A REVIEW OF HIV INFECTION

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Introduction

AIDS is one of the most serious, deadly diseases in human history. More than 20 years ago, doctors in the United States identified the first cases of AIDS in San Francisco and New York. Now there are an estimated 42 million people living with HIV or AIDS worldwide, and more than 3 million die every year from AIDS - related illnesses. AIDS is caused by the human immunodeficiency virus (HIV). HIV destroys a type of d efense cell in the body called a CD4 helper lymphocyte. These lymphocytes are part of the body's immune system, the defense system that fights infectious diseases. But as HIV destroys these lymphocytes, people with the virus begin to get serious infections that they normally wouldn't - that is, they become immune deficient. The name for this condition is acquired immunodeficiency syndrome (AIDS).As the medical community learns more about how HIV works, they've been able to develop drugs to inhibit it (meani ng they interfere with its growth). These drugs have been successful in slowing the progress of the disease, and people with the disease now live much longer. But there is still no cure for HIV and AIDS.

HIV is a Retrovirus

HIV belongs to a class of viru ses called retroviruses. Retroviruses are RNA (ribonucleic acid) viruses, and in order to replicate (duplicate), they must make a DNA (deoxyribonucleic acid) copy of their RNA. It is the DNA genes that allow the virus to replicate.

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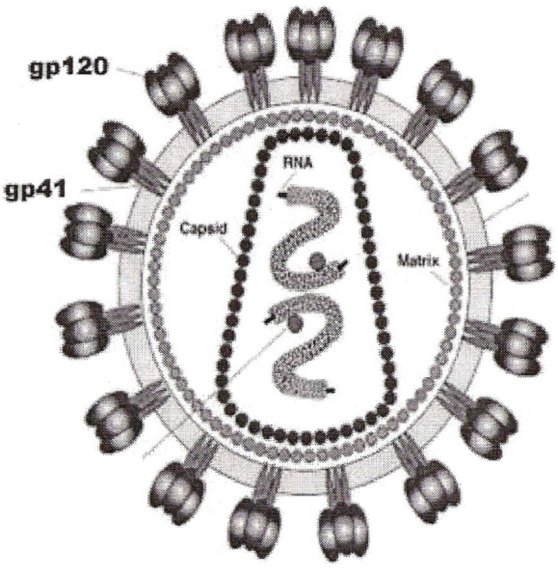
Like all viruses, HIV can replicate only inside cells, commanding the cell's machinery to reproduce. Only HIV and other retroviruses, however, once inside a cell, use an enzyme called reverse transcriptase to convert their RNA into DNA, which can be incorporated into the host cell's genes.

Structure of HIV



The viral envelope

HIV has a diameter of 1/10,000 of a millimeter and is spherical in shape. The outer coat of the virus, known as the viral envelope, is composed of two layers of fatty molecules called lipids, taken from the membrane of a human cell when a newly formed virus particle buds from the cell. HIV may enter and exit cells through special areas of the cell membrane known as "lipid rafts." These rafts are high in cholesterol and glycolipids and may provide a new target for blocking HIV.

Embedded in the viral envelope are proteins from the host cell, as well as 72 copies (on average) of a complex HIV protein (frequently called "spikes") that protrudes through the surface of the virus particle (virion). This protein, known as Env, consists of a cap made of three molecules called glycoprotein (gp) 120, and a stem consisting of three gp41 molecules that anchor the structure in the viral envelope. Much of the research to develop a vaccine against HIV has focused on these envelope proteins.

The viral core

Within the envelope of a mature HIV particle is a bullet -shaped core or capsid, made of 2,000 copies of another viral protein, p24. The capsid surrounds two single strands of HIV RNA, each of which has a copy of the virus's nine genes. Three of these genes, gag, pol, and env, contain information needed to make structural proteins for new virus particles. Six regulatory genes, *tat, rev, nef, vif, vpr*, and *vpu*, contain information necessary to produce proteins that control the ability of HI V to infect a cell, produce new copies of virus, or cause disease. The core of HIV also includes a protein called p7, the HIV nucleocapsid protein. Three enzymes carry out later steps in the virus's life cycle: reverse transcriptase, integrase, and protease. Another HIV protein called p 17, or the HIV matrix protein, lies between the viral core and the viral envelope.

Replication Cycle of HIV

Entry of HIV into cells

Infection typically begins when an HIV particle, which contains two copies of the HIV RNA , encounters a cell with a surface molecule called cluster designation 4 (CD4). Cells carrying this molecule are known as CD4+ cells.

One or more of the virus's **gp120** molecules binds tightly to CD4 molecule(s) on the cell's surface. The binding of gp120 t o CD4 results in a conformational change in the gp120 molecule allowing it to bind to a second molecule on the cell surface known as a co -receptor. The envelope of the virus and the cell membrane then fuse, leading to entry of the virus into the cell. The **gp41** of the envelope is critical to the fusion process. Drugs that block either the binding or the fusion process are being developed and tested in clinical trials.

Once it enters the body, HIV infects a large number of CD4+ cells and replicates rapidly. During this acute or primary phase of infection, the blood contains many viral particles that spread throughout the body, seeding various organs, particularly the lymphoid organs.

Mutations in HIV

HIV replicates rapidly and several billion new virus particles may be produced every day. In addition, the HIV reverse transcriptase enzyme makes many mistakes while making DNA copies from HIV RNA. As a consequence, many variants or strains of HIV develop in a person, some of which may escape destruction by antibodies or killer T cells. Additionally, different strains of HIV can recombine to produce a wide range of variants.

During the course of HIV disease, viral strains emerge in an infected person that differ widely in their ability to infect and kill different cell types, as well as in their rate of replication

One reason that HIV is unique is the fact that despite the body's aggressive immune responses, which are sufficient to clear most viral infections, some HIV invariably escapes. This is due in large part to the high rate of mutations that occur during the process of HIV replication. Even when the virus does not avoid the immune system by mutating, the body's best soldiers in the fight against HIV - certain subsets of killer T cells that recognize HIV -may be depleted or become dysfunctional.

Finally, the virus may hide within the chromosomes of an infected cell and be shielded from surveillance by the immune system. Such cells can be considered as a latent reservoir of the virus.

Conclusion

Factors such as age or genetic differences among individuals, the level of virulence of an individual strain of virus, and co-infection with other microbes may influence the rate and severity of disease progression. Drugs that fight the infections associated with AIDS have improved and prolonged the lives of HIV-infected people by preventing or treating conditions such as Pneumocystis carinii pneumonia, cytomegalovirus disease, and diseases caused by a number of fungi. But there is still no complete cure for AIDS.

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