HIV (AIDS)
HIV (1)’s first emergence was in 1959 from a man in Kinshasa, Democratic Republic of Congo. Although its genetic basis suggests it derived from a single virus in the late 1940’s. In 1999 an international research discovered the origin of HIV -1, the predominant strain of HIV (AIDS). HIV-1 was traced back to a subspecies of chimpanzees native to west equatorial Africa. The disease was transferred to humans when the human population came into contact with the infected chimpanzee blood. [1]

The virus made its presence noticeable in the Unites States in the mid 1970’s. Starting in the early 1980’s rare forms of diseases such as pneumonia and cancer were being reported in the countries metropolitan centers. In 1982 the term “acquired immunodeficiency syndrome” (AIDS) was introduced. By 1985 serological assays became available to test for HIV infection. These techniques immediately were immediately employed to screen blood transfusions. [2]

The earliest antiviral drugs to treat HIV and AIDS were utterly disappointing. It wasn’t until 1987 with the FDA approved zidovudine (AZT, or azidothymidine) that a real and effective treatment for HIV infection became readily available. [2] Since HIV’s startling appearance in the mid 1970’s more than 12 million people have died due to this retrovirus. [10]

**Physical Structure of Disease**

The physical structure of the HIV-1 virus has been determined to be about one ten-thousandth’s of a millimeter across in a roughly spherical shape through electron microscopy. The viral envelope is made up of a double layer lipid molecule similar to that of human cells. This is highly likely because once infected the virus takes it’s membrane from surrounding human tissues. The lipid bilayer is overwhelmed with proteins, a large portion (class I and Class II major histocompatible complex molecules) of which are of human
origin. These human proteins are essential in triggering the immune response. [5]

The coat of the virion is studded with viral protein spikes projecting into the external medium. Each spike most likely consists of four molecules of gp120 on the outside and the four molecules of gp41 embedded in the membrane. These human glycoproteins are of instrumental importance when HIV binds to and enters target cells.

Below the envelope a layer of p17 creates a matrix surrounding the core. It is shaped like a hollow, empty cone made up of p34, which contains the genetic material of the virus. This genetic material exists as two strands of RNA, about 9,200 bases long residing in the core. The RNA strands are affixed to reverse transcriptase, which transcribes viral RNA into DNA once the virus has entered the host cell. Integrase, protease and ribonuclease enzymes are also present in the core. [5]

The life cycle of HIV begins with viral particle attachment to CD4 receptors on the host cell membrane which forces the viral contents into the host cell. The viral core then partially dismantles to allow reverse transcriptase to produce DNA from the viral RNA. The viral DNA enters the nucleus, and integrates itself into the host genome. Host cell proteins bind the viral DNA and initiate transcription. Short RNA molecules leave the nucleus ordering the creation of viral regulatory proteins. Afterwards larger RNA molecules leave the nucleus and generate structural and enzymatic viral proteins. Viral protease becomes active as RNA and viral proteins enter the budding virus. The viral core and missing components form after the virus has budded from the host cell, using the host membrane as its own. [8]

Means of Infection

**Macro Scale**
The most well known methods of HIV infection are through fluid (sexual intercourse, drug/ blood injection, blood exchange through cuts, etc) exchange between two subjects allowing HIV access into the uninfected individual or through contact with an uninfected person’s mucous membrane. [3] From that moment it begins its destructive course of
reproduction and spreading. In the first few weeks of infection patients experience flu like symptoms as viral levels soar and the body struggles to create enough antibodies to battle the virus. During this time HIV contraction from the newly infected person is most communicable. [8]

**Micro Scale / Process of Infection**

The gp120 protein spike on the envelope can tightly bind to CD4, a protein found on certain immune system cells. On binding the two membranes fuse governed by the gp41 envelope protein. On fusion the virus core and contents are then injected into the host cell. [8]

Dendritic cells present throughout the body’s mucosal surfaces, since they carry the CD-4 molecule themselves it is possible they are the initial site for HIV infection during sexual transmission. Macrophages and monocytes carry the CD4 molecule as well making them similarly vulnerable. This vulnerability allows HIV to harbor a ride into other parts of the human system not to exclude the brain. However, HIV’s main targets are the CD4-bearing helper T lymphocytes (T4 cells). These cells are instrumental in activating other parts of the immune system, including killer T cells (attack virus-infected cells) and B cells (which produce antibodies) [8]

On initial infection the human system mounts a vigorous defense. During this acute phase of the infection, B cells produce antibodies neutralizing the HIV-1 virus, and activated killer T cells multiply and destroy infected cells as they would in infections. It is possible
for the immune system to successfully fight off HIV at an early stage, however by the
time HIV antibodies are found in the blood, HIV infection is generally permanent.
A current theory explaining how HIV defeats the immune response shows our own body
fighting against itself. Recent experiments in HIV infected models show many T cells,
even those uninfected commit cellular suicide rather than dividing normally. Apoptosis
normally occurs in the thymus gland and serves to eliminate T cells that would attack the
bodies own tissues. [5]

Joseph M. McCune and his colleagues at SyStemix have found evidence
that HIV infection triggers widespread apoptosis in mice that, lack-ing an
immune system, have had transplants of human fetal thymus and liver
cells. [5]

When an infected persons CD4 count drops below 200, or certain diseases such as
tuberculosis or Pneumocystis carinii contracted in conjunction with HIV they are said to
have AIDS. Throughout an infected life cycle one may alternate between HIV and AIDS
ad their CD4 levels rise and drop. A normal uninfected individual’s CD4 count ranges
between 500 and 1800. [11]

**Avoiding Infection Before and after exposure**
Over the past few years processes have developed to treat patients immediately after
possible contraction. Experiments suggest administering anti-HIV drugs either before
exposure or within 24 hours of exposure can protect test animals from HIV infection.
Postexposure prophylaxis (PEP) holds hope for those just infected. [6]

Transmission of HIV from women to their fetus is significantly reduced when the mother
is treated with Zidovudine (AZT) during pregnancy and labor and if the babies are
immediately treated with AZT after conception. The immunity may be due to the amount
of AZT circulating in the baby’s blood during initial infection from the mother. [6]

Further support for PEP comes from healthcare workers exposed to HIV through needle
sticks, or accidental breaks in the skin. Healthcare workers treated with PEP were most
likely to evade infection. [6]

PEP treatment is still experimental as doctors have yet to come to an agreement on the
proper doses for different exposures, and the long term side effects of anti-HIV drugs are
still unknown. [6]

There are many different HIV medications out on the market with new one’s entering
clinical trials and coming on the market daily. The first medications to arrive on the
market range from reverse transcriptase and protease inhibitors, antivirals and Nucleoside
/ Nucleotide Inhibitors (NRTI). [7] [12]

As modern technology advances newer drugs are constantly being developed as we gain
further insight into the HIV virus.
Crystallographic studies of gp41 fragments show that in the process of fusion, two heptad repeat domains (HR1 and HR2) form a helical bundle containing trimers of each domain. [12]

With this new data newer drugs are being developed to interfere with the fusion of the membranes by inhibiting the HR1 and HR2 domains.

In two Phase III studies that led to its FDA approval, the addition of enfuvirtide to an optimized antiretroviral regimen reduced plasma HIV-1 RNA levels by about $1.5 \log_{10}$ in persons who had previously experienced failure of therapy with each of the three original drug classes. [12]

One of the newest vaccines to complete its trials was AIDSVAX which consists of pieces of the gp120 protein. With the hopes it would trigger an immune response in the body, creating antibodies against the virus before actual infection, resulting in immunity. The trials proved unfortunately proved ineffective. [4]

Of the 3,330 people who received AIDSVAX, 5.7 percent had nonetheless become infected with HIV within three years, a rate almost identical to the 5.8 percent seen among 1,679 individuals who received a placebo. [4]

Even though the vaccine proved relatively ineffective, there was a silver lining. Apparently AIDSVAX worked better among African and Asian Americans.

Although only 327 blacks, Asians and people of other ethnicities received the vaccine, VaxGen said it protected 67 percent of them (3.7 percent got infected as compared with 9.9 percent of controls). AIDSVAX was articularly effective among African-Americans, preventing 78 percent of the 203 individuals in the study from contracting HIV. (Only two of the 53 Asians became infected, whereas six of the 71 people classified as “other minorities” did.) [4]

Currently there is a debate between scientists over immediately placing newly infected individuals on anti-HIV medications and allowing their body to manually fight the infection only beginning medication once one’s immune system begins to falter.

Since the immediate increase in HIV infection numerous state organizations have launched campaigns to help prevent HIV infection. These campaigns include comprehensive sex education, peer influence and community action, targeting education, testing and follow-up counseling, advertising and marketing, abstinence only programs and access to free condoms and clean needles.

In Thailand the Ministry of Public Health has attempted to inspire 100 percent condom use in brothels. It provides condoms and advocates safer sex practices through the media. [9]
Employing coercive measures to identify those infected as well as their partners has backfired, as it infringes on human rights. To this day the most effective way to control this epidemic is altering behavior. [9]
Sources:

2.) http://hivinsite.ucsf.edu/InSite?page=kb-03-01-01#; Hare, Bradley C.; April 2004.


12.) http://hivinsite.ucsf.edu/InSite?page=kb-03-02-07#S1X; Shafer, Robert W., April 2004.