single-stranded DNA (ssDNA) as their genome. They convert their single-stranded genomes into a dsDNA intermediate before transcription to mRNA can occur.

Group III viruses use dsRNA as their genome. The strands separate, and one of them is used as a template for the generation of mRNA using the RNA-dependent RNA polymerase encoded by the virus.

Group IV viruses have ssRNA as their genome with a *positive polarity*, which means that the genomic RNA can serve directly as mRNA. Intermediates of dsRNA, called ***replicative intermediates***, are made in the process of copying the genomic RNA. Multiple, full-length RNA strands of *negative polarity* (complementary to the positive-stranded genomic RNA) are formed from these intermediates, which may then serve as templates for the production of RNA with positive polarity, including both full-length genomic RNA and shorter viral mRNAs.

Group V viruses contain ssRNA genomes with a **negative polarity**, meaning that their sequence is complementary to the mRNA. As with Group IV viruses, dsRNA intermediates are used to make copies of the genome and produce mRNA. In this case, the negative-stranded genome can be converted directly to mRNA. Additionally, full-length positive RNA strands are made to serve as templates for the production of the negative-stranded genome.

Group VI viruses have diploid (two copies) ssRNA genomes that must be converted, using the enzyme **reverse transcriptase**, to dsDNA; the dsDNA is then transported to the nucleus of the host cell and inserted into the host genome. Then, mRNA can be produced by transcription of the viral DNA that was integrated into the host genome.

Group VII viruses have partial dsDNA genomes and make ssRNA intermediates that act as mRNA, but are also

converted back into dsDNA genomes by reverse transcriptase, necessary for genome replication.

The characteristics of each group in the Baltimore classification are summarized in Table 21.3 with examples of each group.

Baltimore Classification

Group	Characteristics	Mode of mRNA Production	Example
I	Double-stranded DNA	mRNA is transcribed directly from the DNA template	Herpes simplex (herpesvirus)
II	Single-stranded DNA	DNA is converted to double-stranded form before RNA is transcribed	Canine parvovirus (parvovirus)
III	Double-stranded RNA	mRNA is transcribed from the RNA genome	Childhood gastroenteritis (rotavirus)
IV	Single stranded RNA (+)	Genome functions as mRNA	Common cold (picornavirus)
V	Single stranded RNA (-)	mRNA is transcribed from the RNA genome	Rabies (rhabdovirus)
VI	Single stranded RNA viruses with reverse transcriptase	Reverse transcriptase makes DNA from the RNA genome; DNA is then incorporated in the host genome; mRNA is transcribed from the incorporated DNA	Human immunodeficiency virus (HIV)
VII	Double stranded DNA viruses with reverse transcriptase	The viral genome is double-stranded DNA, but viral DNA is replicated through an RNA intermediate; the RNA may serve directly as mRNA or as a template to make mRNA	Hepatitis B virus (hepadnavirus)

Table 21.3

21.2 | Virus Infections and Hosts

By the end of this section, you will be able to do the following:

- List the steps of replication and explain what occurs at each step
- Describe the lytic and lysogenic cycles of virus replication
- Explain the transmission of plant and animal viruses
- Discuss some of the diseases caused by plant and animal viruses
- Discuss the economic impact of plant and animal viruses

Viruses are obligate, intracellular parasites. A virus must first recognize and attach to a specific living cell prior to entering it. After penetration, the invading virus must copy its genome and manufacture its own proteins. Finally, the progeny virions must escape the host cell so that they can infect other cells. Viruses can infect only certain species of hosts and only certain cells within that host. Specific host cells that a virus must occupy and use to replicate are called **permissive**. In most cases, the molecular basis for this specificity is due to a particular surface molecule known as the *viral receptor* on the host cell surface. A specific viral receptor is required for the virus to attach. In addition, differences in metabolism and host-cell immune responses (based on differential gene expression) are a likely factor in determining which cells a virus may target for replication.

Steps of Virus Infections

A virus must use its host-cell processes to replicate. The viral replication cycle can produce dramatic biochemical and structural changes in the host cell, which may cause cell damage. These changes, called **cytopathic effects**, can change cell functions or even destroy the cell. Some infected cells, such as those infected by the common cold virus known as rhinovirus, die through **lysis** (bursting) or **apoptosis** (programmed cell death or "cell suicide"), releasing all progeny virions at once. The symptoms of viral diseases result both from such cell damage caused by the virus and from the immune response to the virus, which attempts to control and eliminate the virus from the body.

Many animal viruses, such as **HIV (human immunodeficiency virus)**, leave the infected cells of the immune system by a process known as ***budding***, where virions leave the cell individually. During the budding process, the cell does not undergo lysis and is not immediately killed. However, the damage to the cells that the virus infects may make it impossible for the cells to function normally, even though the cells remain alive for a period of time. Most productive viral infections follow similar steps in the virus replication cycle: *attachment, penetration, uncoating, replication, assembly, and release* (**Figure 21.8**).

Attachment

A virus attaches to a specific receptor site on the host cell membrane through attachment proteins in the capsid or via glycoproteins embedded in the viral envelope. The specificity of this interaction determines the host—and the cells within the host—that can be infected by a particular virus. This can be illustrated by thinking of several keys and several locks, where each key will fit only one specific lock.

This **video (http://openstaxcollege.org/l/influenza)** explains how influenza attacks the body.

Entry

Viruses may enter a host cell either with or without the viral capsid. The nucleic acid of bacteriophages enters the host cell "naked," leaving the capsid outside the cell. Plant and animal viruses can enter through *endocytosis* (as you may recall, the cell membrane surrounds and engulfs the entire virus). Some enveloped viruses enter the cell when the viral envelope fuses directly with the cell membrane. Once inside the cell, the viral capsid degrades, and then the viral nucleic acid is released and becomes available for replication and transcription.

Replication and Assembly

The replication mechanism depends on the viral genome. DNA viruses usually use host-cell proteins and enzymes to replicate the viral DNA and to transcribe viral mRNA, which is then used to direct viral protein synthesis. RNA viruses usually use the RNA core as a template for synthesis of viral genomic RNA and mRNA. The viral mRNA directs the host cell to synthesize viral enzymes and capsid proteins, and assemble new virions.

Of course, there are exceptions to this pattern. If a host cell does not provide the enzymes necessary for viral replication, viral genes supply the information to direct synthesis of the missing proteins. Retroviruses, such as HIV (group VI of the Baltimore classification scheme), have an RNA genome that must be reverse transcribed into DNA, which then is incorporated into the host cell genome. To convert RNA into DNA, retroviruses must contain genes that encode the virus-specific enzyme reverse transcriptase that transcribes an RNA template to DNA. Reverse transcription never occurs in uninfected host cells—the enzyme reverse transcriptase is only derived from the expression of viral genes within the infected host cells. The fact that HIV produces some of its own enzymes not found in the host has allowed researchers to develop drugs that inhibit these enzymes without affecting the host's metabolism.

This approach has led to the development of a variety of drugs used to treat HIV and has been effective at reducing the number of infectious virions (copies of viral RNA) in the blood to non-detectable levels in many HIV-infected individuals.

Egress

The last stage of viral replication is the release of the new virions produced in the host organism, where they are

able to infect adjacent cells and repeat the replication cycle. As you've learned, some viruses are released when the host cell dies, and other viruses can leave infected cells by budding through the membrane without directly killing the cell.

visual CONNECTION

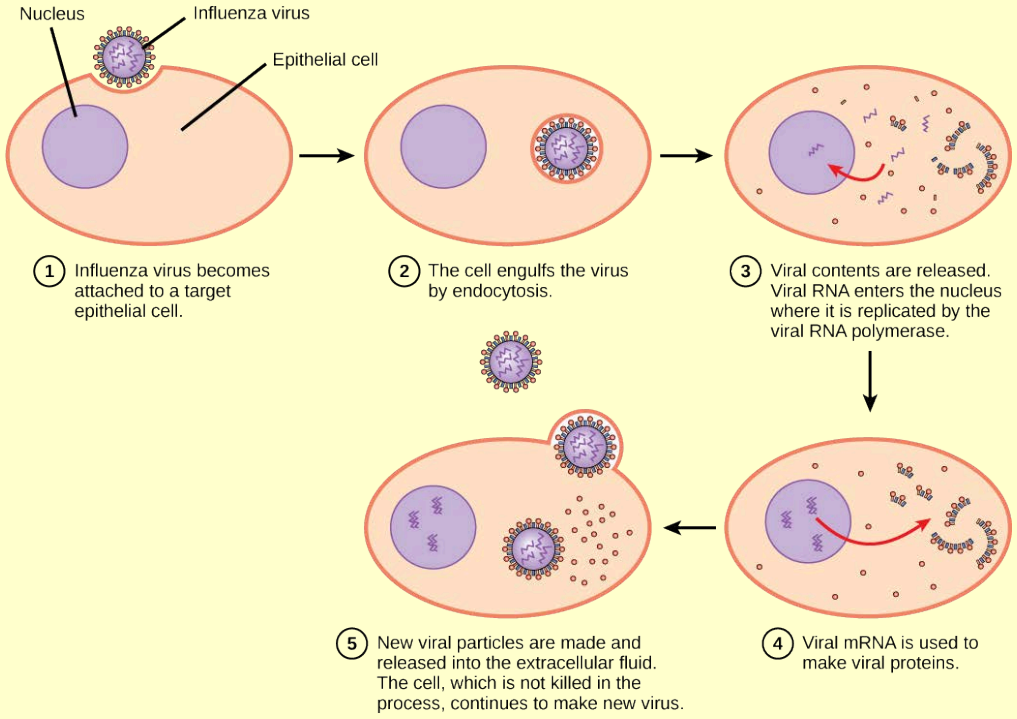


Figure 21.8 The influenza reproductive cycle. In influenza virus infection, glycoproteins on the capsid attach to a host epithelial cell. Following this, the virus is engulfed. RNA and proteins are then made and assembled into new virions.

Influenza virus is packaged in a viral envelope that fuses with the plasma membrane. This way, the virus can exit the host cell without killing it. What advantage does the virus gain by keeping the host cell alive?

LINK TO LEARNING

Watch a **video (https://www.khanacademy.org/science/biology/her/tree-of-life/v/viruses)** on viruses, identifying structures, modes of transmission, replication, and more.

Different Hosts and Their Viruses

As you've learned, viruses often infect very specific hosts, as well as specific cells within the host. This feature of a virus makes it specific to one or a few species of life on Earth. On the other hand, so many different types of viruses exist on Earth that nearly every living organism has its own set of *viruses* trying to infect its cells. Even prokaryotes, the smallest and simplest of cells, may be attacked by specific types of viruses. In the following section, we will look at some of the features of viral infection of prokaryotic cells. As we have learned, viruses that infect bacteria are called *bacteriophages* (**Figure 21.9**). Archaea have their own similar viruses.

Bacteriophages

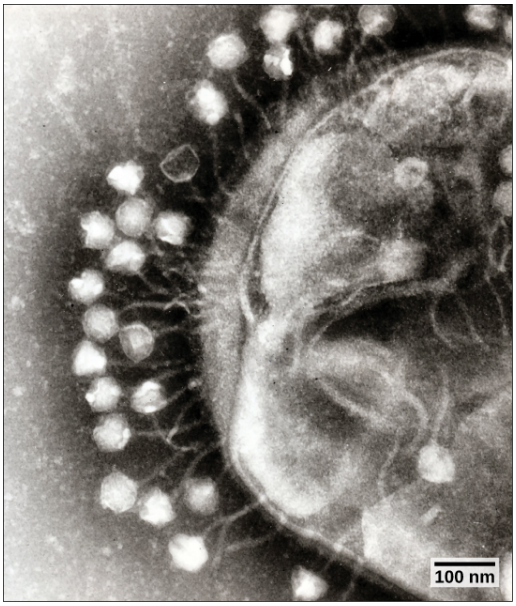


Figure 21.9 Bacteriophages attached to a host cell (transmission electron micrograph). In bacteriophage with tails, like the one shown here, the tails serve as a passageway for transmission of the phage genome. (credit: modification of work by Dr. Graham Beards; scale-bar data from Matt Russell)

Most bacteriophages are dsDNA viruses, which use host enzymes for DNA replication and RNA transcription. Phage particles must bind to specific surface receptors and actively insert the genome into the host cell. (The complex tail structures seen in many bacteriophages are actively involved in getting the viral genome across the prokaryotic cell wall.) When infection of a cell by a bacteriophage results in the production of new virions, the infection is said to be ***productive***. If the virions are released by bursting the cell, the virus replicates by means of a ***lytic cycle*** (**Figure 21.10**). An example of a lytic bacteriophage is T4, which infects *Escherichia coli* found in the human intestinal tract. Sometimes, however, a virus can remain within the cell without being released. For example, when a temperate bacteriophage infects a bacterial cell, it replicates by means of a ***lysogenic cycle*** (**Figure 21.10**), and the viral genome is incorporated into the genome of the host cell. When the phage DNA is incorporated into the host-cell genome, it is called a **prophage**. An example of a lysogenic bacteriophage is the λ (lambda) virus, which also infects the *E. coli* bacterium. Viruses that infect plant or animal cells may sometimes undergo infections where they are not producing virions for long periods. An example is the animal *herpesviruses*, including herpes simplex viruses, the cause of oral and genital herpes in humans. In a process called **latency**, these viruses can exist in nervous tissue for long periods of time without producing new virions, only to leave latency periodically and cause lesions in the skin where the virus replicates. Even though there are similarities between lysogeny and latency, the term lysogenic cycle is usually reserved to describe bacteriophages. Latency will be described in more detail in the next section.

visual CONNECTION

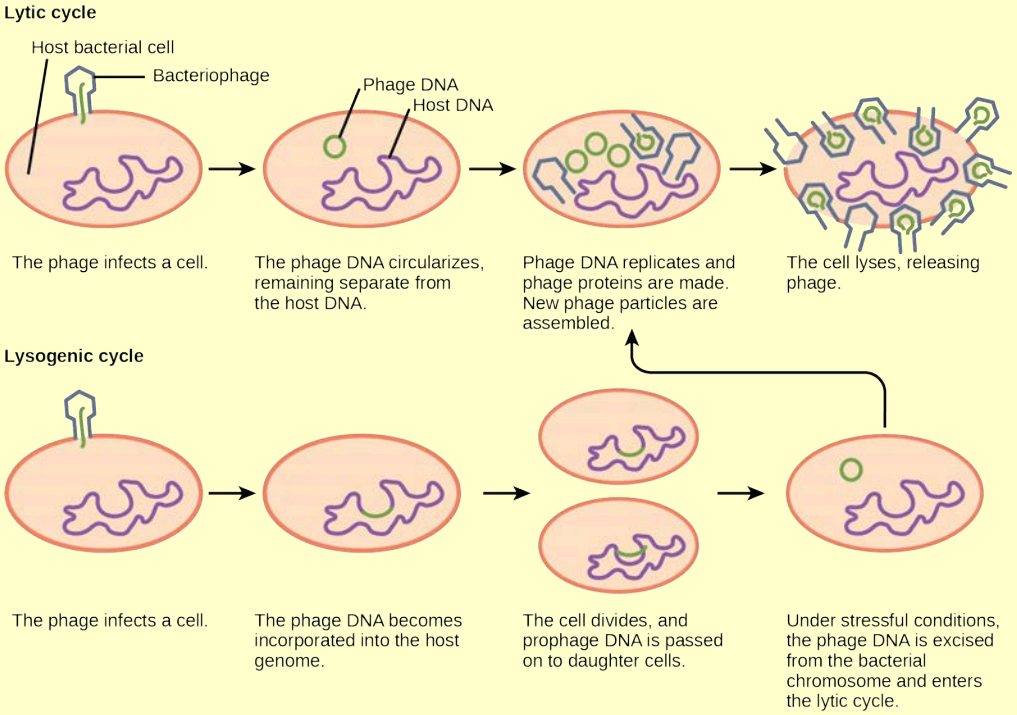


Figure 21.10 A temperate bacteriophage has both lytic and lysogenic cycles. In the lytic cycle, the phage replicates and lyses the host cell. In the lysogenic cycle, phage DNA is incorporated into the host genome, where it is passed on to subsequent generations. Environmental stressors such as starvation or exposure to toxic chemicals may cause the prophage to excise and enter the lytic cycle.

Which of the following statements is false?

a. In the lytic cycle, new phages are produced and released into the environment.
b. In the lysogenic cycle, phage DNA is incorporated into the host genome.
c. An environmental stressor can cause the phage to initiate the lysogenic cycle.
d. Cell lysis only occurs in the lytic cycle.

Plant Viruses

Most plant viruses, like the tobacco mosaic virus, have single-stranded (+) RNA genomes. However, there are also plant viruses in most other virus categories. Unlike bacteriophages, plant viruses do not have active mechanisms for delivering the viral genome across the protective cell wall. For a plant virus to enter a new host plant, some type of mechanical damage must occur. This damage is often caused by weather, insects, animals, fire, or human activities like farming or landscaping. Movement from cell to cell within a plant can be facilitated by viral modification of plasmodesmata (cytoplasmic threads that pass from one plant cell to the next). Additionally, plant offspring may inherit viral diseases from parent plants. Plant viruses can be transmitted by a variety of vectors, through contact with an infected plant's sap, by living organisms such as insects and nematodes, and through pollen. The transfer of a virus from one plant to another is known as **horizontal transmission**, whereas the inheritance of a virus from a parent is called **vertical transmission**.

Symptoms of viral diseases vary according to the virus and its host (Table 21.4). One common symptom is ***hyperplasia***, the abnormal proliferation of cells that causes the appearance of plant tumors known as **galls**. Other viruses induce ***hypoplasia***, or decreased cell growth, in the leaves of plants, causing thin, yellow areas to appear. Still other viruses affect the plant by directly killing plant cells, a process known as ***cell necrosis***. Other symptoms of plant viruses include malformed leaves; black streaks on the stems of the plants; altered growth of stems, leaves, or fruits; and ring spots, which are circular or linear areas of discoloration found in a leaf.

Some Common Symptoms of Plant Viral Diseases

Symptom	Appears as
Hyperplasia	Galls (tumors)
Hypoplasia	Thinned, yellow splotches on leaves
Cell necrosis	Dead, blackened stems, leaves, or fruit
Abnormal growth patterns	Malformed stems, leaves, or fruit
Discoloration	Yellow, red, or black lines, or rings in stems, leaves, or fruit

Table 21.4

Plant viruses can seriously disrupt crop growth and development, significantly affecting our food supply. They are responsible for poor crop quality and quantity globally, and can bring about huge economic losses annually. Others viruses may damage plants used in landscaping. Some viruses that infect agricultural food plants include the name of the plant they infect, such as tomato spotted wilt virus, bean common mosaic virus, and cucumber mosaic virus. In plants used for landscaping, two of the most common viruses are peony ring spot and rose mosaic virus. There are far too many plant viruses to discuss each in detail, but symptoms of bean common mosaic virus result in lowered bean production and stunted, unproductive plants. In the ornamental rose, the rose mosaic disease causes wavy yellow lines and colored splotches on the leaves of the plant.

Animal Viruses

Animal viruses, unlike the viruses of plants and bacteria, do not have to penetrate a cell wall to gain access to the host cell. The virus may even induce the host cell to cooperate in the infection process. Non-enveloped or “naked” animal viruses may enter cells in two different ways. As a protein in the viral capsid binds to its receptor on the host cell, the virus may be taken inside the cell via a vesicle during the normal cell process of *receptor-mediated endocytosis*. An alternative method of cell penetration used by non-enveloped viruses is for capsid proteins to undergo shape changes after binding to the receptor, creating channels in the host cell membrane. The viral genome is then “injected” into the host cell through these channels in a manner analogous to that used by many bacteriophages.

Enveloped viruses also have two ways of entering cells after binding to their receptors: receptor-mediated endocytosis, or **fusion**. Many enveloped viruses enter the cell by receptor-mediated endocytosis in a fashion similar to that seen in some non-enveloped viruses. On the other hand, fusion only occurs with enveloped virions. These viruses, which include HIV among others, use special fusion proteins in their envelopes to cause the envelope to fuse with the plasma membrane of the cell, thus releasing the genome and capsid of the virus into the cell cytoplasm.

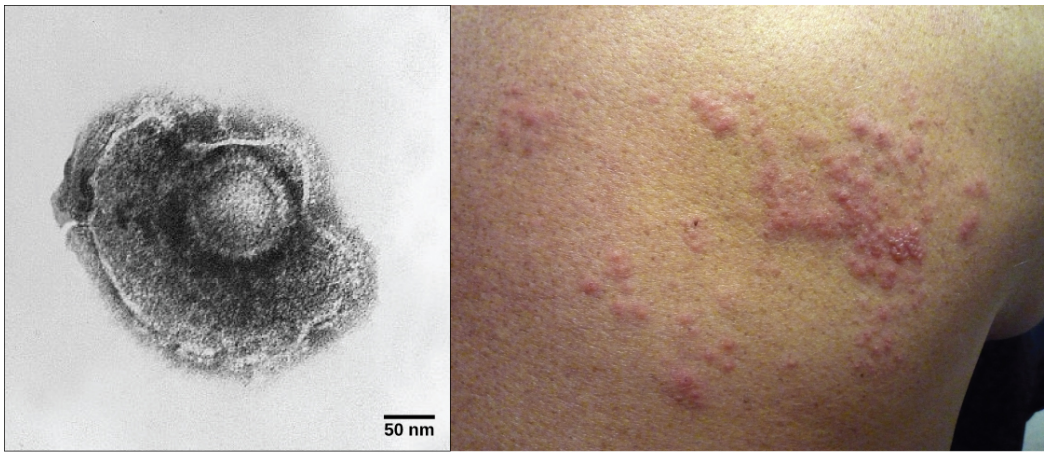
After making their proteins and copying their genomes, animal viruses complete the assembly of new virions and exit the cell. As we have already discussed using the example the influenza virus, enveloped animal viruses may bud from the cell membrane as they assemble themselves, taking a piece of the cell’s plasma membrane in the process. On the other hand, non-enveloped viral progeny, such as rhinoviruses, accumulate in infected cells until there is a signal for lysis or apoptosis, and all virions are released together.

As you will learn in the next module, animal viruses are associated with a variety of human diseases. Some of them follow the classic pattern of **acute disease**, where symptoms get increasingly worse for a short period followed by the elimination of the virus from the body by the immune system and eventual recovery from the infection. Examples of acute viral diseases are the common cold and influenza. Other viruses cause long-term **chronic infections**, such as the virus causing hepatitis C, whereas others, like herpes simplex virus, only cause **intermittent** symptoms. Still other viruses, such as human herpesviruses 6 and 7, which in some cases can cause the minor childhood disease roseola, often successfully cause productive infections without causing any symptoms at all in the host, and thus we say these patients have an **asymptomatic infection**.

In hepatitis C infections, the virus grows and reproduces in liver cells, causing low levels of liver damage. The damage is so low that infected individuals are often unaware that they are infected, and many infections are detected only by routine blood work on patients with risk factors such as intravenous drug use. On the other hand, since many of the symptoms of viral diseases are caused by immune responses, a lack of symptoms is an indication of a weak immune response to the virus. This allows the virus to escape elimination by the

immune system and persist in individuals for years, all the while producing low levels of progeny virions in what is known as a chronic viral disease. Chronic infection of the liver by this virus leads to a much greater chance of developing liver cancer, sometimes as much as 30 years after the initial infection.

As already discussed, herpes simplex virus can remain in a state of latency in nervous tissue for months, even years. As the virus “hides” in the tissue and makes few if any viral proteins, there is nothing for the immune response to act against, and immunity to the virus slowly declines. Under certain conditions, including various types of physical and psychological stress, the latent herpes simplex virus may be reactivated and undergo a lytic replication cycle in the skin, causing the lesions associated with the disease. Once virions are produced in the skin and viral proteins are synthesized, the immune response is again stimulated and resolves the skin lesions in a few days or weeks by destroying viruses in the skin. As a result of this type of replicative cycle, appearances of cold sores and genital herpes outbreaks only occur intermittently, even though the viruses remain in the nervous tissue for life. Latent infections are common with other herpesviruses as well, including the varicella-zoster virus that causes chickenpox. After having a chickenpox infection in childhood, the varicella-zoster virus can remain latent for many years and reactivate in adults to cause the painful condition known as “shingles” (**Figure 21.11**).



(a) (b)

Figure 21.11 A latent virus infection. (a) Varicella-zoster, the virus that causes chickenpox, has an enveloped icosahedral capsid visible in this transmission electron micrograph. Its double-stranded DNA genome becomes incorporated in the host DNA and can reactivate after latency in the form of (b) shingles, often exhibiting a rash. (credit a: modification of work by Dr. Erskine Palmer, B. G. Martin, CDC; credit b: modification of work by “rosmary”/Flickr; scale-bar data from Matt Russell)

Some animal-infecting viruses, including the hepatitis C virus discussed above, are known as **oncogenic viruses**: They have the ability to cause cancer. These viruses interfere with the normal regulation of the host cell cycle either by introducing genes that stimulate unregulated cell growth (oncogenes) or by interfering with the expression of genes that inhibit cell growth. Oncogenic viruses can be either DNA or RNA viruses. Cancers known to be associated with viral infections include cervical cancer, caused by human papillomavirus (HPV) (**Figure 21.12**), liver cancer caused by hepatitis B virus, T-cell leukemia, and several types of lymphoma.

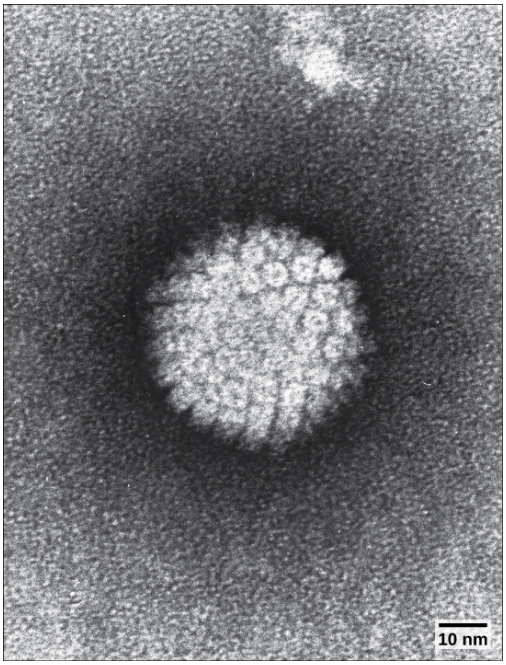


Figure 21.12 HPV, or human papillomavirus, has a naked icosahedral capsid visible in this transmission electron micrograph and a double-stranded DNA genome that is incorporated into the host DNA. The virus, which is sexually transmitted, is oncogenic and can lead to cervical cancer. (credit: modification of work by NCI, NIH; scale-bar data from Matt Russell)

LINK TO LEARNING

Visit the interactive **animations (http://openstaxcollege.org/l/animal_viruses)** showing the various stages of the replicative cycles of animal viruses and click on the flash animation links.

21.3 | Prevention and Treatment of Viral Infections

By the end of this section, you will be able to do the following:

- Identify major viral illnesses that affect humans
- Compare vaccinations and anti-viral drugs as medical approaches to viruses

Viruses cause a variety of diseases in animals, including humans, ranging from the common cold to potentially fatal illnesses like meningitis (**Figure 21.13**). These diseases can be treated by antiviral drugs or by vaccines; however, some viruses, such as HIV, are capable both of avoiding the immune response and of mutating within the host organism to become resistant to antiviral drugs.

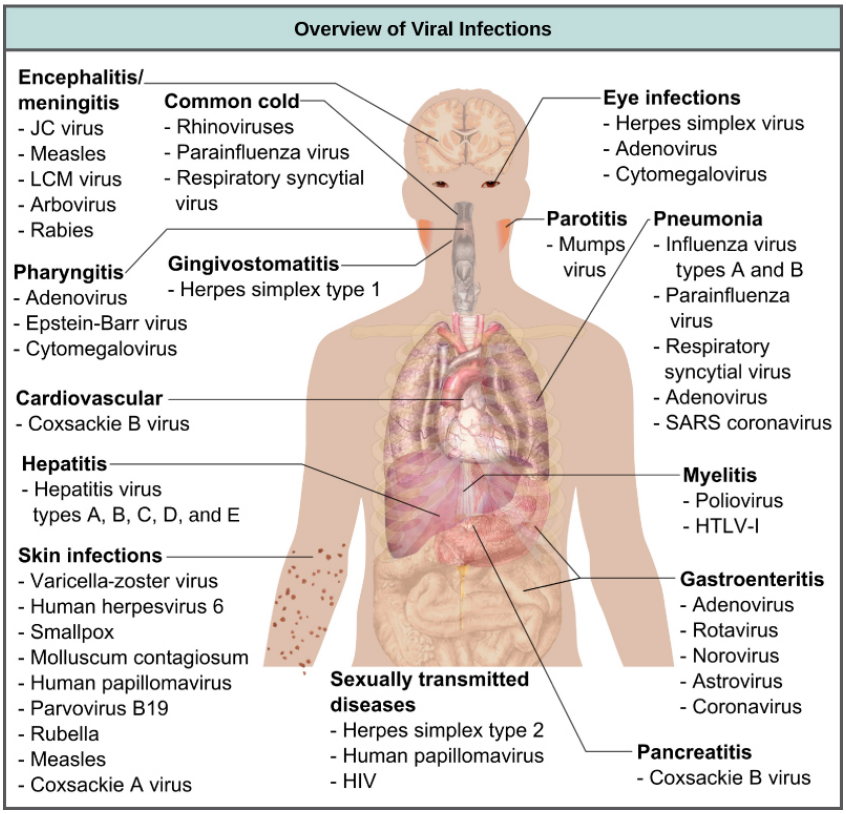


Figure 21.13 A sampling of human viruses. Viruses can cause dozens of ailments in humans, ranging from mild illnesses to serious diseases. (credit: modification of work by Mikael Häggström)

Vaccines for Prevention

The primary method of controlling viral disease is by **vaccination**, which is intended to prevent outbreaks by building immunity to a virus or virus family (**Figure 21.14**). **Vaccines** may be prepared using live viruses, killed viruses, or molecular subunits of the virus. Note that the killed viral vaccines and subunit viruses are both incapable of causing disease, nor is there any valid evidence that vaccinations contribute to autism.

Live viral vaccines are designed in the laboratory to cause few symptoms in recipients while giving them protective immunity against future infections. Polio was one disease that represented a milestone in the use of vaccines. Mass immunization campaigns in the 1950s (killed vaccine) and 1960s (live vaccine) significantly reduced the incidence of the disease, which caused muscle paralysis in children and generated a great amount of fear in the general population when regional epidemics occurred. The success of the polio vaccine paved the way for the routine dispensation of childhood vaccines against measles, mumps, rubella, chickenpox, and other diseases.

The issue with using live vaccines (which are usually more effective than killed vaccines), is the low but significant danger that these viruses will revert to their disease-causing form by **back mutations**. Live vaccines are usually made by **attenuating** (weakening) the “wild-type” (disease-causing) virus by growing it in the laboratory in tissues or at temperatures different from what the virus is accustomed to in the host. Adaptations to these new cells or temperatures induce mutations in the genomes of the virus, allowing it to grow better in the laboratory while inhibiting its ability to cause disease when reintroduced into conditions found in the host. These attenuated viruses thus still cause infection, but they do not grow very well, allowing the immune response to develop in time to prevent major disease. Back mutations occur when the vaccine undergoes mutations in the host such that it readapts to the host and can again cause disease, which can then be spread to other humans in an epidemic. This type of scenario happened as recently as 2007 in Nigeria where mutations in a polio vaccine led to an epidemic of polio in that country.

Some vaccines are in continuous development because certain viruses, such as influenza and HIV, have a high mutation rate compared to that of other viruses and normal host cells. With influenza, mutations in the surface molecules of the virus help the organism evade the protective immunity that may have been obtained in a previous influenza season, making it necessary for individuals to get vaccinated every year. Other viruses,

such as those that cause the childhood diseases measles, mumps, and rubella, mutate so infrequently that the same vaccine is used year after year.

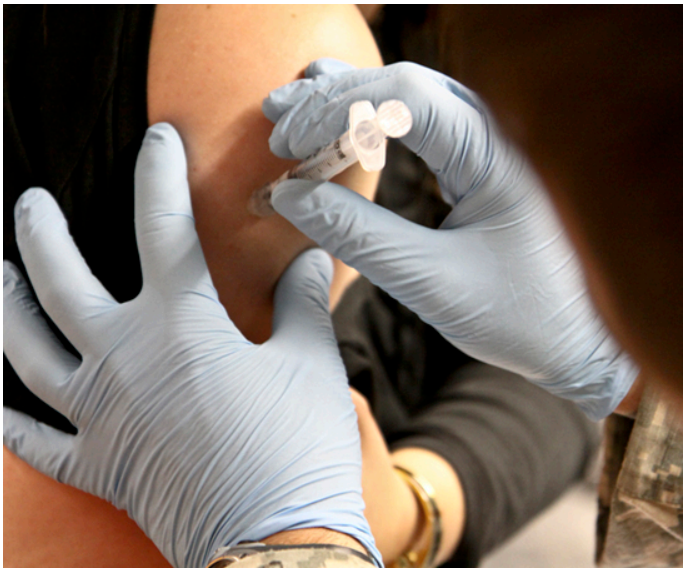


Figure 21.14 Vaccinations are designed to boost immunity to a virus to prevent infection. (credit: USACE Europe District)

LINK TO LEARNING

Watch this NOVA **video (http://openstaxcollege.org/l/1918_flu)** to learn how microbiologists are attempting to replicate the deadly 1918 Spanish influenza virus so they can understand more about virology.

Vaccines and Antiviral Drugs for Treatment

In some cases, vaccines can be used to treat an active viral infection. The concept behind this is that by giving the vaccine, immunity is boosted without adding more disease-causing virus. In the case of *rabies*, a fatal neurological disease transmitted via the saliva of rabies virus-infected animals, the progression of the disease from the time of the animal bite to the time it enters the central nervous system may be two weeks or longer. This is enough time to vaccinate individuals who suspect that they have been bitten by a rabid animal, and their boosted immune response is sufficient to prevent the virus from entering nervous tissue. Thus, the potentially fatal neurological consequences of the disease are averted, and the individual only has to recover from the infected bite. This approach is also being used for the treatment of Ebola, one of the fastest and most deadly viruses on Earth. Transmitted by bats and great apes, this disease can cause death in 70 to 90 percent of infected humans within two weeks. Using newly developed vaccines that *boost the immune response* in this way, there is hope that affected individuals will be better able to control the virus, potentially saving a greater percentage of infected persons from a rapid and very painful death.

Another way of treating viral infections is the use of antiviral drugs. Because viruses use the resources of the host cell for replication and the production of new virus proteins, it is difficult to block their activities without damaging the host. However, we do have some effective antiviral drugs, such as those used to treat HIV and influenza. Some antiviral drugs are specific for a particular virus and others have been used to control and reduce symptoms for a wide variety of viral diseases. For most viruses, these drugs can inhibit the virus by blocking the actions of one or more of its proteins. *It is important to note that the targeted proteins be encoded by viral genes and that these molecules are not present in a healthy host cell.* In this way, viral growth is inhibited without damaging the host.

Antivirals have been developed to treat genital herpes (herpes simplex II) and influenza. For genital herpes,

drugs such as acyclovir can reduce the number and duration of episodes of active viral disease, during which patients develop viral lesions in their skin cells. As the virus remains latent in nervous tissue of the body for life, this drug is not curative but can make the symptoms of the disease more manageable. For influenza, drugs like Tamiflu (oseltamivir) (**Figure 21.15**) can reduce the duration of "flu" symptoms by one or two days, but the drug does not prevent symptoms entirely. Tamiflu works by inhibiting an enzyme (viral neuraminidase) that allows new virions to leave their infected cells. Thus, Tamiflu inhibits the spread of virus from infected to uninfected cells. Other antiviral drugs, such as Ribavirin, have been used to treat a variety of viral infections, although its mechanism of action against certain viruses remains unclear.

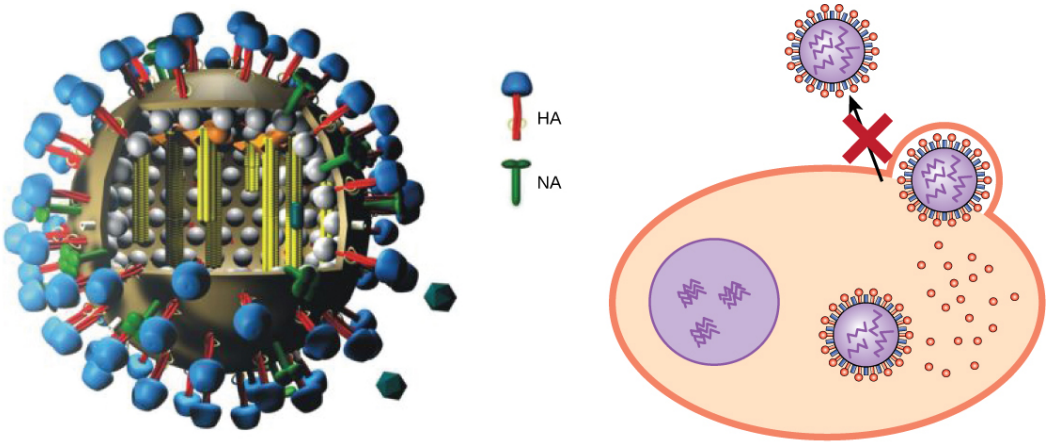


Figure 21.15 Action of an antiviral drug. (a) Tamiflu inhibits a viral enzyme called neuraminidase (NA) found in the influenza viral envelope. (b) Neuraminidase cleaves the connection between viral hemagglutinin (HA), also found in the viral envelope, and glycoproteins on the host cell surface. Inhibition of neuraminidase prevents the virus from detaching from the host cell, thereby blocking further infection. (credit a: modification of work by M. Eickmann)

By far, the most successful use of antivirals has been in the treatment of the retrovirus HIV, which causes a disease that, if untreated, is usually fatal within 10 to 12 years after infection. Anti-HIV drugs have been able to control viral replication to the point that individuals receiving these drugs survive for a significantly longer time than the untreated.

Anti-HIV drugs inhibit viral replication at many different phases of the HIV replicative cycle (**Figure 21.16**). Drugs have been developed that inhibit the fusion of the HIV viral envelope with the plasma membrane of the host cell (fusion inhibitors), the conversion of its RNA genome into double-stranded DNA (reverse transcriptase inhibitors, like AZT), the integration of the viral DNA into the host genome (integrase inhibitors), and the processing of viral proteins (protease inhibitors).

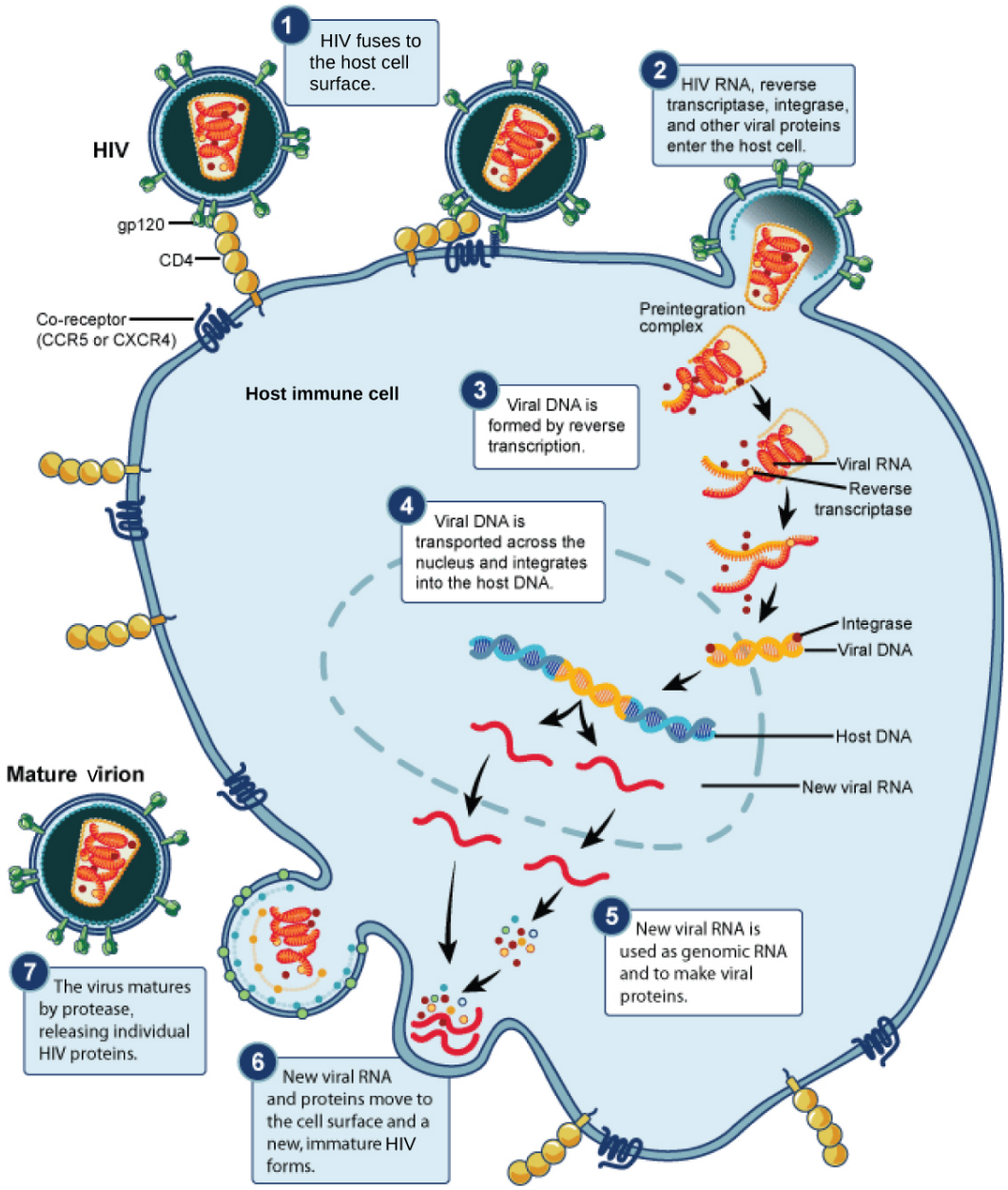


Figure 21.16 Life cycle of HIV. HIV, an enveloped, icosahedral virus, attaches to the CD4 receptor of an immune cell and fuses with the cell membrane. Viral contents are released into the cell, where viral enzymes convert the single-stranded RNA genome into DNA and incorporate it into the host genome. (credit: NIAID, NIH)

Unfortunately, when any of these drugs are used individually, the high mutation rate of the virus allows it to easily and rapidly develop resistance to the drug, limiting the drug's effectiveness. The breakthrough in the treatment of HIV was the development of HAART, *highly active anti-retroviral therapy*, which involves a mixture of different drugs, sometimes called a drug "cocktail." By attacking the virus at different stages of its replicative cycle, it is much more difficult for the virus to develop resistance to multiple drugs at the same time. Still, even with the use of combination HAART therapy, there is concern that, over time, the virus will develop resistance to this therapy. Thus, new anti-HIV drugs are constantly being developed with the hope of continuing the battle against this highly fatal virus.

everyday CONNECTION

Applied Virology:

The study of viruses has led to the development of a variety of new ways to treat non-viral diseases. Viruses have been used in **gene therapy**. Gene therapy is used to treat genetic diseases such as severe combined immunodeficiency (SCID), a heritable, recessive disease in which children are born with severely compromised immune systems. One common type of SCID is due to the lack of an enzyme, adenosine deaminase (ADA), which breaks down purine bases. To treat this disease by gene therapy, bone marrow cells are taken from a SCID patient and the ADA gene is inserted. This is where viruses come in, and their use relies on their ability to penetrate living cells and bring genes in with them. Viruses such as adenovirus, an upper-respiratory human virus, are modified by the addition of the ADA gene, and the virus then transports this gene into the cell. The modified cells, now capable of making ADA, are then given back to the patients in the hope of curing them. Gene therapy using viruses as carriers of genes (viral vectors), although still experimental, holds promise for the treatment of many genetic diseases. Still, many technological problems need to be solved for this approach to be a viable method for treating genetic disease.

Another medical use for viruses relies on their specificity and ability to kill the cells they infect. **Oncolytic viruses** are engineered in the laboratory specifically to attack and kill cancer cells. A genetically modified adenovirus known as H101 has been used since 2005 in clinical trials in China to treat head and neck cancers. The results have been promising, with a greater short-term response rate to the combination of chemotherapy and viral therapy than to chemotherapy treatment alone. This ongoing research may herald the beginning of a new age of cancer therapy, where viruses are engineered to find and specifically kill cancer cells, regardless of where in the body they may have spread.

A third use of viruses in medicine relies on their specificity and involves using bacteriophages in the treatment of bacterial infections. Bacterial diseases have been treated with antibiotics since the 1940s. However, over time, many bacteria have evolved resistance to antibiotics. A good example is methicillin-resistant *Staphylococcus aureus* (MRSA, pronounced “mersa”), an infection commonly acquired in hospitals. This bacterium is resistant to a variety of antibiotics, making it difficult to treat. The use of bacteriophages specific for such bacteria would bypass their resistance to antibiotics and specifically kill them. Although **phage therapy** is in use in the Republic of Georgia to treat antibiotic-resistant bacteria, its use to treat human diseases has not been approved in most countries. However, the safety of the treatment was confirmed in the United States when the U.S. Food and Drug Administration approved spraying meats with bacteriophages to destroy the food pathogen *Listeria.* As more and more antibiotic-resistant strains of bacteria evolve, the use of bacteriophages might be a potential solution to the problem, and the development of phage therapy is of much interest to researchers worldwide.

21.4 | Other Acellular Entities: Prions and Viroids

By the end of this section, you will be able to do the following:

- Describe prions and their basic properties
- Define viroids and their targets of infection

Prions and viroids are **pathogens** (agents with the ability to cause disease) that have simpler structures than viruses but, in the case of prions, still can produce deadly diseases.

Prions

Prions, so-called because they are proteinaceous, are infectious particles—smaller than viruses—that contain no nucleic acids (neither DNA nor RNA). Historically, the idea of an infectious agent that did not use nucleic acids was considered impossible, but pioneering work by Nobel Prize-winning biologist Stanley Prusiner has convinced the majority of biologists that such agents do indeed exist.

Fatal neurodegenerative diseases, such as kuru in humans and bovine spongiform encephalopathy (BSE) in cattle (commonly known as “mad cow disease”) were shown to be transmitted by prions. The disease was spread by the consumption of meat, nervous tissue, or internal organs between members of the same species. Kuru, native to humans in Papua New Guinea, was spread from human to human via ritualistic cannibalism. BSE, originally detected in the United Kingdom, was spread between cattle by the practice of including cattle nervous tissue in feed for other cattle. Individuals with kuru and BSE show symptoms of loss of motor control and unusual behaviors, such as uncontrolled bursts of laughter with kuru, followed by death. Kuru was controlled by inducing the population to abandon its ritualistic cannibalism.

On the other hand, BSE was initially thought to only affect cattle. Cattle dying of the disease were shown to have developed lesions or “holes” in the brain, causing the brain tissue to resemble a sponge. Later on in the outbreak, however, it was shown that a similar encephalopathy in humans, known as variant Creutzfeldt-Jakob disease (CJD), could be acquired from eating beef from animals infected with BSE, sparking bans by various countries on the importation of British beef and causing considerable economic damage to the British beef industry (**Figure 21.17**). BSE still exists in various areas, and although a rare disease, individuals that acquire CJD are difficult to treat. The disease can be spread from human to human by blood, so many countries have banned blood donation from regions associated with BSE.

The cause of spongiform encephalopathies, such as kuru and BSE, is an infectious structural variant of a normal cellular protein called PrP (prion protein). It is this variant that constitutes the prion particle. PrP exists in two forms, **PrP^{C}**, the normal form of the protein, and **PrP^{SC}**, the infectious form. Once introduced into the body, the PrP^{SC} contained within the prion binds to PrP^{C} and converts it to PrP^{SC}. This leads to an exponential increase of the PrP^{SC} protein, which aggregates. PrP^{SC} is folded abnormally, and the resulting conformation (shape) is directly responsible for the lesions seen in the brains of infected cattle. Thus, although not without some detractors among scientists, the prion seems likely to be an entirely new form of infectious agent, the first one found whose transmission is not reliant upon genes made of DNA or RNA.

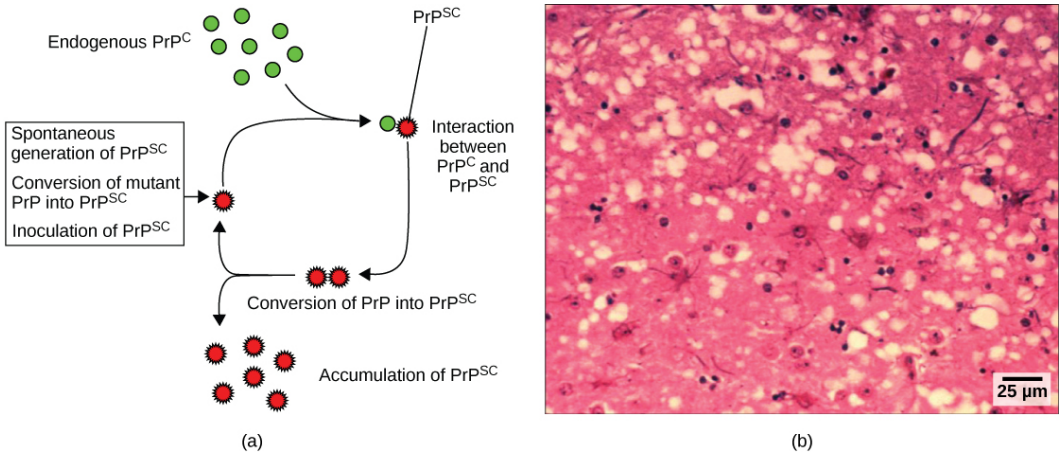


Figure 21.17 Mad Cow Disease in humans. (a) Endogenous normal prion protein (PrP^{C}) is converted into the disease-causing form (PrP^{SC}) when it encounters this variant form of the protein. PrP^{SC} may arise spontaneously in brain tissue, especially if a mutant form of the protein is present, or it may occur via the spread of misfolded prions consumed in food into brain tissue. (b) This prion-infected brain tissue, visualized using light microscopy, shows the vacuoles that give it a spongy texture, typical of transmissible spongiform encephalopathies. (credit b: modification of work by Dr. Al Jenny, USDA APHIS; scale-bar data from Matt Russell)

Viroids

Viroids are plant pathogens: small, single-stranded, circular RNA particles that are much simpler than a virus. They do not have a capsid or outer envelope, but like viruses can reproduce only within a host cell. Viroids do not, however, manufacture any proteins, and they only produce a single, specific RNA molecule. Human diseases caused by viroids have yet to be identified.

Viroids are known to infect plants (**Figure 21.18**) and are responsible for crop failures and the loss of millions of dollars in agricultural revenue each year. Some of the plants they infect include potatoes, cucumbers, tomatoes, chrysanthemums, avocados, and coconut palms.

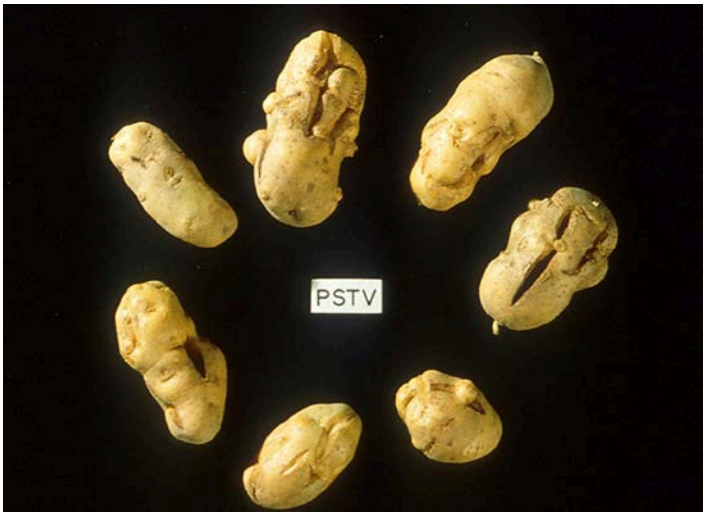


Figure 21.18 These potatoes have been infected by the potato spindle tuber viroid (PSTV), which is typically spread when infected knives are used to cut healthy potatoes, which are then planted. (credit: Pamela Roberts, University of Florida Institute of Food and Agricultural Sciences, USDA ARS)

career CONNECTION

Virologist

Virology is the study of viruses, and a virologist is an individual trained in this discipline. Training in virology can lead to many different career paths. Virologists are actively involved in academic research and teaching in colleges and medical schools. Some virologists treat patients or are involved in the generation and production of vaccines. They might participate in epidemiologic studies (**Figure 21.19**) or become science writers, to name just a few possible careers.

Figure 21.19 This virologist is engaged in fieldwork, sampling eggs from this nest for avian influenza. (credit: Don Becker, USGS EROS, U.S. Fish and Wildlife Service)

If you think you may be interested in a career in virology, find a mentor in the field. Many large medical centers have departments of virology, and smaller hospitals usually have virology labs within their microbiology departments. Volunteer in a virology lab for a semester or work in one over the summer. Discussing the profession and getting a first-hand look at the work will help you decide whether a career in virology is right for you. The American Society of Virology's **website (http://openstaxcollege.org/l/asv)** is a good resource for information regarding training and careers in virology.

KEY TERMS

acellular lacking cells

acute disease disease where the symptoms rise and fall within a short period of time

asymptomatic disease disease where there are no symptoms and the individual is unaware of being infected unless lab tests are performed

attenuation weakening of a virus during vaccine development

AZT anti-HIV drug that inhibits the viral enzyme reverse transcriptase

back mutation when a live virus vaccine reverts back to it disease-causing phenotype

bacteriophage virus that infects bacteria

budding method of exit from the cell used in certain animal viruses, where virions leave the cell individually by capturing a piece of the host plasma membrane

capsid protein coating of the viral core

capsomere protein subunit that makes up the capsid

cell necrosis cell death

chronic infection describes when the virus persists in the body for a long period of time

cytopathic causing cell damage

envelope lipid bilayer that encircles some viruses

fusion method of entry by some enveloped viruses, where the viral envelope fuses with the plasma membrane of the host cell

gall appearance of a plant tumor

gene therapy treatment of genetic disease by adding genes, using viruses to carry the new genes inside the cell

group I virus virus with a dsDNA genome

group II virus virus with an ssDNA genome

group III virus virus with a dsRNA genome

group IV virus virus with an ssRNA genome with positive polarity

group V virus virus with an ssRNA genome with negative polarity

group VI virus virus with an ssRNA genome converted into dsDNA by reverse transcriptase

group VII virus virus with a single-stranded mRNA converted into dsDNA for genome replication

horizontal transmission transmission of a disease between unrelated individuals

hyperplasia abnormally high cell growth and division

hypoplasia abnormally low cell growth and division

intermittent symptom symptom that occurs periodically

latency virus that remains in the body for a long period of time but only causes intermittent symptoms