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## Sexually transmitted disease: Acquired immune deficiency syndrome: A Review

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### ABSTRACT

Acquired immune deficiency syndrome, a disease in which there is a severe loss of the body's cellular immunity, greatly lowering the resistance to infection and malignancy. The cause is a human immune deficiency virus, or HIV transmitted in blood and in sexual fluids. AIDS was first reported June 5, 1981. A combination of several antiretroviral drugs, called highly active antiretroviral therapy (HAART), has been very effective in reducing the number of HIV particles in the bloodstream. The best treatment for AIDS in humans is prevention by vaccination.

**Key words:** AIDS, Human immune deficiency virus, Sexually transmitted disease, Sexual infection, Immune disease.

### INTRODUCTION

CDC defines a case of AIDS as a disease, at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that disease. Such diseases include KS [Kaposi's sarcoma], PCP [Pneumocystis carinii pneumonia], and serious OOI [other opportunistic infections]. (Holmes et al., 2003). These infections include pneumonia, meningitis, or encephalitis due to one or more of the following: aspergillosis, candidiasis, cryptococcosis, cytomegalovirus, norcardiosis, strongyloidosis, toxoplasmosis, zygomycosis, or atypical mycobacteriosis (species other than tuberculosis or lepra); esophagitis due to candidiasis, cytomegalovirus, or herpes simplex virus; progressive multifocal leukoencephalopathy, chronic enterocolitis (more than 4 weeks) due to cryptosporidiosis; or unusually extensive mucocutaneous herpes simplex of more than 5 weeks duration. Diagnoses are considered to fit the case definition only if based on sufficiently reliable methods (generally histology or culture). (Heath et al., 2002) However, this case definition may not include the full spectrum of AIDS manifestations, which may range from absence of symptoms (despite laboratory evidence of immune deficiency) to nonspecific symptoms (e.g., fever, weight loss, generalized, persistent lymphadenopathy) to specific diseases that are insufficiently predictive of cellular immunodeficiency to be included in incidence monitoring (e.g., tuberculosis, oral candidiasis, herpes zoster) to malignant neoplasms that cause, as well as result from, immunodeficiency. Acquired immune deficiency syndrome, a disease in which there is a severe loss of the body's cellular immunity, greatly lowering the resistance to infection and malignancy. (Ho-Yen et al., 2008) The cause is a virus (the human immunodeficiency virus, or HIV) transmitted in blood and in sexual fluids. a disease of the human immune system that is characterized cytologically especially by reduction in the numbers of CD4-bearing helper T cells to 20 percent or less of normal thereby rendering the subject highly vulnerable to life-threatening conditions (as Pneumocystis carinii pneumonia) and to some (as Kaposi's sarcoma) that become life-threatening and that is caused by infection with HIV commonly transmitted in infected blood

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especially during illicit intravenous drug use and in bodily secretions (as semen) during sexual intercourse. The human immunodeficiency virus (HIV) eats away at the T-cells of the body's immune system, thereby exposing it to infections. (Charles Gilks., 1991) Twenty-six diseases are now on the list of these "opportunistic" infections. Some of them are not actually infectious — Kaposi's sarcoma and cervical cancer, for example. (Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection 2005-11-03) Others are — tuberculosis, herpes, pneumonia, and candidiasis among them. So, if you have one of these diseases, and you are HIV positive, and, in time, your T-cell count dips below a certain level, then you have AIDS. (Altman., 1982)

### Signs and Symptoms

- The **symptoms of AIDS** are primarily the result of conditions that do not normally develop in individuals with healthy immune systems
- Most of these conditions are infections caused by bacteria, viruses, fungi and parasites that are normally controlled by the elements of the immune system that HIV damages.
- A person may remain asymptomatic, feel, and appear healthy for even years even though he or she is infected with HIV. While he or she does not exhibit AIDS, the immune system starts to be impaired.
- The person may exhibit neurological symptoms such as memory loss, altered gait, depression, sleep disorders or chronic diarrhea.
- This set of symptoms is often called **AIDS-related Complex (ARC)** by clinicians. As the symptom progress, the patient becomes an AIDS patient.

### Minor Signs

1. Persistent Cough for one month
2. Generalized pruritic dermatitis
3. Recurrent herpes zoster
4. Oropharyngeal candidiasis
5. Chronic disseminated herpes simplex
6. Generalized lymphadenopathy

### Major Signs

1. Loss of weight – 10 percent of body weight
2. Chronic diarrhea for more than one month
3. Prolonged fever for one month

### Common Opportunistic Infections

1. Pneumocystis carinii pneumonia
2. Oral candidiasis
3. Toxoplasmosis of the CNS
4. Chronic diarrhea/wasting syndrome
5. Pulmonary/extra-pulmonary tuberculosis
6. Cancers

- a. **Kaposi's sarcoma** – affects small blood vessels and internal organs.
- b. Cervical dysplasia and cancer. Researchers found out that women with HIV have higher rates of this type of cancer. Cervical carcinoma is associated with Human Papilloma Virus (HPV).

Non-Hodgkin's lymphoma – cancerous tumor of the lymph nodes. This is usually a late manifestation of HIV infection. (Boshoff et al., 2002).

### CAUSES

AIDS is the ultimate clinical consequence of infection with HIV. HIV is a retrovirus that primarily infects vital organs of the human immune system such as CD4<sup>+</sup> T cells (a subset of T cells), macrophages and dendritic cells. It directly and indirectly destroys CD4<sup>+</sup> T cells. Once the number of CD4<sup>+</sup> T cells per microliter (μL) of blood drops below 200, cellular immunity is lost. Acute HIV infection usually progresses over time to clinical latent HIV infection and then to early symptomatic HIV infection and later to AIDS, which is identified either on the basis of the amount of CD4<sup>+</sup> T cells remaining in the blood, and/or the presence of certain infections, as noted above. In the absence of antiretroviral therapy, the median time of progression from HIV infection to AIDS is nine to ten years, and the median survival time after developing AIDS is only 9.2 months. However, the rate of clinical disease progression varies widely between individuals, from two weeks up to 20 years. Many factors affect the rate of progression. These include factors that influence the body's ability to defend against HIV such as the infected person's general immune function. Older people have weaker immune systems, and therefore have a greater risk of rapid disease progression than younger people. Poor access to health care and the existence of coexisting infections such as tuberculosis also may predispose people to faster disease progression. The infected person's genetic inheritance plays an important role and some people are resistant to certain strains of HIV. An example of this is people with the homozygous CCR5-Δ32 variation are resistant to infection with certain strains of HIV. HIV is genetically variable and exists as different strains, which cause different rates of clinical disease progression. There are a number HIV and AIDS misconceptions. Three of the most common are that AIDS can spread through casual contact, that sexual intercourse with a virgin will cure AIDS, and that HIV can infect only homosexual men and drug users. Other misconceptions are that any act of anal intercourse between gay men can lead to AIDS infection, and that open discussion of homosexuality and HIV in schools will lead to increased rates of homosexuality and AIDS (WHO, 1985).

### Sexual transmission

Sexual transmission occurs with the contact between sexual secretions of one person with the rectal, genital or oral mucous membranes of another. Unprotected sexual acts are riskier

for the receptive partner than for the insertive partner, and the risk for transmitting HIV through unprotected anal intercourse is greater than the risk from vaginal intercourse or oral sex. However, oral sex is not entirely safe, as HIV can be transmitted through both insertive and receptive oral sex. Sexual assault greatly increases the risk of HIV transmission as condoms are rarely employed and physical trauma to the vagina or rectum occurs frequently, facilitating the transmission of HIV. Drug use has been studied as a possible predictor of HIV transmission. Perry N. Halkitis found that methamphetamine usage does significantly relate to unprotected sexual behavior. The study found methamphetamine users to be at a higher risk for contracting HIV.

Other sexually transmitted infections (STI) increase the risk of HIV transmission and infection, because they cause the disruption of the normal epithelial barrier by genital ulceration and/or micro-ulceration; and by accumulation of pools of HIV-susceptible or HIV-infected cells (lymphocytes and macrophages) in semen and vaginal secretions. Epidemiological studies from sub-Saharan Africa, Europe and North America suggest that genital ulcers, such as those caused by syphilis and/or chancroid, increase the risk of becoming infected with HIV by about fourfold. There is also a significant although lesser increase in risk from STIs such as gonorrhoea, chlamydia and trichomoniasis, which all cause local accumulations of lymphocytes and macrophages.

Transmission of HIV depends on the infectiousness of the index case and the susceptibility of the uninfected partner. Infectivity seems to vary during the course of illness and is not constant between individuals. An undetectable plasma viral load does not necessarily indicate a low viral load in the seminal liquid or genital secretions. However, each 10-fold increase in the level of HIV in the blood is associated with an 81% increased rate of HIV transmission. Women are more susceptible to HIV-1 infection due to hormonal changes, vaginal microbial ecology and physiology, and a higher prevalence of sexually transmitted diseases. People who have been infected with one strain of HIV can still be infected later on in their lives by other, more virulent strains. Infection is unlikely in a single encounter. High rates of infection have been linked to a pattern of overlapping long-term sexual relationships. This allows the virus to quickly spread to multiple partners who in turn infect their partners. A pattern of serial monogamy or occasional casual encounters is associated with lower rates of infection. HIV spreads readily through heterosexual sex in Africa, but less so elsewhere. One possibility being researched is that schistosomiasis, which affects up to 50% of women in parts of Africa, damages the lining of the vagina. (WHO., 1986)

### Blood products

This transmission route is particularly relevant to intravenous drug users, hemophiliacs and recipients of blood transfusions and blood products. Sharing and reusing syringes contaminated with HIV-infected blood represents a major risk for infection with HIV. Needle sharing is the cause of one third of all new HIV-infections in North America, China, and Eastern Europe.

The risk of being infected with HIV from a single prick with a needle that has been used on an HIV-infected person is thought to be about 1 in 150 (see table above). Post-exposure prophylaxis with anti-HIV drugs can further reduce this risk. This route can also affect people who give and receive tattoos and piercings. (india.gov.in., 2010) .Universal precautions are frequently not followed in both sub-Saharan Africa and much of Asia because of both a shortage of supplies and inadequate training. The WHO estimates that approximately 2.5% of all HIV infections in sub-Saharan Africa are transmitted through unsafe healthcare injections.<sup>[90]</sup> Because of this, the United Nations General Assembly has urged the nations of the world to implement precautions to prevent HIV transmission by health workers. The risk of transmitting HIV to blood transfusion recipients is extremely low in developed countries where improved donor selection and HIV screening is performed. However, according to the WHO, the overwhelming majority of the world's population does not have access to safe blood and between 5% and 10% of the world's HIV infections come from transfusion of infected blood and blood products. (Weiss., 1993)

### Perinatal transmission

The transmission of the virus from the mother to the child can occur *in utero* during the last weeks of pregnancy and at childbirth. In the absence of treatment, the transmission rate between a mother and her child during pregnancy, labor and delivery is 25%. However, when the mother takes antiretroviral therapy and gives birth by caesarean section, the rate of transmission is just 1%. The risk of infection is influenced by the viral load of the mother at birth, with the higher the viral load, the higher the risk. Breastfeeding also increases the risk of transmission by about 4%. (Decker et al., 2000)

### Pathophysiology

The pathophysiology of AIDS is complex, as is the case with all syndromes. Ultimately, HIV causes AIDS by depleting CD4<sup>+</sup> T helper lymphocytes. (Del Rio et al., 2009). This weakens the immune system and allows opportunistic infections. (Gray et al., 2001) T lymphocytes are essential to the immune response and without them, the body cannot fight infections or kill cancerous cells. The mechanism of CD4<sup>+</sup> T cell depletion differs in the acute and chronic phases. During the acute phase, HIV-induced cell lysis and killing of infected cells by cytotoxic T cells accounts for CD4<sup>+</sup> T cell depletion, although apoptosis may also be a factor. (Feldman., 2005). During the chronic phase, the consequences of generalized immune activation coupled with the gradual loss of the ability of the immune system to generate new T cells appear to account for the slow decline in CD4<sup>+</sup> T cell numbers. (Gazzard et al., 2010).

Although the symptoms of immune deficiency characteristic of AIDS do not appear for years after a person is infected, the bulk of CD4<sup>+</sup> T cell loss occurs during the first weeks of infection, especially in the intestinal mucosa, which harbors the

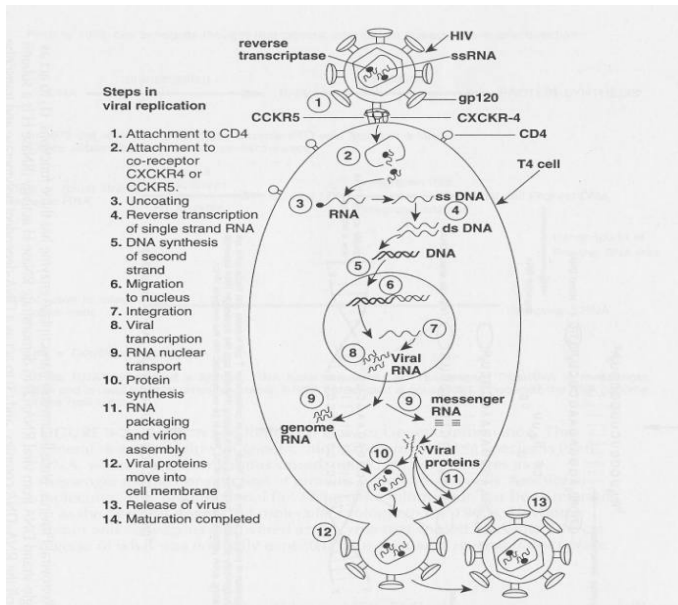


Fig 3. Shows HIV Virus Replication ( Guss., 1994).

majority of the lymphocytes found in the body (Guerrant et al., 1990). The reason for the preferential loss of mucosal CD4<sup>+</sup> T cells is that a majority of mucosal CD4<sup>+</sup> T cells express the CCR5 coreceptor, whereas a small fraction of CD4<sup>+</sup> T cells in the bloodstream do so. HIV seeks out and destroys CCR5 expressing CD4<sup>+</sup> cells during acute infection. A vigorous immune response eventually controls the infection and initiates the clinically latent phase. However, CD4<sup>+</sup> T cells in mucosal tissues remain depleted throughout the infection; although enough remain to initially ward off life-threatening infections. Continuous HIV replication results in a state of generalized immune activation persisting throughout the chronic phase. Immune activation, which is reflected by the increased activation state of immune cells and release of proinflammatory cytokines, results from the activity of several HIV gene products and the immune response to ongoing HIV replication. Another cause is the breakdown of the immune surveillance system of the mucosal barrier caused by the depletion of mucosal CD4<sup>+</sup> T cells during the acute phase of disease. This results in the systemic exposure of the immune system to microbial components of the gut's normal flora, which in a healthy person is kept in check by the mucosal immune system. The activation and proliferation of T cells that results from immune activation provides fresh targets for HIV infection. However, direct killing by HIV alone cannot account for the observed depletion of CD4<sup>+</sup> T cells since only 0.01–0.10% of CD4<sup>+</sup> T cells in the blood are infected. A major cause of CD4<sup>+</sup> T cell loss appears to result from their heightened susceptibility to apoptosis when the immune system remains activated. Although new T cells are continuously produced by the thymus to replace the ones lost, the regenerative capacity of the thymus is slowly destroyed by direct infection of its thymocytes by HIV. Eventually, the minimal number of CD4<sup>+</sup> T cells necessary to maintain a sufficient immune response is lost, leading to AIDS (Ghosh., 1986).

### Cells affected

The virus, entering through which ever route, acts primarily on the following cells: Lymphoreticular system:

- CD<sub>4</sub><sup>+</sup> T-Helper cells
- Macrophages
- Monocytes
- B-lymphocytes
  - Certain endothelial cells
  - Central nervous system:
- Microglia of the nervous system
- Astrocytes
- Oligodendrocytes

Neurons – indirectly by the action of cytokines and the gp-120.( Goldman et al., 2007)

### The effect

The virus has cytopathic effects but how it does it is still not quite clear. It can remain inactive in these cells for long periods, though. This effect is hypothesized to be due to the CD<sub>4</sub>-gp120 interaction. The most prominent effect of HIV is its T-helper cell suppression and lysis. The cell is simply killed off or deranged to the point of being function-less (they do not respond to foreign antigens). The infected B-cells cannot produce enough antibodies either. Thus the immune system collapses leading to the familiar AIDS complications, like infections and neoplasms (vide supra) (Grant I et al., 2005).

- Infection of the cells of the CNS cause acute aseptic meningitis, subacute encephalitis, vacuolar myelopathy and peripheral neuropathy. Later it leads to even AIDS dementia complex.

The CD<sub>4</sub>-gp120 interaction (see above) is also permissive to other viruses like Cytomegalovirus, Hepatitis virus, Herpes simplex virus, etc. These viruses lead to further cell damage i.e. cytopathy. (Wadia et al., 2001)

### DIAGNOSIS & TESTS

HIV is most commonly diagnosed by testing your blood or saliva for the presence of antibodies to the virus. Unfortunately, these types of HIV tests aren't accurate immediately after infection because it takes time for your body to develop these antibodies — usually up to 12 weeks. In rare cases, it can take up to six months for an HIV antibody test to become positive. A newer type of test checks for HIV antigen, a protein produced by the virus immediately after infection. This test can confirm a diagnosis within days of infection. An earlier diagnosis may prompt people to take extra precautions to prevent transmission of the virus to others. (Zaidi et al., 2002)

### Tests to tailor treatment

These tests include:

- **CD4 count.** CD4 cells are a type of white blood cell that's specifically targeted and destroyed by HIV. A healthy person's

CD4 count can vary from 500 to more than 1,000. Even if a person has no symptoms, HIV infection progresses to AIDS when his or her CD4 count becomes less than 200.

- **Viral load.** This test measures the amount of virus in your blood. Studies have shown that people with higher viral loads generally fare more poorly than do those with a lower viral load.
- **Drug resistance.** This type of test determines if your strain of HIV is resistant to any anti-HIV medications.

### HIV antibody test

HIV antibody tests are the most appropriate test for routine diagnosis of HIV among adults. Antibody tests are inexpensive and very accurate. The ELISA antibody test (enzyme-linked immunosorbent) also known as EIA (enzyme immunoassay) was the first HIV test to be widely used.

### How do antibody tests work?

When a person is infected with HIV, their body responds by producing special proteins that fight infection, called antibodies. An HIV antibody test looks for these antibodies in blood, saliva or urine. If antibodies to HIV are detected, it means a person has been infected with HIV. There are only two exceptions to this rule:

- Babies born to HIV infected mothers retain their mother's antibodies for up to 18 months, which means they may test positive on an HIV antibody test, even if they are actually HIV negative. Normally babies who are born to HIV positive mothers receive a PCR test (see below) after birth.
- Some people who have taken part in HIV vaccine trials may have HIV antibodies even if they are not infected with the virus.

Most people develop detectable HIV antibodies within 6 to 12 weeks of infection. In *very* rare cases, it can take up to 6 months and there are nearly always very particular reasons for antibodies developing so late such as other auto-immune disorders. It is exceedingly unlikely that someone would take longer than 6 months to develop antibodies.

### What is a window period?

The 'window period' is a term used to describe the period of time between HIV infection and the production of antibodies. During this time, an antibody test may give a 'false negative' result, which means the test will be negative, even though a person is infected with HIV. To avoid false negative results, antibody tests are recommended three months after potential exposure to HIV infection. A negative test at three months will almost always mean a person is not infected with HIV. If an individual's test is still negative at six months, and they have not been at risk of HIV infection in the meantime, it means they are not infected with HIV. It is very important to note that if a person is infected with HIV, they can still transmit the virus to others during the window period.

### How accurate are antibody tests?

Antibody tests are extremely accurate when it comes to detecting the presence of HIV antibodies. ELISA tests are very sensitive and so will detect very small amounts of HIV antibody. This high level of sensitivity however, means that their specificity (ability to distinguish HIV antibodies from other antibodies) is slightly lowered. There is therefore a very small chance that a result could come back as 'false positive'.

A false positive result means that although a person may not be infected with HIV, their antibody test may come back positive. All positive test results are followed up with a confirmatory test, such as:

- A Western blot assay – One of the oldest but most accurate confirmatory antibody tests. It is complex to administer and may produce indeterminate results if a person has a transitory infection with another virus.
- An indirect immunofluorescence assay – Like the Western blot, but it uses a microscope to detect HIV antibodies.
- A line immunoassay - Commonly used in Europe. Reduces the chance of sample contamination and is as accurate as the Western Blot.
- A second ELISA – In resource-poor settings with relatively high prevalence, a second ELISA test may be used to confirm a diagnosis. The second test will usually be a different commercial brand and will use a different method of detection to the first.

When two tests are combined, the chance of getting an inaccurate result is less than 0.1%. (King et al., 2003)

### Rapid HIV tests

These tests are based on the same technology as ELISA tests, but instead of sending the sample to a laboratory to be analysed, the rapid test can produce results within 20 minutes. Rapid tests can use either a blood sample or oral fluids. They are easy to use and do not require laboratory facilities or highly trained staff. All positive results from a rapid test must be followed up with a confirmatory test, the results of which can take from a few days to a few weeks. (Kwara et al., 2010)

### Antigen test (P24 test)

Antigens are the substances found on a foreign body or germ that trigger the production of antibodies in the body. The antigen on HIV that most commonly provokes an antibody response is the protein P24. Early in HIV infection, P24 is produced in excess and can be detected in the blood serum (although as HIV becomes fully established in the body it will fade to undetectable levels). P24 antigen tests are not usually used for general HIV diagnostic purposes, as they have a very low sensitivity and they only work before antibodies are produced in the period immediately after HIV infection. They are now most often used as a component of 'fourth generation' tests (Luft et al., 2000).

#### Fourth generation tests

Some of the most modern HIV tests combine P24 antigen tests with standard antibody tests to reduce the 'diagnostic window'. Testing for antibodies and P24 antigen simultaneously has the advantage of enabling earlier and more accurate HIV detection. In the UK, fourth generation tests are the primary recommendation for HIV testing among individuals, but are not offered by all testing sites. During June 2010, the FDA approved the first fourth generation test in the United States.

#### PCR test

A PCR test (Polymerase Chain Reaction test) can detect the genetic material of HIV rather than the antibodies to the virus, and so can identify HIV in the blood within two or three weeks of infection. The test is also known as a viral load test and HIV NAAT (nucleic acid amplification testing). Babies born to HIV positive mothers are usually tested using a PCR test because they retain their mother's antibodies for several months, making an antibody test inaccurate. Blood supplies in most developed countries are screened for HIV using PCR tests. However, they are not often used to test for HIV in individuals, as they are very expensive and more complicated to administer and interpret than a standard antibody test.

#### HIV home sampling and HIV home testing

It is generally recommended that an HIV test is carried out in a healthcare setting. However, in some countries home sampling and home testing kits are available.

#### Home sampling

With a home sampling kit, a person can take a sample (usually a blood sample) and send it to a laboratory for testing. They can phone up for the results a few days later. If the result is positive then a professional counsellor will provide emotional support and referrals. The main advantages of home sampling are convenience, speed, privacy and anonymity.

#### Home testing

A home self-test involves a person conducting a rapid antibody HIV test in their home. The person takes either a blood or saliva sample and can interpret the result within minutes. A positive result will require a further confirmatory blood-test in a clinic. In many countries it is illegal to sell HIV test kits to the public. If a test is purchased over the internet, there is no guarantee that the test kit is genuine or will provide accurate results. (McAllister et al., 2008)

### TREATMENT

#### Antiviral therapy

Current treatment for HIV infection consists of highly active antiretroviral therapy, or HAART. This has been highly beneficial to many HIV-infected individuals since its introduction in 1996 when the protease inhibitor-based HAART initially

became available. Current optimal HAART options consist of combinations (or "cocktails") consisting of at least three drugs belonging to at least two types, or "classes," of antiretroviral agents. Typical regimens consist of two nucleoside analogue reverse transcriptase inhibitors (NRTIs or NRTIs) plus either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor (NNRTI). (Bhargava et al. 2010) Because HIV disease progression in children is more rapid than in adults, and laboratory parameters are less predictive of risk for disease progression, particularly for young infants, treatment recommendations are more aggressive for children than for adults.

In developed countries where HAART is available, doctors assess the viral load, CD4 counts, rapidity of CD4 decline and patient readiness while deciding when to recommend initiating treatment. Traditionally, treatment has been recommended for otherwise asymptomatic patients when CD4 cell counts fall to 200-250 cells per microliter of blood. However, beginning treatment earlier (at a CD4 level of 350 cells/microliter) may significantly reduce the risk of death. Standard goals of HAART include improvement in the patient's quality of life, reduction in complications, and reduction of HIV viremia below the limit of detection, but it does not cure the patient of HIV nor does it prevent the return, once treatment is stopped, of high blood levels of HIV, often HAART resistant. Moreover, it would take more than the lifetime of an individual to be cleared of HIV infection using HAART. Despite this, many HIV-infected individuals have experienced remarkable improvements in their general health and quality of life, which has led to the plummeting of HIV-associated morbidity and mortality.

In the absence of HAART, progression from HIV infection to AIDS occurs at a median of between nine to ten years and the median survival time after developing AIDS is only 9.2 months. HAART is thought to increase survival time by between 4 and 12 years. For some patients, which can be more than fifty percent of patients, HAART achieves far less than optimal results, due to medication intolerance/side effects, prior ineffective antiretroviral therapy and infection with a drug-resistant strain of HIV. Non-adherence and non-persistence with therapy are the major reasons why some people do not benefit from HAART. The reasons for non-adherence and non-persistence are varied. Major psychosocial issues include poor access to medical care, inadequate social supports, psychiatric disease and drug abuse. HAART regimens can also be complex and thus hard to follow, with large numbers of pills taken frequently. Side effects can also deter people from persisting with HAART, these include lipodystrophy, dyslipidaemia, diarrhoea, insulin resistance, an increase in cardiovascular risks and birth defects. Anti-retroviral drugs are expensive, and the majority of the world's infected individuals do not have access to medications and treatments for HIV and AIDS. However, the costs of anti-retroviral drugs have fallen recently in low-income countries. Moreover, patients' quality of life indices benefit from anti-retroviral treatment especially if healthcare services are adequate. In the absence of a cure for AIDS, anti-retroviral treatment is likely to be a cost-effective strategy for

enhancing well-being of AIDS patients and their dependents. There are currently more than 20 approved antiretroviral drugs in the US and Europe (including combined formulations) and many more in the expanded access programmes and trials. Most antiretroviral drugs have at least three names. Sometimes a drug is referred to by its research or chemical name, such as AZT. (Bonnet et al., 2004) The second name is the generic name for all drugs with the same chemical structure; for example AZT is also known as zidovudine. The third name is the brand name given by the pharmaceutical company; one of the brand names for zidovudine is Retrovir. Lastly, an abbreviation of the common name might sometimes also be used, such as ZDV, which is the fourth name given to zidovudine. The drugs listed here are those approved by the US Food and Drug Administration (FDA). This list does not contain new drugs that are currently under development and still in clinical trials, which are covered in our new AIDS drugs page. Further information should be available from your doctor. (A Pocket Guide., 2006)

### Nucleoside Reverse Transcriptase Inhibitors (NRTI)

These drugs interrupt the virus from duplicating, which may slow the spread of HIV in the body. They include:

- Abacavir (Ziagen, ABC)
- Didanosine (Videx, dideoxyinosine, ddI)
- Emtricitabine (Emtriva, FTC)
- Lamivudine (Epivir, 3TC)
- Stavudine (Zerit, d4T)
- Tenofovir (Viread, TDF)
- Zalcitabine (Hivid, ddC)
- Zidovudine (Retrovir, ZDV or AZT).

Combinations of NRTIs make it possible to take lower doses and maintain effectiveness. These drugs include Combivir (Zidovudine and Lamivudine), Trizivir (Zidovudine, Lamivudine and Abacavir), Epzicom (Abacavir and Lamivudine) and Truvada (Tenofovir and Lamivudine). We expect more combination drugs to be available in the future (Yarchoan et al., 2005)

### Side Effects of NRTIs (Palefsky 2007).

Side effects from taking NRTIs vary, depending on the individual. We recommend that you consult with your doctor regarding any side effects you experience. Common side effects include:

- **Abacavir (Ziagen, ABC)** — Side effects may include fever, rash, fatigue, vomiting, diarrhea, abdominal pain, malaise or fatigue, loss of appetite and respiratory symptoms.
- **Dideoxyinosine (Videx, ddI)** — Side effects may include nausea, vomiting and bloating. More serious side effects include pancreatitis and peripheral neuropathy. Peripheral neuropathy is a common neurological disorder resulting from damage to the peripheral nerves. Symptoms of peripheral neuropathy include a sharp, burning pain sensation in the hands or legs.

- **Lamivudine (Epivir, 3TC)** — Side effects may include cough, diarrhea, dizziness, headache, loss of appetite, mild stomach cramps or pain and trouble sleeping. More serious side effects include burning, tingling, or pain in the hands, arms, feet, or legs; chills; ear, nose, or throat problems; fever; muscle aches; nausea; pale skin; severe stomach pain; skin rash; unusual tiredness or weakness; vomiting; and yellow eyes or skin.
- **Stavudine (Zerit, d4T)** — Side effects may include peripheral neuropathy. Symptoms of peripheral neuropathy include a sharp, burning pain sensation in the hands or legs. In rare cases, Stavudine also may cause pancreatitis.
- **Tenofovir (Viread, TDF)** — Side effects may include weakness and lack of energy, headache, diarrhea, nausea, vomiting and intestinal gas. More serious side effects include liver or kidney failure and pancreas disease.
- **Zalcitabine (Hivid, ddC)** — Side effects may include oral ulcers and peripheral neuropathy. Symptoms of peripheral neuropathy include a sharp, burning pain sensation in the hands or legs.
- **Zidovudine (Retrovir, ZDV or AZT)** — Side effects may include diarrhea, nausea, vomiting, headache, insomnia, weakness and fatigue, bone marrow suppression, anemia and neutropenia. Neutropenia refers to an abnormally low number of neutrophils in the blood. Neutrophils, a type of white blood cell, help fight bacterial infections. Neutropenia isn't a disease but a sign of an underlying problem. In mild cases, it may cause no symptoms. Severe neutropenia increases the risk of infection of the lungs, kidneys, blood and skin.

### Protease Inhibitors (PI)

These FDA-approved drugs interrupt virus replication at a later step in the virus life cycle. Protease inhibitors include:

- Amprenavir (Agenerase, APV)
- Atazanavir (Reyataz, ATV)
- Fosamprenavir (Lexiva, FOS)
- Indinavir (Crixivan, IDV)
- Lopinavir (Kaletra, LPV/r)
- Ritonavir (Norvir, RIT)
- Saquinavir (Fortovase, Invirase, SQV) (Palella et al., 1998)

### Side Effects of PIs

Side effects from protease inhibitors vary, depending on the individual. We recommend that you consult with your doctor to discuss any side effects you may experience. The following is a list of protease inhibitors and their possible side effects:

- **Amprenavir (Agenerase, APV)** — Side effects include nausea, diarrhea, vomiting, rash, numbness around the mouth and abdominal pain. About 1 percent of people have serious skin reactions, including Stevens-Johnson syndrome.

- **Atazanavir (Reyataz, ATV)** — Side effects include headache, rash, stomach pain, vomiting, depression, increased cough, trouble sleeping, tiredness, back pain, joint pain, as well as numbness, tingling or burning of the hands or feet. More serious side effects include yellowing of the eyes or skin, change in heart rhythm, diabetes and high blood sugar, diarrhea, infection, nausea and blood in the urine.
- **Fosamprenavir (Lexiva, FOS)** — Side effects may include rash, nausea and diarrhea.
- **Indinavir (Crixivan, IDV)** — Side effects include change in sense of taste, diarrhea, nausea, vomiting, dizziness or drowsiness, general feeling of weakness, headache, stomach pain and trouble sleeping. More serious side effects include kidney stones, changes in body fat, increased bleeding in patients with hemophilia, high sugar and fat levels in the blood, and onset or worsening of diabetes.
- **Lopinavir (Kaletra, LPV/r)** — Side effects include abdominal pain, abnormal stools or bowel movements, diarrhea, feeling weak or tired, headache and nausea. In addition, patients taking Lopinavir should be monitored for possible liver problems. People taking the drug who have liver disease, such as hepatitis B or hepatitis C, may experience a worsening of their liver condition. A small number of patients have experienced severe liver problems.
- **Nelfinavir (Viracept, NFV)** — Side effects include diarrhea, weakness, headache, nausea and abdominal pain.
- **Ritonavir (Norvir, RIT)** — Ritonavir often is used in combination with other protease inhibitors — an approach called "Ritonavir boosting." Studies have shown that small amounts of Ritonavir, taken in combination with other PIs, can boost or increase the strength and effectiveness of some drugs and may overcome drug and food interactions. In some cases, "Ritonavir boosting" reduces the number of pills necessary or how often they're taken. The disadvantage is that Ritonavir interacts with many drugs, both prescription and over the counter. It is important that you speak with your doctor about all your medications before taking Ritonavir. Side effects include general weakness, burning or prickling sensation in the hands and feet, stomach pain, diarrhea, constipation, indigestion, flatulence, nausea, vomiting, loss of appetite, change in sense of taste, headache, dizziness, drowsiness, insomnia, fever, throat irritation, abnormal thinking, rash, sore throat and sweating. More serious effects include pancreas disease, changes in body fat, increased bleeding in patients with hemophilia, high sugar and fat levels in the blood, and onset or worsening of diabetes.
- **Saquinavir (Fortovase, Invirase, SQV)** — Side effects are related to the stomach and intestinal system, including diarrhea, nausea, stomach-intestinal pain, heartburn, rectal gas, vomiting, altered taste sensation, headache, fatigue, depression, sleep disturbance including insomnia, anxiety, sex

drive disorder, muscle aches, rash, hepatitis and abnormal fat redistribution.( Panda et al., 2002)

## Other AIDS Medications

### *Fusion Inhibitors*

Fusion inhibitors are a new class of drugs that act against HIV by preventing the virus from fusing with the inside of a cell, preventing it from replicating. The group of drugs includes Enfuvirtide, also known as Fuzeon or T-20. (Piot et al., 2007)

### *Highly Active Antiretroviral Therapy (HAART)*

In 1996, highly active antiretroviral therapy (HAART) was introduced for people with HIV and AIDS. HAART — often referred to as the anti-HIV "cocktail" — is a combination of three or more drugs, such as protease inhibitors and other anti-retroviral medications. The treatment is highly effective in slowing the rate at which the HIV virus replicates itself, which may slow the spread of HIV in the body. (Sadler June 1997). The goal of HAART is to reduce the amount of virus in your body, or the viral load, to a level that can no longer be detected with blood tests. (Pollok. , 2001).

### *Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)*

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) block the infection of new cells by HIV. These drugs may be prescribed in combination with other anti-retroviral drugs. NNRTIs include:

- Delvaridine (Rescriptor, DLV)
- Efavirenz (Sustiva, EFV)
- Nevirapine (Viramune, NVP) (Satishchandra et al., 2000).

## Future Aspects

The HIV/AIDS pandemic, though global, is overwhelmingly concentrated in sub-Saharan Africa. Although this situation has exacted a terrible human cost, the rest of the world has been largely unaffected by Africa's tragedy. (Sepkowitz., 2001). Things will be very different, however, in the next major area of HIV infection. Eurasia (which for the purposes of this essay is considered to be the territory encompassing the continent of Asia, plus Russia) will likely be home to the largest number of HIV victims in the decades ahead. Driven by the spread of the disease in the region's three largest countries -- China, India, and Russia -- the coming Eurasian pandemic threatens to derail the economic prospects of billions and alter the global military balance. And although the devastating costs of HIV/AIDS are clear, it is unclear that much will be done to head off the looming catastrophe.( Sterling et al., 2009)

## CONCLUSION

Without treatment, the net median survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype, and the median survival rate after diagnosis of AIDS in resource-limited settings where treatment is not available ranges between 6 and 19 months, depending on the study. In areas where it is widely available, the development of HAART as



effective therapy for HIV infection and AIDS reduced the death rate from this disease by 80%, and raised the life expectancy for a newly diagnosed HIV-infected person to about 20 years.

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