8.7: Viruses

Learning Objectives

- Define viruses and understand how they infect and multiply, including reverse transcription.
- Understand the basic structural features, infection ways, and treatment of two viral infections, including covid-19 and HAIDS.

What is a virus?

> A **virus** is a tiny infectious microbe that consists of a genetic material (DNA or RNA) surrounded by a protein coat called the **capsid** that covers and protects the genetic material.

A single virus outside the cell that has genetic material and capsid surrounding it is also called a **virus particle** or a virion**.** As Figure $8.7.1$ illustrates, viruses have various shapes.

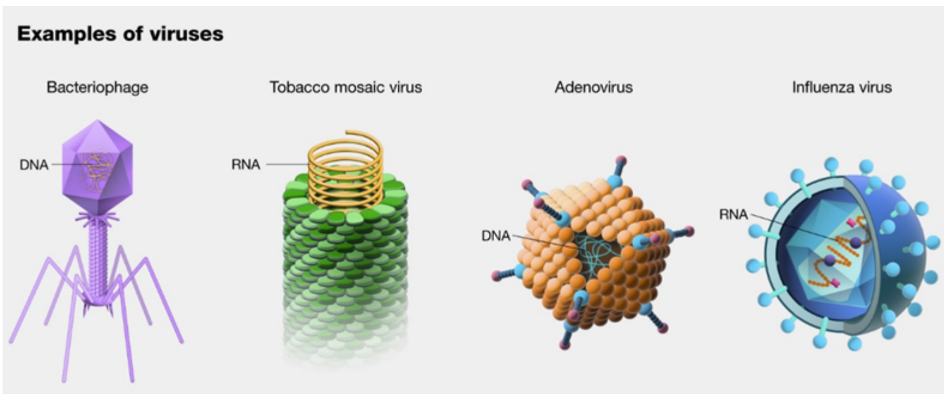


Figure $8.7.1$: Some examples of viruses having genetic material (DNA or RNA) surrounded by protein coats in various shapes. (Copyright; National Human Genome Research Institute, Public domain)

A virus does not have the machinery to replicate and synthesize proteins, so it injects its genetic material into a host cell and hijacks its nucleic acid and protein synthesis machinery to reproduce. Viruses infect nearly all life forms, including humans, animals, plants, bacteria, and fungi. Figure $8.7.2$. illustrates some of the human viral infections.

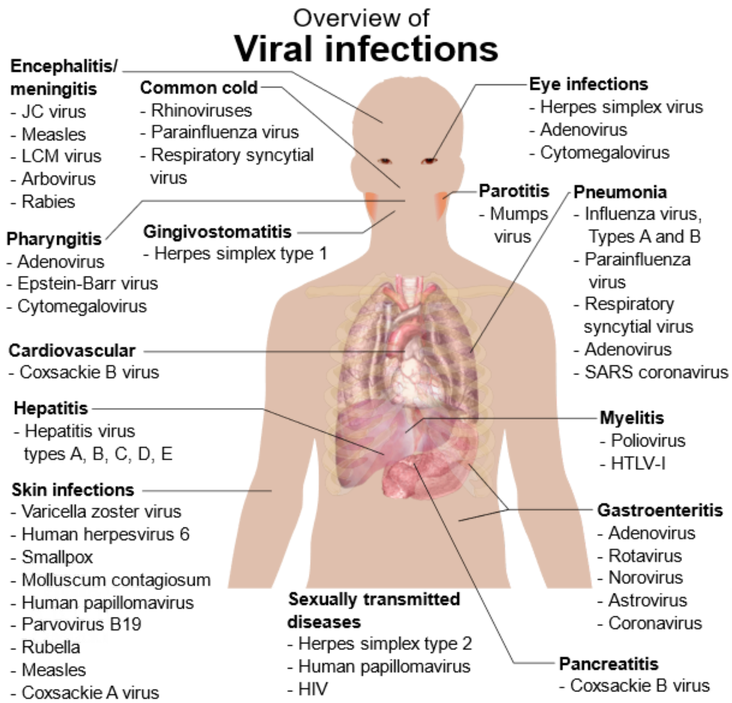


Figure 8.7.2: A simplified overview of human viral infections. (Copyright; Mikael Häggström, Public domain via Wikimedia Commons)

How do viruses infect and multiply?

The virus infection of cells begins with the attachment of the virus to the receptors at the host cell surface, followed by penetrating the cell membrane or cell wall. The protein coat (capsid) is removed, and the genetic material is injected into the host cell. The host cell replicates the viral DNA producing copies of it, and also translates it, making the proteins that the newborn virus needs. New viruses are assembled using the viral DNA and the protein coat produced by the host cell. They ultimately kill the host cell by bursting out of it in a lysis process, as illustrated in Figure 8.7.3. Some viruses take a portion of the host cell membrane to form an envelope around the capsid during lysis.

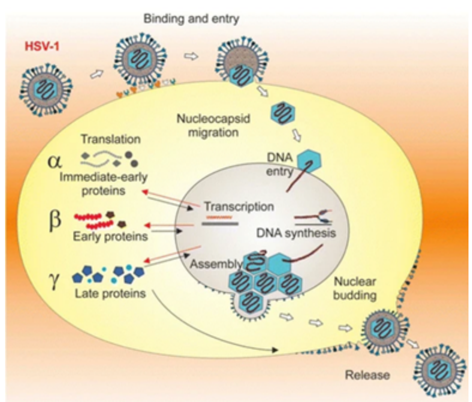


Figure 8.7.3: Illustration of virus multiplication using the host cell's machinery to replicate and translate its genetic material. (Copyright; Giovanna De Chiara, Maria Elena Marcocci, Rossella Sgarbanti, Livia Civitelli, Cristian Ripoli, Roberto Piacentini, Enrico Garaci, Claudio Grassi, Anna Teresa Palamara, CC BY 2.5, via Wikimedia Commons)

Reverse transcription

Viruses that contain viral RNA as their genetic material are called **retroviruses**. Once inside the host cell, the retroviruses first synthesize DNA using the viral RNA as a template, the reverse transcriptase enzyme in the virus, and the nucleotides in the host cell. The single DNA strand forms a double-strand viral DNA called a **provirus**. The provirus integrates with the DNA of the host cell using enzyme ligase, which is also present in the virus. Then the viral DNA directs the synthesis of viral RNA and the proteins needed to assemble new virus particles, as illustrated in Figure 8.7.4. Finally, the newborn virus particles burst out of the host cell and infect other cells.

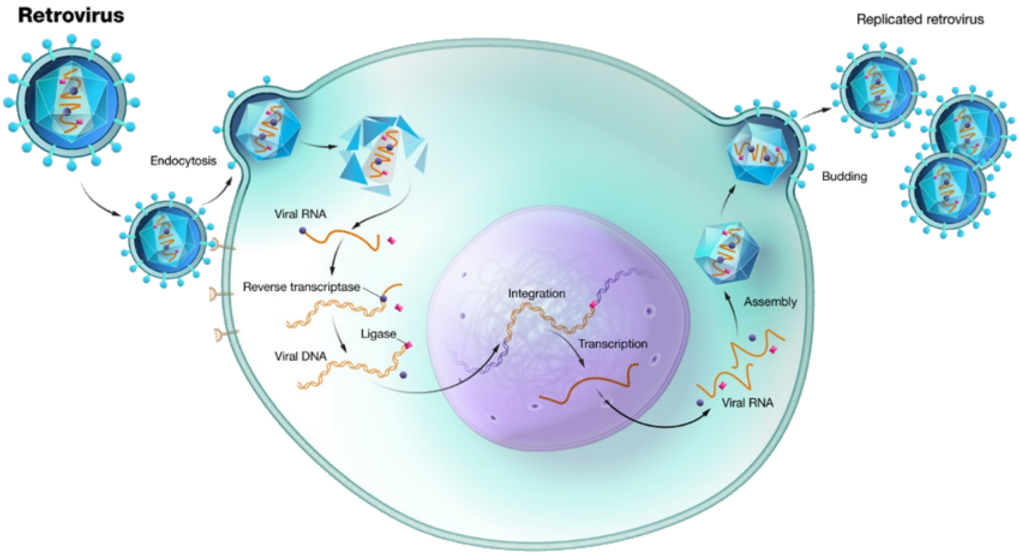


Figure 8.7.4: Illustration of reverse transcription of retroviruses. (Copyright; National Human Genome Research Institute, Public domain)

Examples of viral infections

Viruses are responsible for various human infections, as illustrated in Figure 8.7.2, and also in animals, plants, fungi, and bacteria. Two well-known example diseases caused by viruses, COVID-19 and AIDS, are described briefly here.

COVID-19

Coronavirus disease 2019, commonly known as COVID-19, is caused by SARS-CoV-2, which was discovered in Wuhan, China, in December 2019 and has spread worldwide. SARS-CoV2 is a member of a family of viruses that cause various diseases, from head or chest colds to more severe conditions like severe acute respiratory syndrome (SARS). SARS-CoV-2, also called coronavirus, spreads through droplets expelled or projected out of the mouth or nose of an infected person during breathing, coughing, sneezing, or speaking.

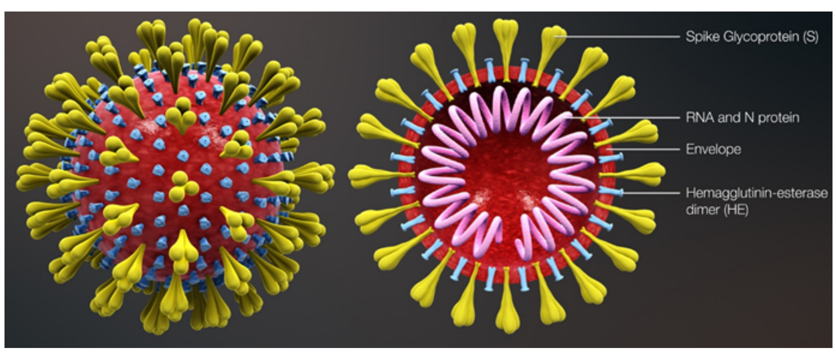


Figure 8.7.5: Images combined from a 3D medical animation depicting the coronavirus's shape and the cross-sectional view. The image shows the major elements, including the Spike S protein, HE protein, viral envelope, and helical RNA. (Copyright; https://www.scientificanimations.com, CC BY-SA 4.0, via Wikimedia Commons)

The common name coronavirus refers to the crown-shaped spike proteins sticking out of the virus, as illustrated in Figure 8.7.5. Coronavirus uses these spike proteins to attach to the host cells to infect them. Like other viruses, it replicates by reverse transcription inside the host cell, as illustrated in Figure 8.7.6. Genetic changes happen to the virus over time, resulting in variants that have different attributes regarding how fast the virus spreads or how severe the illness it causes. The virus and its variants are constantly monitored to update or improve its treatment as it changes over time.

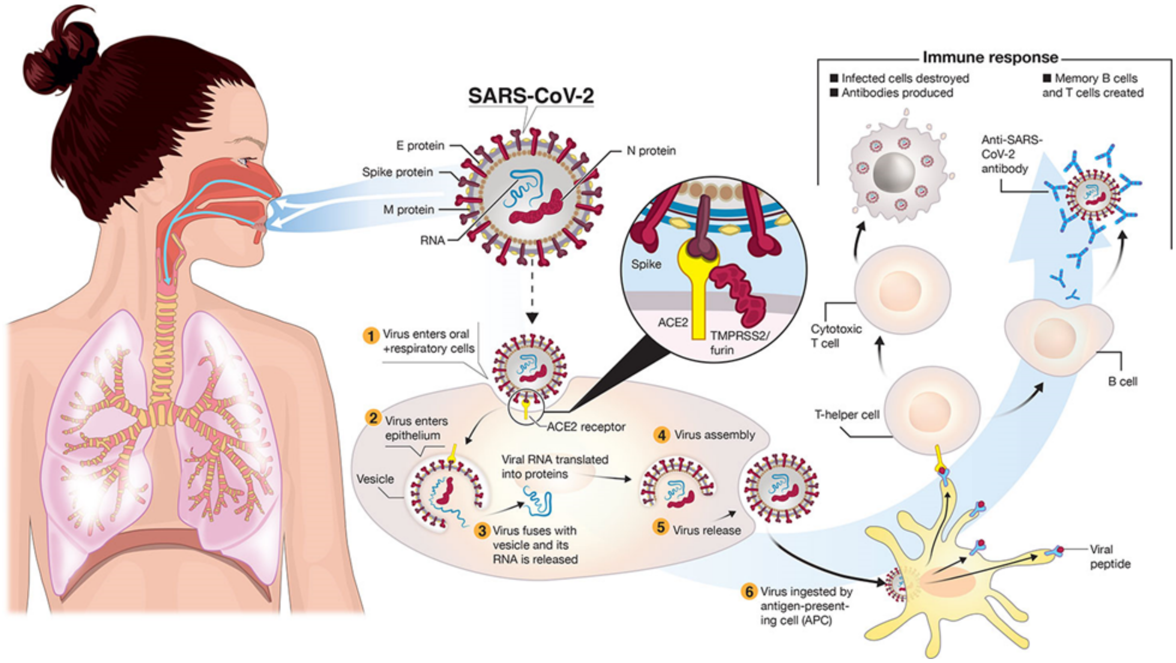


Figure 8.7.6: A simplified depiction of the virus's life cycle and potential immune responses elicited. (Copyright; Colin D. Funk, Craig Laferrière, and Ali Ardakani. Graphic by Ian Dennis - http://www.iandennisgraphics.com, CC BY 4.0, via Wikimedia Commons)

According to CDC, some antibodies can protect from coronavirus by targeting these spike proteins, but the best protection is vaccines. Several COVID-19 vaccines have been developed. The most common COVID-19 vaccines, i.e., Pfizer and Moderna vaccines, use either self-replicating RNA or mRNA, which cause the cells to produce SARS-CoV-2 spike protein. This process teaches the body's immune system how to identify and destroy the pathogen. RNA vaccines usually use modified nucleotides in mRNA.

AIDS

Acquired immunodeficiency syndrome (AIDS) is the late stage of the **human immunodeficiency virus** (HIV) when the virus badly damages the body's immune system. HIV infection is transmitted through sexual activity, blood transfusion, mother to child, etc., and primarily destroys $CD4^+$ T cells, components of the human immune system.

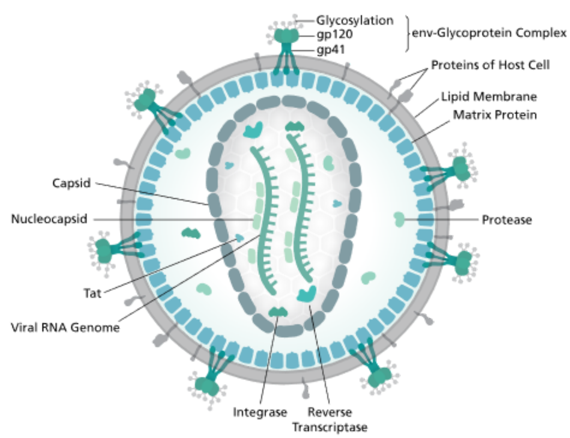


Figure 8.7.7: Diagram of the HIV virion. (Copyright; Thomas Splettstoesser (www.scistyle.com), CC BY-SA 4.0, via Wikimedia Commons)

HIV is a spherical retrovirus, as illustrated in Figure 8.7.7. It has two copies of RNA enclosed by a nucleocapsid and bound to enzymes needed for its development surrounded in a conical capsid. It also has an envelope of lipid bilayer taken from the cell membrane of the host cell. It also has proteins from the host cell, like glycoproteins, gp120 and gp41, that allow it to attach to the target cell to begin the infection. Destruction of $CD4^+$ T cells by HIV infection makes the person's immune system ineffective. It increases the risk of common diseases such as tuberculosis, tumors, pneumonia, skin cancer, etc., that are rare, as illustrated in Figure 8.7.8.

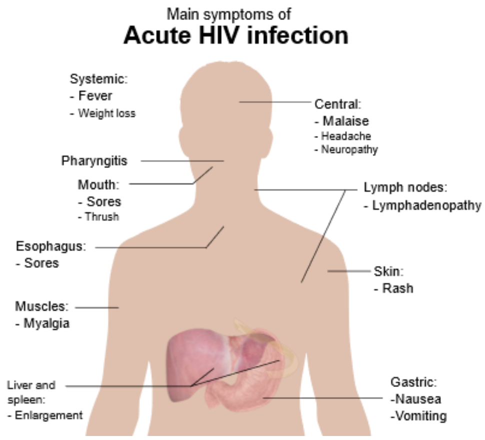
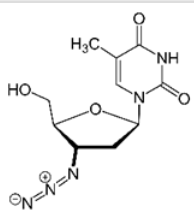
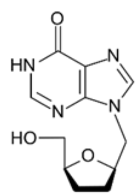
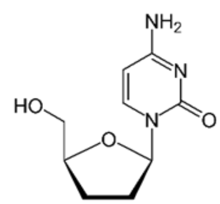
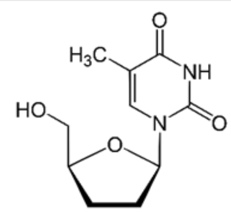


Figure 8.7.8: Main symptoms of acute HIV infection. (Copyright; Mikael Häggström, Public domain, via Wikimedia Commons)

There is no cure for AIDS, it stays for life long, but its progress can be slowed down by treatments that interfere with the life cycle of HIV at different stages. These include drugs that inhibit entry, reverse transcription, and translation. Entry inhibitors include enfuvirtide (Fuzeon) and maraviroc (Selzentry). Transcription inhibitors include nucleosides analogous to natural nucleosides, e.g., 3'-azido-2'deoxythymidine (AZT), 2',3'-dideoxyinosine (ddC), 2',3'-dideoxycytidine (ddC) and 2',3'-didehydro-2'3'-dideoxythymidine (d4T), illustrated below. They incorporate into viral DNA and prevent the formation of a sugar-phosphate backbone as they do not have $-OH$ groups at the 3' position of the sugar needed for this purpose. The translation inhibitors include saquinavir (Invirase), ritonavir (Norvir), fosamprenavir (Lexiva), etc.

 3'-azido-2'deoxythymidine (AZT)	 2',3'-dideoxyinosine (ddC)	 2',3'-dideoxycytidine (ddC)	 2',3'-didehydro-2'3'-dideoxythymidine (d4T)