

➤ **AIDS = Acquired Immune Deficiency Syndrome**

• **AIDS YESTERDAY AND TODAY**

- The **Centers for Disease Control and Prevention (CDC)**, which is responsible for the monitoring and prevention of epidemics of diseases in the U.S. first saw evidence of AIDS in 1981.
- In June of 1981, 5 cases of *Pneumocystis carinii* appeared in homosexual men in Los Angeles. This type of pneumonia was rare and only treatable with a drug which could be specially ordered from the CDC. Additionally, there was a large increase in the number of **Kaposi sarcoma (KS)** cases in New York and California. KS and *Pneumocystis* pneumonia are now widely recognized as hallmarks of HIV infection and AIDS.
- **In 1982, the disease was given the name Acquired Immune Deficiency Syndrome (AIDS) and studies had shown that it was transmitted by sexual or blood to blood contact.**
- Worldwide surveillance of AIDS is monitored by the Global Program on AIDS (GPA) which is a part of the World Health Organization (WHO) in Geneva, Switzerland.
- At least 1.3 million people died worldwide from AIDS in 1995. It is estimated that over 3 million people became infected with HIV worldwide in 1996.
- Urban centers such as New York, Los Angeles, San Francisco, Miami, and Chicago are areas with the greatest rates of HIV transmission.
- HIV transmission has tended to level off in the homosexual and hemophiliac population since the beginning of the epidemic.
- Currently, the rate of HIV transmission is the greatest in young people (particularly young gay men) and women. AIDS is one of the leading causes of death in young people in the U.S.
- The cumulative number of AIDS cases reported to CDC is **774,467**. Adult and adolescent AIDS cases total **765,559** with **635,451** cases in males and **130,104** cases in females. Through the same time period, **8,908** AIDS cases were reported in children under age 13.
- Total deaths of persons reported with AIDS are **448,060**, including **442,882** adults and adolescents, and **5,178** children under age 15, and 412 persons whose age at death is unknown.

- Of the total AIDS cases reported through December 2000, patients' ages at time of diagnosis were distributed as follows:

- **CUMULATIVE AIDS CASES BY AGE**

AGE	# of CUMULATIVE AIDS CASES
Under 5:	6,872
Ages 5 to 12:	2,036
Ages 13 to 19:	4,061
Ages 20 to 24:	27,232
Ages 25 to 29:	101,494
Ages 30 to 34:	172,310
Ages 35 to 39:	173,512
Ages 40 to 44:	128,177
Ages 45 to 49:	74,724
Ages 50 to 54:	39,625
Ages 55 to 59:	21,685
Ages 60 to 64:	12,023
Ages 65 or older:	10,711

Race or ethnicity of persons reported with AIDS as of December 2000 was:

CUMULATIVE AIDS CASES BY RACE or ETHNICITY

RACE or ETHNICITY	# of CUMULATIVE AIDS CASES
White, not Hispanic	331,160
Black, not Hispanic	292,522
Hispanic	141,694
Asian/Pacific Islander	5,728
American Indian/Alaska Native	2,337
Race/ethnicity unknown	1,025

- **WORLDWIDE HIV/AIDS CASES**

- Today, **36.1 million people are estimated to be living with HIV/AIDS**. Of these, 34.7 million are adults. 16.4 million are women, and 1.4 million are children under 15.
- An estimated **21.8 million people have died from AIDS** since the epidemic began. 17.5 million were adults, including 9 million women. 4.3 million were children under 15.
- During 2000, **AIDS caused the deaths of an estimated 3 million people**, including 1.3 million women and 500,000 children under 15.
- Women are becoming increasingly affected by HIV. Approximately **47%, or 16.4 million**, of the 34.7 million adults living with HIV or AIDS worldwide are women.
- The overwhelming majority of people with HIV - approximately 95% of the global total - now live in the developing world.

- **AIDS HIGH RISK GROUPS**

- **In Western countries** (Pattern I of the epidemic) = homosexual and bisexual men, intravenous drug users, and to a lesser extent, recipients of blood transfusion products such as hemophiliacs. However, women and young people (less than 25 years of age) are the groups in which HIV transmission is currently increasing at the fastest rate in the U.S.

- **In African countries** (Pattern II of the epidemic) = prostitutes, men or women with multiple sexual partners

Heterosexual transmission of HIV is the primary route of transmission in Africa.

Sub-saharan Africa has been devastated by AIDS. Two-thirds of the roughly 16 million people infected with HIV worldwide live in Africa. AIDS tends to strike young adults between 20 and 40 years of age in the prime of their productive lives. This decreases economic productivity and perpetuates the problem. In some parts of Africa, 1 in 3 people has AIDS. Since the transmission of HIV in Africa is mainly heterosexual, the number of peri-natal (mother to child) cases is also higher than in Western countries.

The number of orphans in Africa due to the AIDS epidemic is nearly impossible to calculate. Africa is in desperate need of education, money, drugs, and hospitals.

- **HIV TRANSMISSION AND PREVENTION**

- Currently, there is no 100% effective vaccine or cure for AIDS or HIV infection. Promising new drugs such as protease inhibitors have helped slow or halt the progress of the disease in some individuals. Recently developed combination therapies which include the use of protease inhibitors together with antiviral drugs have shown new hope for suppressing the activity of the virus. Unfortunately, these new therapies are also quite expensive (tens of thousands of dollars per year).

- **Avoid behaviors that are risky such as:**

- 1. Any type of sex without a latex condom**

Anal sex is the most risky followed by vaginal sex and then oral sex.

There are a few documented cases of HIV transmission by oral sex, although the risk of transmission is probably lower than anal or vaginal sex.

- 2. Intravenous (IV) drug use**

- 3. Multiple sexual partners**

- 4. Drug or alcohol use in social situations which may lower your inhibitions and prevent you from controlling your sexual/drug use behavior.**

- If you have sex, always wear a latex condom. It is suggested that you use a condom which is prelubricated with the spermicide called **NONOXYNOL-9**. Nonoxynol-9 has been shown to kill HIV in culture.

- **There is no evidence to show that you can become infected with HIV by:**

shaking hands, hugging, social kissing (no exchange of saliva), coughing, sneezing, toilet seats, doorknobs, telephones, furniture, insects, or swimming in a pool with a person who is HIV infected.

- **THE ORIGIN OF HIV**

- The origin of HIV is very difficult to determine. There are theories that HIV originated in Central Africa as a mutant form of SIV (Simian Immunodeficiency Virus) in monkeys that crossed the species barrier. New genetic evidence from molecular biology studies comparing the gene sequences of SIVs and HIV clearly supports this hypothesis.
- The first laboratory demonstration of human infection by detection of antibodies was from an archived blood serum sample from a person in Zaire in 1959.
- There is little doubt that the epidemic of AIDS began in humans in the late 1970's and has increased in extent since then, partly due to the sexual revolution of the 1970's.

- **HIV INFECTION VERSUS AIDS**

- It is important to distinguish between HIV infection and having the clinical disease known as AIDS
- HIV infection implies that a person has been exposed to and infected by HIV. A person may be infected by HIV and remain asymptomatic (that is, they show no signs of immunosuppression = AIDS). A person may be infected with HIV for many years before they develop AIDS. The average period of latency is about 10 years.
- AIDS is a clinically defined disease that is characterized by a decrease in the ability of the immune system to fight against opportunistic infections.
- The T4 helper cell count is about 1,000 cells per microliter in a normal person. A person is generally considered to have crossed the line to AIDS from HIV infection when their T4 helper cell count falls below 200 cells per microliter. At this point, the viral count rises as the virus wins the battle against the immune system.
- Recently it has been recognized that 10-15% of HIV-infected people do not progress to having AIDS after 10 years = **non-progressors**. About 10% of HIV-infected people develop AIDS within 2-3 years = **rapid progressors**.
- Rapid progressors tend to have low concentrations of anti-HIV antibodies with higher plasma concentrations of actual HIV as compared with non-progressors.

- **HIV (Human Immunodeficiency Virus)**

- HIV was first discovered by **Luc Montagnier** at the Pasteur Institute in France and **Robert Gallo** at the National Cancer Institute (part of the National Institutes of Health) in the U.S. in 1984.
- A blood test to determine if a person has been infected with HIV was first developed in 1984. The blood test does not directly detect the virus, but rather detects antibodies to the virus. If a person has been infected with HIV, their immune system will make antibodies to the virus and these will be detected by the blood test. There are other blood tests (Western blots and PCR) which can actually detect the virus.
- **HIV is a type of retrovirus.** Basically, HIV is an RNA molecule surrounded by a protein coat. HIV requires a host cell to survive.
- Like other viruses, HIV will only infect certain cells that have certain proteins on their cell surfaces. HIV only infects cells that have the CD4 molecule in their cell membranes. The T4 helper cells have many CD4 molecules on their cell surfaces. There is a protein on HIV called gp120 that binds to the CD4 protein molecule and allows HIV to infect the T4 helper cells.
- HIV infects and can destroy the T4 helper cells. Since the T4 helper cells are the mediators and coordinators of the immune response, an HIV infected person can lose their immunity and become immunosuppressed. This causes a person to become susceptible to a number of **opportunistic infections**. A person with AIDS does not die of HIV infection, but rather dies due to an opportunistic infection.

- **Retroviruses** have to make their RNA genetic material into DNA genetic material in order to infect a host cell. HIV uses an enzyme called **reverse transcriptase** to convert it's RNA into DNA so that it can infect the T4 helper cells of the immune system. The life cycle and molecular biology of HIV is complex and not completely understood.
- There are at least two known basic strains of HIV:
 1. **HIV-1** which is present worldwide, but predominantly in Western countries.
 2. **HIV-2** which is present mainly in Africa.
- There are other, more rare strains of HIV, but they infect very few people worldwide as compared with HIV-1 and HIV-2. These rare strains appear to be transmitted via the same routes as HIV-1 and HIV-2.
- Although there are two basic forms of HIV, HIV has an incredible ability to mutate and there are literally thousands of slightly different variants of the virus. When a person first becomes infected with HIV, they may be infected by perhaps ten different mutant forms of HIV. By the time a person has progressed to having full blown AIDS, they may have thousands of mutant HIV forms in their body.
- **HIV INFECTION**
 - When HIV infects a T4 helper cell, it injects it's viral RNA into the cell. Using the enzyme called **reverse transcriptase**, the viral RNA is made into viral DNA. This viral DNA can then be incorporated into the normal, genomic DNA of the helper cell.
 - When HIV infects a T4 helper cell, there are three possible outcomes for the helper cell:
 1. **LATENCY** = the virus remains dormant. No viral replication takes place.
 2. **CONTROLLED REPLICATION (LYSOGENESIS)** = the viral DNA is used to make new virus particles at a controlled rate. This process takes place slowly and the host cell is spared.
 3. **LYSIS** = the viral DNA is used to make new viruses so fast, that the helper cell fills up with virus particles and eventually bursts. This allows the virus to rapidly spread to other cells.
 - The course of HIV infection typically runs many years, during most of which the patient has no symptoms, but can still spread the virus. The levels of antibodies, cytotoxic T cells and helper cells (T4 cells) remain strong during the asymptomatic stage (no symptoms are evident). However, as the immune defenses lose control of the virus, which replicates quickly and mutates wildly, the levels of antibodies, helper T cells and cytotoxic T cells declines. This leaves the person defenseless against a number of opportunistic infections.
 - It is very difficult for the immune system to destroy HIV because it mutates so rapidly. Even if the immune system learns to destroy a specific strain of HIV, HIV can still remain in the body because it mutates so rapidly that it can avoid detection by the immune system. The high mutation rate of HIV also makes it difficult to formulate an effective vaccine against the virus.
 - HIV can infect the central nervous system where it has serious effects that lead to dementia. Dementia can be mild to severe, but tends to worsen as the disease progresses.

- **OPPORTUNISTIC INFECTIONS ASSOCIATED WITH HIV**

- Opportunistic infections are caused by organisms which commonly occur in the environment. People with normal immune systems have a natural resistance to these organisms. Only when a person's immune system is suppressed can these viruses, fungi, bacteria, and protozoa seize the opportunity to cause infection

- **Viral Opportunistic Infections associated with AIDS**

1. *Cytomegalovirus* and *Epstein-Barr virus* = mononucleosis-like symptoms such as sore throat, sweats, loss of appetite, swollen glands and severe fatigue
2. *Herpes Simplex I and II* = oral and genital herpes sores (last longer in people with AIDS)
3. *Shingles* = reactivation of the dormant chicken pox virus (a type of herpes virus)

- **Fungal Opportunistic Infection associated with AIDS**

1. *Candida* = "thrush"; same fungus that causes yeast infections in women; creamy, white patches in mucous membranes of mouth and vagina. Can infect organs of the gastrointestinal tract in people with AIDS.

- **Protozoan Opportunistic Infections associated with AIDS**

1. *Pneumocystis carinii* = clogs lungs with fluid. Causes pneumonia which develops slowly and is not easily recognized in its early stages.
2. *Toxoplasmosis* = transmitted from hand to mouth, usually from cat feces. Causes brain inflammation with fever in people with AIDS.

- **Bacterial Opportunistic Infections associated with AIDS**

1. *Pulmonary Tuberculosis*
2. Many blood-borne bacteria

- **Kaposi's Sarcoma (KS)**

- KS is an aggressive tumor of epithelial cells seen in people with AIDS.
- Tumor lesions arise primarily from the inner wall of blood vessels and appear as reddish purple, coin sized spots on the skin. Lesions may appear anywhere on the body and frequently involve the internal organs.
- Can spread rapidly in people with AIDS, even though they cause no discomfort.

- **PROBLEMS IN FINDING THERAPIES FOR AIDS**

- HIV mutates very rapidly and while an individual may initially be infected by only a few different strains of the virus, they may have thousands of slightly different molecular variants in their bodies by the time they develop full blown AIDS. It is very difficult for the immune system to recognize so many slightly different types of the same virus.

- There are only a handful of antiviral agents available (ddI, ddC, AZT, acyclovir, etc.).
- Retroviruses such as HIV are elusive and can lie dormant for years.
- Infection of a number of different tissue types, including the CNS that can be protected by the blood-brain barrier.
- Secondary opportunistic infections may lead to complications that may be difficult to eradicate.

- **THERAPIES FOR AIDS**

- Since viruses depend on their hosts for survival and replication, it is difficult to find a drug which will destroy the virus without destroying the host cells and subsequently the host organism.
- **AZT (Zidovudine)** was the first available (in 1986) and most widely used anti-viral drug used to block the replication of HIV.
- Many new drugs are currently available which block viral replication including: ddI, ddC, acyclovir, protease inhibitors, synovir, etc. Many more drugs are under investigation to prevent or treat AIDS.
- AZT, ddI, ddC and other anti-viral drugs work by blocking the **reverse transcriptase** enzyme that whose function is necessary to convert viral RNA into viral DNA during T cell infection. Blocking this enzyme blocks viral replication at an early stage in the viral life cycle. However, these drugs are fairly toxic and do not work well in all patients.
- Protease inhibitors block a protease enzyme (an enzyme that cuts proteins) whose function is necessary for the virus to assemble new viral particles that can bud off of infected cells. Blocking this enzyme blocks viral replication at a later stage in the viral life cycle. Protease inhibitors have been found to be potent drugs that can decrease the number of viruses in the body, mainly when they are used in conjunction with a reverse transcriptase inhibitor.
- There is great hope for the use of combination therapies which use multiple anti-viral drugs to combat the disease. Combination therapy has been very effective in treating some individuals with AIDS. These therapies usually involve the use of two different reverse transcriptase inhibitors and one protease inhibitor drug.
- Unfortunately, these “cocktail” drugs:
 - do not work in all patients
 - they may have side effects in some patients
 - they may stop working after a few years
 - they must be taken everyday for the rest of the patients life
 - they are expensive
 - there is already evidence that the virus will be able to mutate and form viral strains that are resistant to these new drugs.
 - The cocktail is not a cure.
- Other drugs in development or use are targeted against preventing or curing opportunistic infections as well as developing new reverse transcriptase inhibitors and protease inhibitors.
- AIDS therapy is now focussed on long-term management of the disease as well as a cure.

- **AIDS (more correctly, HIV) VACCINES**

- Currently, there is no vaccine available to prevent HIV infection. Many vaccines have been tried, most with little or no success. The high mutation rate of HIV and a lack of a complete understanding of how HIV destroys the immune system are the biggest stumbling blocks to developing an effective vaccine against HIV.
 - There are vaccines against HIV in clinical trials, but they show only limited promise.
- **Don't forget, HIV is not the only sexually transmitted disease and a condom can help protect against chlamydia, herpes, gonorrhoea, syphilis, genital warts, and pelvic inflammatory disease (PID).**