

Chapter 34 Viruses

I. What Are Viruses?

- A. Viruses are obligate parasites that are not cells or organisms.
- B. Viruses are called particles or agents.
- C. Viruses have a genome, but must use the ATP and carbon compounds of their host to copy and translate their genome. (**Table 35.1**)
- D. Nearly all known organisms are parasitized by at least one kind of virus.
 1. Virtually every human tissue and organ system can be infected. (**Fig. 35.1**)
 2. Bacteria are infected by bacteriophages.

II. Why Do Biologists Study Viruses?

- A. Recent Viral Epidemics in Humans
 1. Epidemics describe diseases that infect a large number of people at one time.
 2. Measles, smallpox, and other viral diseases were epidemics in Native American tribes; these epidemics were triggered by the immigration of European settlers.
 3. In 1918-1919, the Spanish flu killed more people than died in World War I.
 - a. The flu is a respiratory disease.
 - b. The Spanish flu was highly virulent and would suffocate victims within hours of the first symptom.
- B. Current Viral Epidemics in Humans
 1. It is believed that the AIDS epidemic will eventually surpass the Spanish flu epidemic in regard to numbers of people affected.
 - a. The human immunodeficiency virus (HIV) causes acquired immune deficiency syndrome. (**Fig. 35.2**)
 - b. HIV is currently the single most studied virus in the world.
 2. How does HIV cause disease?
 - a. HIV infects helper T cells and macrophages of the immune system.
 - b. Helper T cells and macrophages usually help combat bacterial and viral infections.
 - c. But, with HIV infection, these immune cells die when the virus replicates and new viral particles lyse the cell to go infect other cells.
 - d. This decreases the number of helper T cells, making the immune system deficient in its ability to fight other infections. (**Fig. 35.3**)
 - e. AIDS occurs when there are too few helper T cells to fight other infections.
 - f. AIDS victims usually die of secondary infections or diseases such as pneumonia or cancer.
 3. What is the scope of the AIDS epidemic?
 - a. AIDS has already killed 25 million people worldwide.
 - b. In east and central Africa, the epidemic is at its worst. (**Fig. 35.4**)
 - c. As many as 42 million people worldwide may be infected with HIV.
 - d. The epidemic is on the rise in southern and eastern Asia.

III. How Do Biologists Study Viruses?

- A. The Research Goals
 1. To develop vaccines that will help host cells fight a viral infection.
 2. To develop antiviral drugs that will stop the virus from replicating once the host is infected.
- B. Nanobiology

1. Viruses are extremely small: 50-100 nm. (**Fig. 35.5**)
 2. Viruses can be isolated to confirm that they cause a certain disease.
 - a. Infected cells are grown in culture.
 - b. The cultured cells and viruses are passed over a filter that will allow the virus through, but trap cells.
 - c. The resulting filtrate has the isolated viral particles.
 - d. Scientists can then use the isolated virus to test their virulence using Koch's postulates.
 3. Viruses come in a variety of shapes. (**Fig. 35.6**)
 4. Two basic viral structures have been identified using electron microscopy.
 - a. Nonenveloped or naked viruses are simply a genome enclosed by a protein shell called a capsid. (**Fig. 35.7a**)
 - b. Enveloped viruses consist of a genome enclosed in a capsid that is all surrounded by a phospholipid bilayer called an envelope.
 - (1) The envelope is derived from the host's plasma membrane.
 - (2) HIV is an enveloped virus. (**Fig. 35.7b**)
 5. Understanding viral morphology and replication cycles allows scientists to attempt to develop a vaccine. (**Box 35.1, Fig. 35.8**)
 - a. Vaccines prime the host's immune system, so that it will be prepared in the event of an infection.
 - b. Currently biologists have not been able to make vaccines to many common viruses because they mutate too quickly and use too much of the host-cell machinery.
- C. How do viruses replicate once they've infected their host?
1. Some viruses show a lytic replication cycle. (**Fig. 35.8a**)
 - a. Once the virus has infected the cell, viral or host enzymes replicate the viral genome.
 - b. The host cell manufactures viral proteins.
 - c. New viral particles are built with these proteins.
 - d. The new particles break open or lyse the host cell, to go infect other cells.
 - e. The viral exit usually kills the host cell.
 2. Other viruses show a lysogenic replication cycle. (**Fig. 35.9b**)
 - a. Once the virus has infected the cell, its genome becomes incorporated into the host cell's chromosomes.
 - b. The viral genome is replicated when the host's genome is replicated in S phase preceding mitosis.
 - c. During the lysogenic cycle, the virus is quiescent; it is allowing the host cell to replicate its genome and pass it to subsequent generations of cells.
 - d. If the host cell becomes damaged, or begins to starve, the virus may switch to a lytic replication cycle and assemble new viral particles that can exit that cell to infect others.
 - e. Many bacteriophages show lysogeny.
 - (1) This type of replication cycle allows the virus to take advantage of the bacteria's rapid division.
 - (2) The switch to lytic growth allows the virus to continue to replicate even if its host stops dividing.
 - f. Lysogenic infections cannot be treated with drugs because the virus is dormant.
- D. Analyzing the Phases of the Lytic Cycle in Order to Develop Antiviral Drugs
1. How do viruses enter a cell?
 - a. Plant viruses enter cells by following sucking insects that have disrupted the cell wall.
 - b. Viruses enter bacterial and animal cells by binding to cell-surface molecules.
 - (1) After binding, naked viruses simply dump their genome into the cell, leaving the capsid at the cell surface.
 - (2) When an enveloped virus binds, the entire capsid enters the cell.
 - c. What cell-surface molecules do viruses use?

- (1) Researchers found that people with AIDS lacked T cells with the CD4 surface protein.
 - (2) This led to the discovery that HIV uses CD4 as a "doorknob" to enter cells.
 - (3) If CD4 is blocked, can HIV still enter cells? (**Fig. 35.10**)
 - (a) No, antibodies to CD4 blocked HIV infection in culture.
 - (b) Antibodies for many other surface proteins did not block HIV entry into cells in culture.
 - (4) Subsequent research showed that the virus binds to another protein in addition to CD4.
 - (a) This protein is called a co-receptor.
 - (b) The search is on for compounds that will block the co-receptor.
 - (5) When the virus binds to CD4 and the co-receptor, the viral membrane and the host membrane fuse, and the viral contents enter the cell.
2. How do viruses copy their genomes?
 - a. Many viruses use their own DNA polymerase and the host's nucleotides to replicate their genome.
 - b. Some viruses have RNA genomes.
 - (1) Some of these viruses replicate their genome via an enzyme called RNA replicase.
 - (2) Other RNA viruses have a special enzyme called reverse transcriptase, an RNA polymerase that transcribes RNA into complementary DNA (cDNA).
 - (a) These are called retroviruses.
 - (b) HIV is a retrovirus.
 - (c) The first HIV drugs were reverse transcriptase inhibitors.
 - (d) After reverse transcriptase makes the cDNA, it is incorporated into the host's genome, at which point the virus is lysogenic.
 - (e) After some time, the virus will become lytic in order to infect more cells.
 3. Producing viral proteins
 - a. Ribosomes lack the translational machinery so must use the host's.
 - b. Viral envelope proteins are made in the same way that the host's membrane proteins are made. (**Fig. 35.12a**)
 - (1) Viral mRNAs are translated on ribosomes bound to the endoplasmic reticulum.
 - (2) Proteins are processed through the ER and Golgi apparatus and delivered to the plasma membrane.
 - (3) Once at the plasma membrane, the envelope proteins are assembled into the envelope.
 - c. Viral capsid and inner core proteins are translated on free ribosomes. (**Fig. 35.12b**)
 - (1) Long viral polypeptides are cut by viral proteases into smaller, functional proteins.
 - (2) These proteins are then assembled into the viral capsid and inner core.
 - (3) Protease inhibitors are a major class of HIV drug. (**Box 35.2**)
 - (a) X-ray crystallographic studies elucidated the structure of HIV protease. (**Fig. 35.13a**)
 - (b) Scientists searched for molecules that would fit into the protease active site. (**Fig. 35.13b**)
 4. How are viruses transmitted to new hosts?
 - a. Viruses leave a cell in one of two ways.
 - (1) Enveloped viruses bud off from the host cell, taking some host-cell membrane with them along with the newly synthesized envelope proteins. (**Fig. 35.15a**)
 - (2) Nonenveloped or naked viruses burst from the cell, lysing it in the process. (**Fig. 35.15b**)
 - b. In multicellular organisms, the new virions travel through the host via the bloodstream or lymphatic system.
 - (1) If the virus meets a matching antibody, it is targeted for destruction by the immune system.

- (2) If the virus meets a new target cell, it binds to it and the replication cycle starts over again.
- c. Sneezing, coughing, and wiping runny noses allow viruses to leave their current host and infect a new host.
 - (1) Infecting new hosts increases the reproductive success of that virus.
 - (2) Natural selection favors viruses that can successfully replicate within their host and infect new hosts.
 - (3) Blocking viral transmission is a major public health campaign.
- d. In unicellular organisms, released particles can be transmitted to new hosts.

IV. What Themes Occur in the Diversification of Viruses?

A. The Nature of Viral Genetic Material (Table 35.2)

- 1. Some viruses break the central dogma.
 - a. In the 1950s researchers demonstrated that some viruses had RNA genomes.
 - b. This RNA was the infective agent, the genetic material of the virus.
- 2. Virus genomes can be DNA or RNA, single stranded or double stranded.
- 3. Three different variations of single-stranded viral genomes exist.
 - a. Positive-sense viruses have genomes that contain the same sequence of mRNA.
 - b. Negative-sense viruses have genomes that contain the complementary sequence to the mRNA.
 - c. Ambisense genomes have segments that are positive-sense and others that are negative-sense.
- 4. The number of genes in a viral genome varies from 3 to 343.

B. Where Did Viruses Come From?

- 1. The escaped-gene hypothesis
 - a. Many biologists believe that viruses are closely related to plasmids and transposable elements.
 - b. Many viruses are identical to plasmids except for their protein coat.
 - c. Escaped-gene hypothesis: Viral genomes descended from clusters of genes that escaped from bacterial or eukaryotic chromosomes long ago.
 - d. The escaped gene sets then took on a mobile, parasitic existence.
 - e. The escaped genes would have had to contain the genes needed to make the viral protein coat.
- 2. Other biologists hypothesize that viruses are derived from free-living bacteria.
 - a. These bacteria used to take up residence in eukaryotic cells.
 - b. These bacteria eventually lost the genes needed to make ATP and other macromolecules since they were able to get these things from their host.
 - c. As a result, these bacteria degenerated into viruses.
- 3. Neither hypothesis has been rigorously tested.

C. Emerging Viruses, Emerging Diseases

- 1. Emerging viruses are those that have switched from their traditional host species and recently are appearing in humans.
 - a. Hantavirus infected dozens of humans in the American Southwest in 1993.
 - b. In 1996, Ebola virus infection in the Congo suddenly infected 200 people, 75% of whom died.
- 2. Hantavirus and Ebola are examples of emerging diseases.
 - a. Emerging diseases are illnesses that have suddenly affected significant numbers of people.
 - b. Some scientists feel that HIV is an emerging virus because it originated in monkeys. (Box 35.3, Fig. 35.16)
- 3. Identifying an unknown virus and determining how it is transmitted
 - a. Doctors report cases to public health officials, who track the outbreak.
 - b. Public health officials identify the pathogen. Example: the hantavirus

- (1) Public health officials noticed the U.S. cases were similar to symptoms caused by the Asian Hantaan virus, which primarily infects rodents.
 - (2) About one-third of mice captured from homes of U.S. victims tested positive for a Hantaan-like virus.
 - (3) The mouse virus DNA was sequenced and was shown to be a new type of hantavirus.
 - (4) The sequences in the mouse virus matched the sequences in the unknown virus in the human victims.
- c. Public health officials then determine how the virus is transmitted.
- (1) An epidemic may occur if . . .
 - (a) A virus that normally parasitizes one species suddenly begins parasitizing humans.
 - (b) Spread between humans is efficient.
 - (2) If transmission takes place only between the normal host and humans, and does not occur between humans, rates of infection are likely to stay low.
 - (3) Detective work is required to determine how a virus is transmitted:
 - (a) Patients are interviewed about their activities and movements.
 - (b) In the hantavirus outbreak, few individuals had contact with each other, suggesting that the spread was not from human to human.
 - (c) Ebola virus was clearly transmitted between humans because many health care workers were infected, and infection was due to contact with bodily fluids from an infected person.

V. Key Lineages of Viruses

A. Double-Stranded DNA (dsDNA) Viruses (Fig. 35.17)

1. Genetic material: Linear or circular dsDNA
2. Host species:
 - a. Almost anything except land plants.
 - b. T and I bacteriophages infect bacteria.
 - c. Pox, herpesviruses and denoviruses infect humans.
3. Replication cycle:
 - a. Viral genes must enter the nucleus to be replicated.
 - b. Viral genes can be replicated only during S phase.
 - c. Therefore, must infect an actively dividing cell to survive.

B. RNA Reverse-Transcribing Viruses (retroviruses) (Fig. 35.18)

1. Genetic material: Diploid, because they have two copies of their single-stranded RNA genome
2. Host species:
 - a. Only vertebrates
 - b. HIV, Rous sarcoma virus, murine leukemia virus
3. Replication cycle:
 - a. Use reverse transcriptase to make a cDNA of their genome
 - b. The cDNA enters the nucleus and becomes part of the host's chromosome with the help of viral integrase.
 - c. The virus may be lysogenic for a time, but will switch to lytic growth to make more viral particles.

C. Double-Stranded RNA (dsRNA) Viruses (Fig. 35.19)

1. Genetic material: Up to 12 dsRNA molecules per genome
2. Host species:
 - a. Fungi, land plants, insects, vertebrates, and bacteria
 - b. These viruses can devastate rice, corn, and sugarcane crops.
3. Replication cycle:

- a. Once in the cytoplasm of the host cell, the viral dsRNA serves as a template for transcription.
 - b. Transcribed ssRNA molecules are used for the translation of viral proteins.
 - c. Viral enzymes then make the ssRNA double stranded to replicate the genome.
- D. **Negative-Sense Single-Stranded RNA Viruses (Fig. 35.20)**
1. Genetic material:
 - a. The negative-sense ssRNA is complementary to the viral mRNA.
 - b. The ssRNA genome must be transcribed into mRNA and translated into protein.
 2. Host species:
 - a. The viruses that cause the flu, mumps, or measles are negative-sense ssRNA viruses.
 - b. Ebola, hanta, and rabies also belong to this group.
 3. Replication cycle:
 - a. Once inside the host's cells, viral RNA polymerase transcribes the genome into mRNA.
 - b. The viral mRNA is also used as a template for the next generation of the ssRNA genome.
- E. **Positive-Sense Single-Stranded RNA Viruses (Fig. 35.21)**
1. Genetic material:
 - a. The positive-sense RNA genome serves as mRNA, so transcription is not necessary.
 - b. ssRNAs are translated directly into proteins.
 2. Host species:
 - a. Mostly plants, but also bacteria, fungi, and animals
 - b. Plant strains are often called spotted, chlorotic, necrotic, or mosaic viruses.
 - c. Colds, polio, and hepatitis A, C, and E are caused by these viruses.
 3. Replication cycle:
 - a. Once in the host's cells, the ssRNA is translated directly into protein.
 - b. Viral enzymes then replicate the viral genome.