Case Study Human Immunodeficiency Virus

Acquired immunodeficiency syndrome, or AIDS, describes a number of disorders associated with infection by the human immunodeficiency virus, or HIV. Two different types of HIV have been identified: HIV-1, discovered in 1981, evolved in chimpanzees before "jumping" species to infect humans; HIV-2, the less prevalent and less virulent form, was described in 1985.

For viruses to survive inside the body, they must be able to evade the defences of the human host. HIV does this in a unique manner—by invading the very cells whose function it is to protect the body from pathogens, or disease-causing agents. Instead of eliminating the virus, this stimulation of host defences actually helps HIV replicate and survive. Although the body does eventually mount an immune response to HIV, the virus is never fully contained, resulting in progressive disease and the development of AIDS. Individuals with HIV or AIDS have damaged immune systems. This condition makes them more susceptible to infections that humans with normal immune systems would be able to fight off. These are known as opportunistic infections. AIDS patients are also at higher risk of developing malignancies (cancers). As of early 2002, there was no cure for AIDS. However, advances in microbiology, genetics, and molecular biology have led to the development of more effective treatment for the disease, and work continues on the development of an HIV vaccine. Prevention of further transmission of HIV and improved treatment of existing cases are difficult challenges presently being tackled.

Unlike the chicken pox and flu viruses, HIV cannot be transmitted through the air, but it is found in human body fluids. It is spread primarily through direct sexual contact and by the introduction of blood or blood components into the bloodstream through blood transfusions or the sharing of needles or syringes for injection drug use. HIV can also be transmitted from infected mothers to their infants during pregnancy, at the time of birth, and through breastfeeding.

The structure of HIV is deceptively simple, consisting of an outer membrane made of proteins and lipids, and an inner coat made of protein that protects an RNA core. RNA encodes the genetic information of the virus. HIV attacks the immune system directly by selectively targeting and infecting helper T cells (**Figure 5**). Helper T cells act as guards against invading pathogens. Thus, HIV destroys the body's own defences, rendering it incapable of defeating other invading organisms.

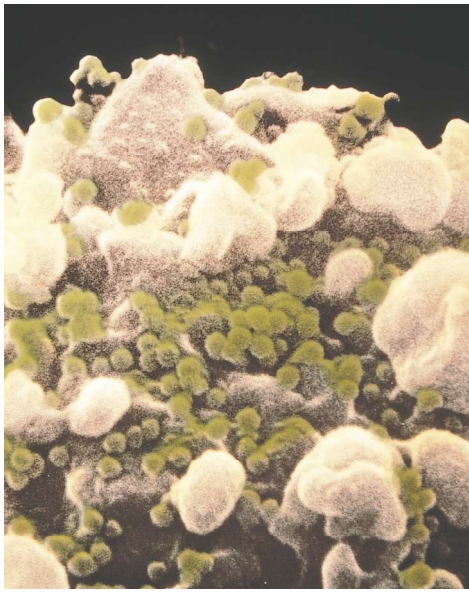


Figure 5
Colour-enhanced scanning electron micrograph of the helper T cell being attacked by HIV particles. The HIV particles appear in green.

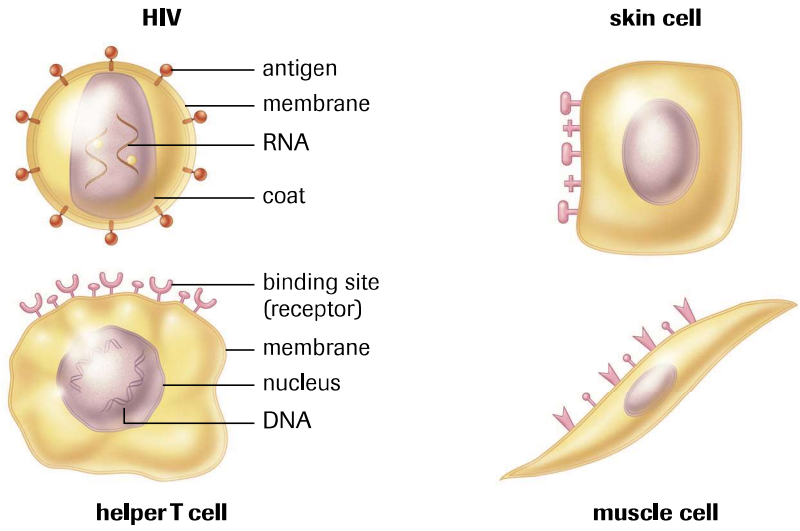


Figure 6
Outer membranes of the helper T cell, skin cell, and muscle cell. Note that the antigens on the HIV membrane are complementary to the binding sites of helper T cells, but not to those of other cells, such as skin or muscle cells.

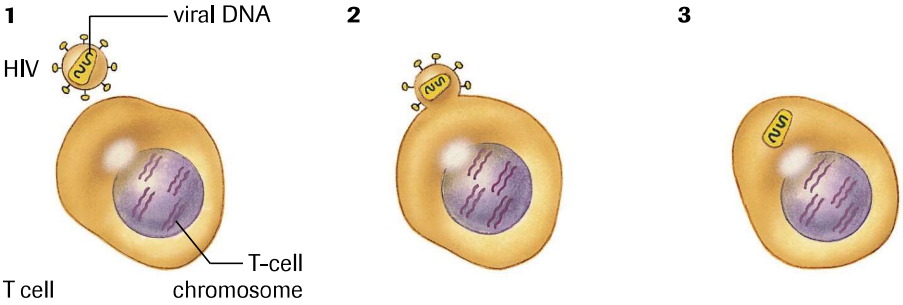


Figure 7
HIV entering the helper T cell

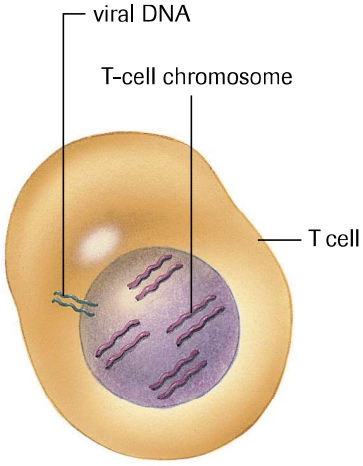


Figure 8
The RNA in HIV is converted into double-stranded DNA.

With infections other than HIV, proteins on the surface of helper T cells recognize foreign substances, which starts a chain of events to produce an immunologic attack and removal of the invading organism. HIV infects helper T cells by locking into specific binding sites on the cell surface, called receptors, much like a key into a lock (**Figure 6**, page 245). Once HIV binds to these sites, the viral and cell membranes fuse. The entire virus enters the cell, where it loses its coat and the RNA core is set free (**Figure 7**).

HIV belongs to a group of viruses known as retroviruses, whose genetic information is composed of RNA instead of DNA. The RNA of retroviruses encodes a special enzyme called reverse transcriptase, which converts the genetic message contained in RNA into a complementary copy of single-stranded DNA. The single-stranded DNA is then converted to double-stranded DNA by the same enzyme (**Figure 8**).

The newly constructed double-stranded viral DNA slips into the nucleus of the infected cell. Here it is spliced into the infected helper T cell's DNA, such that the instructions for HIV proteins are now part of the helper T cell's genome. The virus may remain dormant for many years. When viral DNA is integrated into a host cell's genome it is known as a provirus (**Figure 9**).

Activation of the helper T cells results in transcription of the integrated viral DNA into viral mRNA, which enters the cytoplasm. The transcribed mRNA attaches itself to ribosomes and directs them to produce many copies of viral proteins and enzymes (**Figure 10**). They will form the protective coat for the newly released RNA.

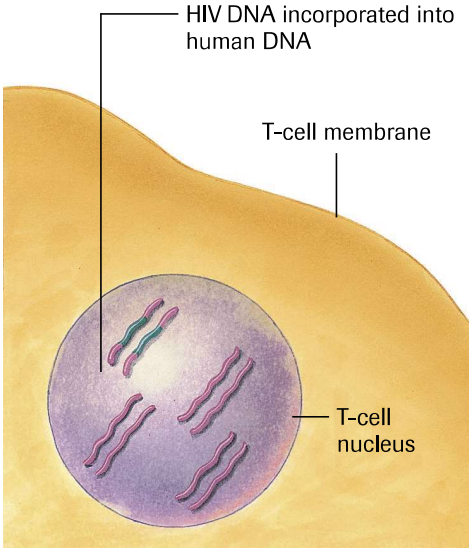


Figure 9
HIV genomic DNA is incorporated into human DNA.

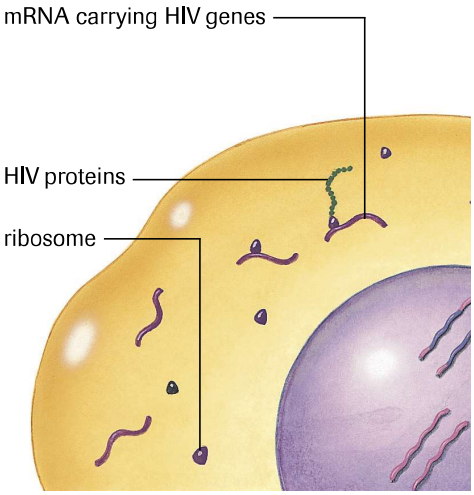
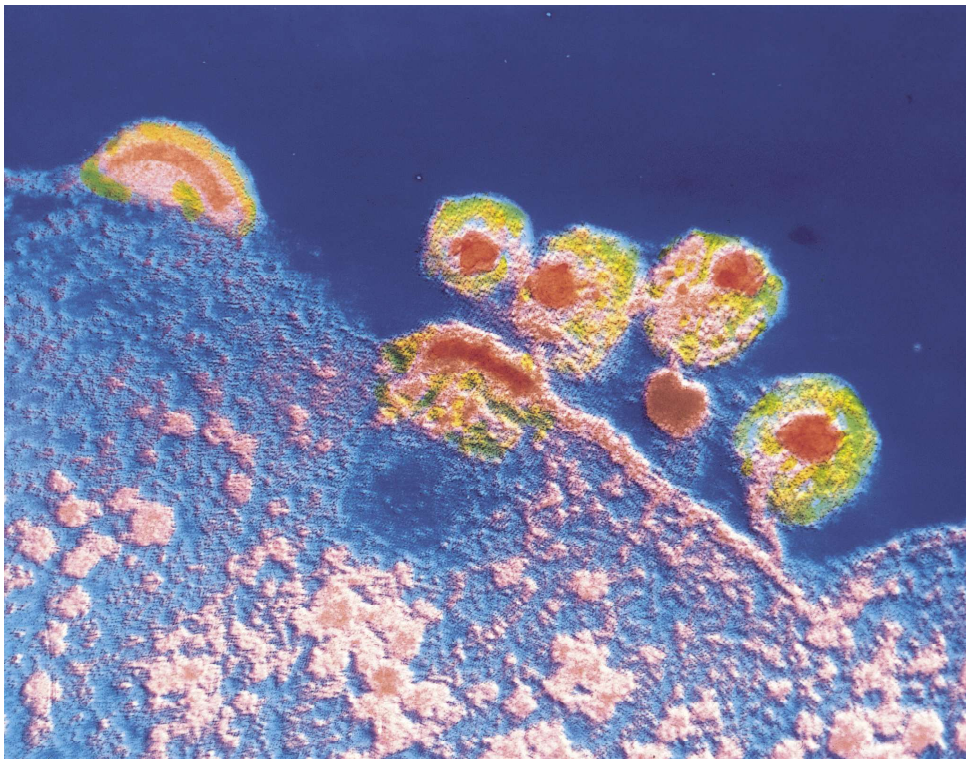
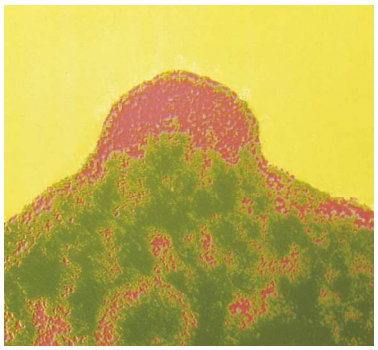


Figure 10
HIV mRNA directs the production of viral proteins and enzymes.



(a)



(b)

(c)

Figure 11
(a) Electron micrograph showing HIV being released from the cell membrane of a helper T cell; **(b)** and **(c)** a closer view of the infected helper T cell as the virus becomes coated by the cell membrane and escapes

Instead of performing T-cell functions, the once-healthy helper T cell is now transformed into an HIV factory. Viral proteins, destined for the HIV membrane, enter the host cell's membrane. Viral RNA and structural proteins migrate to just inside the host cell's membrane, where they pinch off from the cell to form a new viral particle, as illustrated in **Figure 11(a)**. **Figures 11(b)** and **(c)** show that, as the viral particle escapes, it becomes coated by the membrane. The newly released viral particle infects other helper T cells. Release of many viral particles eventually weakens the host T cell and it dies.

One of the challenges of finding a cure for AIDS stems from the ability of HIV to mutate to avoid immune detection and destruction. Examples of such mutations include changes to the proteins on its outer membrane. Killer T cells play an important role in containing HIV replication by recognizing the HIV-infected cells that display remnants of viral protein on their surface. When mutations of viral proteins occur, the killer T cells can no longer recognize HIV-infected cells and the virus escapes immune recognition.

In developed countries, the numbers of new AIDS diagnoses and deaths have been steadily falling. These reductions result from a number of factors, a major one being the development and use of potent anti-HIV drugs. There are several different classes of agents that work by interfering with different stages in the HIV life cycle. Patients usually receive combinations of three or more drugs at one time. Such combinations are known as highly active antiretroviral therapy (HAART). Despite the beneficial effects of HAART, many patients find taking many pills several times a day extremely difficult. As well, the medications are expensive, can have serious or intolerable side effects, and are not curative.

Major breakthroughs in the efforts to limit the spread of AIDS have also come in the form of tests for detecting HIV. Since 1985, blood collected by the Red Cross, and now the Canadian Blood Services, has been screened for the presence of HIV. As a result, the risk of acquiring HIV through a blood transfusion is extremely low.

There are several approaches to HIV prevention. Education about HIV and other sexually transmitted diseases, treatment and clean needle programs for injection drug users, and the use of antiretroviral drugs to prevent transmission of HIV from mother to infant have all proved successful. The development of a safe and effective HIV vaccine remains a priority in AIDS research. Although many of the developed nations of the world have health budgets that allow for HIV/AIDS testing and treatment, less developed countries are struggling to deal with the consequences of having exerted inadequate control over the disease in its early years. Furthermore, since the countries that are most in need cannot afford the costs of HAART and the high expenses associated with HIV, the majority of worldwide infections go untreated. Thus, despite the medical, social, and political advances in HIV management to date, many challenges still need to be addressed before global control of HIV is realized.

Case Study Questions

Understanding Concepts

1. Can HIV attach itself to a muscle cell or a skin cell?
2. Explain why you cannot get AIDS by shaking hands. (Use the information that you have gained about binding sites.)
3. Why is the enzyme that converts the RNA in HIV into DNA referred to as reverse transcriptase?
4. What happens to the viral DNA if the helper T cell divides?
5. Explain why it is possible for a human to be infected with HIV and not exhibit any of the symptoms of AIDS.
6. Indicate why people infected with HIV most often die of another infection, such as pneumonia.
7. David Vetter, "the boy in the plastic bubble," suffered from a disorder called severe combined immunodeficiency syndrome. How does this disorder differ from acquired immunodeficiency syndrome? (Severe combined immunodeficiency syndrome is discussed in more detail in Chapter 10, section 10.1.)
8. Why is it so difficult to destroy a virus that mutates frequently?
9. Canadian Blood Services inquires about a person's travels before blood donations are accepted. Explain why this practice can be classified as preventive.
10. Can HIV be transmitted through either food or beverages? Explain your answer.

Making Connections

11. Should health-care workers, such as doctors, dentists, and nurses, be screened for HIV? Justify your answer. What precautions do medical professionals take to protect themselves from the AIDS virus?
12. How can the spread of AIDS be prevented? List numerous policies that might minimize the spread of the disease.
13. Currently, blood tests are available to screen for the AIDS virus. Although these tests are very effective in detecting the virus, they fail if the virus has been contracted recently. Research how the AIDS test works. Explain why the test may fail to detect the virus after a recent exposure to HIV.

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SUMMARY An Overview of Transcription

1. Initiation of transcription commences when the RNA polymerase binds to the promoter region of the gene to be transcribed. At this point, the DNA is unwound and the double helix is disrupted.
2. RNA polymerase moves past the promoter until it reaches the start sequence of the gene to be transcribed.