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An HIV Information Site & HIV Educational Resource Site (HIS & HERS)

General Information on Human Immunodeficiency Virus (HIV) Infection

History

HIV is short for the Human Immunodeficiency Virus. It is a RNA retrovirus that probably originated in Africa in monkeys and began spreading as early as the late 1950's but with the sexual revolution and rapid international travel by airplane, it really took off in the late 1970's and early 1980's. The first cases of AIDS were recognized in the early and mid-1980's (see **Figure 1**.) Initially the cause was not known or suspected until large numbers of gay men developed the disease. This suggested that it was an infection transmitted by sexual intercourse or other practices, or some other lifestyle issue related to homosexuality. Very shortly after this, HIV was identified (then called HTLV III,) and a blood test became available in 1984. After the test became available it became even more apparent that gay men, recipients of some blood transfusions, most recipients of factor concentrates, and intravenous drug users who shared needles were the highest risk groups for the infection. Prior to the availability of the specific blood test for HIV, T-cells or CD4-lymphocyte tests were used to help diagnose the disease.

After many people had died or already become sick, AZT (also known as Retrovir, zidovudine and ZDV) was tested and approved quickly in 1987 and 1988 in the US (see **Figure 2**.) While AZT was active against the virus, it was very toxic at the doses that were used at that time (the doses were 4 times what is currently used.) Additionally, since only one drug, (or one drug used after another) is not very effective, persons with HIV infection in the USA continued to get sick and die relatively quickly until the latter half of the 1990's. During that time the first protease inhibitors became available and for the first time healthcare providers were able to prescribe several different active drugs at one time (aka the "cocktail" or combination therapy.) Even then, the number of drugs was relatively low and the knowledge to use these drugs was very limited. The advent of the availability of the HIV viral load test at about this time helped everyone to learn how to use the drugs more effectively, more about the way affects the human body, and how to develop and more rapidly bring to market new, more active, and less toxic drugs.

Since the understanding of the necessity of combination therapy and the development of multiple new medications, death and the development of AIDS have dropped off dramatically in the USA and other areas of the world that have access to medications and the infrastructure necessary to provide these medications and monitor them. Currently there are **22 drugs available** in the USA including combinations of existing drugs into one medication. The importance of adherence to medications, resistance testing, and important parameters like when

to begin treatment are the most important non-drug issues that have been clarified in the last few years.

AIDS continues to kill in areas of the world and in the US where there is poor drug availability or lack of skill at using the drugs. As the epidemic reaches into the lower socioeconomic classes of the US, it has become more and more a disease of heterosexuals. Minority women sit at the fastest spreading edge of the infection and disease. Due to disenfranchisement from medical care, these persons often do not seek testing until the disease is advanced.

Effects of HIV on the Human Body

HIV infects and kills several different types of cells in the human body.

1. CD4-lymphocytes or T-cells. As it turns out, if a virus had a brain and it had to choose one type of cell to affect, the smart virus would choose T-cells. T-cells are responsible for coordinating an important part of the immune system called cell-mediated immunity (CMI). This part of the immune system is important for defending humans from viruses, bacteria, fungi, and parasites that we are constantly exposed to. Note that viruses are part of the defenses of CMI. HIV weakens the part of the immune system that can defend the body from HIV itself. This sets into motion a vicious cycle of lowered immunity, more viral reproduction, even more lowered immunity, and even more viral reproduction. More and more virus kills T-cells faster and faster in the untreated human despite valiant efforts by the body to keep up with the losses. Billions of viral particles are produced by the virus every second and only slightly less than that are killed by the immune system; however, over time the losses add up. More and more virus is present at any given time and less and less T-cells are present. When the CD4-count is less than 250 or so, symptoms develop if not already present (see Table below). One definition that the US Centers for Disease Control uses for "full blown" AIDS (acquired immunodeficiency syndrome) is the loss of CD4-cells to less than 200 at any time.

The average rate of loss of T-cells in someone who is not on effective treatment is approximately 50-100 per year. This can vary quite a bit from person to person.

CD4-lymphocyte count Estimated HIV Viral Load	Problems that can occur
>500 cells/cc **<10,000 copies/cc**	Shingles TB Mild risk of cancers like Kaposi's sarcoma or lymphoma Superficial fungal infections Superficial bacterial infections of the skin

300-500 **10,000 - 50,000**	Shingles Possible weight loss Possible lymph node swelling Lymphoepithelial cysts Increased chance of bacterial pneumonia especially in smokers Risk for recurrent herpes TB Higher risk of central nervous system (brain) syphilis Mild risk of cancers like Kaposi's sarcoma or lymphoma Superficial fungal infections Superficial bacterial infections of the skin
200-300 **50,000 - 250,000**	Possible yeast infections in mouth, vagina, or on penis Mild weight loss Unexplained fevers, nightsweats Increased risk of bacterial pneumonia Low probability of pneumocystis pneumonia (a parasitic or fungal pneumonia) Increased diarrhea Higher risk for recurrent herpes TB Higher risk of central nervous system (brain) syphilis Mild risk of cancers like Kaposi's sarcoma or lymphoma Superficial fungal infections Risk of HIV-related peripheral neuropathy
100-200 **100,000 - 750,000**	Increased risk of yeast infections of the mouth, esophagus, genital organs Weight loss Nonspecific skin problems: itchy bumps Unexplained fevers, nightsweats Increased risk of bacterial pneumonia Increasing risk of pneumocystis pneumonia Diarrheal problems Mild risk of deep-seated fungal infections like cryptococcosis Recurrent herpes, frequently TB Higher risk of central nervous system (brain) syphilis Higher risk of cancers like Kaposi's sarcoma or lymphoma Risk of AIDS enteropathy Risk of HIV encephalitis or dementia Higher risk of HIV-related peripheral neuropathy Risk of progressive multifocal leukoencephalopathy

<100 **>750,000**	Highest risk for oral and esophageal yeast infections Worsening nonspecific skin problems: itchy bumps Highest risk of pneumocystis pneumonia Risk for severe diarrheal problems like cryptosporidiosis High risk for viral infections like recurrent herpes and cytomegalovirus (CMV) Highest risk for deep-seated fungal infections including cryptococcosis, histoplasmosis and coccidioidomycosis High risk of disseminated mycobacterial infection (Mycobacterium avium complex or MAC) Risk of toxoplasmic encephalitis Wasting Risk of AIDS enteropathy TB Highest risk of cancers like Kaposi's sarcoma or lymphoma Highest risk of HIV encephalitis or dementia Highest risk of HIV-related peripheral neuropathy Risk of HIV-related myelopathy (lower extremity weakness, bowel/bladder dysfunction) Risk of progressive multifocal leukoencephalopathy

2. Besides the T-cells, HIV also infects cells within the nervous system: Over long periods of time, nervous cells die or become sick due to the steady attack. Many problems can develop due to this ongoing nerve damage. As you can see from the table above, the items in green type illustrate the problems within the nervous system caused directly or indirectly by HIV.

The more common problems include the following:

1. Peripheral neuropathy is characterized by numbness and/or pain that usually begins in the soles of the feet and may rise to involve the entire and the legs.
2. HIV encephalitis is an inflammatory condition of the brain that over long periods of time results in actual death of brain cells; when this process goes on long enough, the afflicted person may develop short term memory problems, confusion or other more "localized" problems like seizures. Dementia may be the end result.
3. In addition to direct attack on the nervous system by HIV, many of the opportunistic infections listed above localize there also (cryptococcosis, toxoplasmosis, progressive multifocal leukoencephalopathy).
4. Cytomegalovirus (CMV) can infect the eyes ("retinitis") and cause blindness. Rarely it can cause encephalitis also.

3. Another target of HIV is the gastrointestinal (GI) tract: The gastrointestinal tract consists

of the entire "tube" from the mouth to the anus. The GI tract is surrounded by lymph tissue which is one of the best reproductive grounds for HIV. Problems with the GI tract include reduced absorption of nutrients and drugs. This malabsorption impairs the immune system further and sets into play another vicious cycle of weight loss and debilitation. Reduced absorption or malabsorption usually results in diarrhea. The entire GI tract including the liver and the bile ducts may be affected by HIV as well as opportunistic infections such as cytomegalovirus, cryptosporidiosis, or relatives of tuberculosis (mycobacteria.)

4. Other organs are affected also: It is also known that the skin, bone marrow, muscles, and genital organs are also targeted by HIV's destructive effects. As the skin is affected, its integrity is compromised and bothersome symptoms develop. Itchy red bumps can become extremely bothersome. Superficial infections of the skin as well as deeper-seated ones like staph boils are much more common. Occasionally localized staph infections start to invade the body through the bloodstream. The bone marrow gets suppressed more and more so that white cells, red blood cells and platelet cells are affected and lowered more and more. The hormones in the body are affected and in particular the male sex hormone (testosterone) is lowered in many men with AIDS so that they lose weight and become depressed.

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