



MEDICAL VIROLOGY (450)



The Supervision Of :

Nora Al-Kubaisi

<u>NO</u>	<u>STUDANET NAME</u>	<u>ID NUMBER</u>
<u>1</u>	ABRAR SHAHEEN	431200651
<u>2</u>	KHOLOUD AL TUWALAH	432201194
<u>3</u>	REHAM ALFLAJ	432200929
<u>4</u>	SEHAM ALBOGAMI	431200804
<u>5</u>	NOUF ALQADI	432202083

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Introduction

WHAT IS HIV ?

It is “**Human Immunodeficiency Virus**” And also they have other names for HIV:

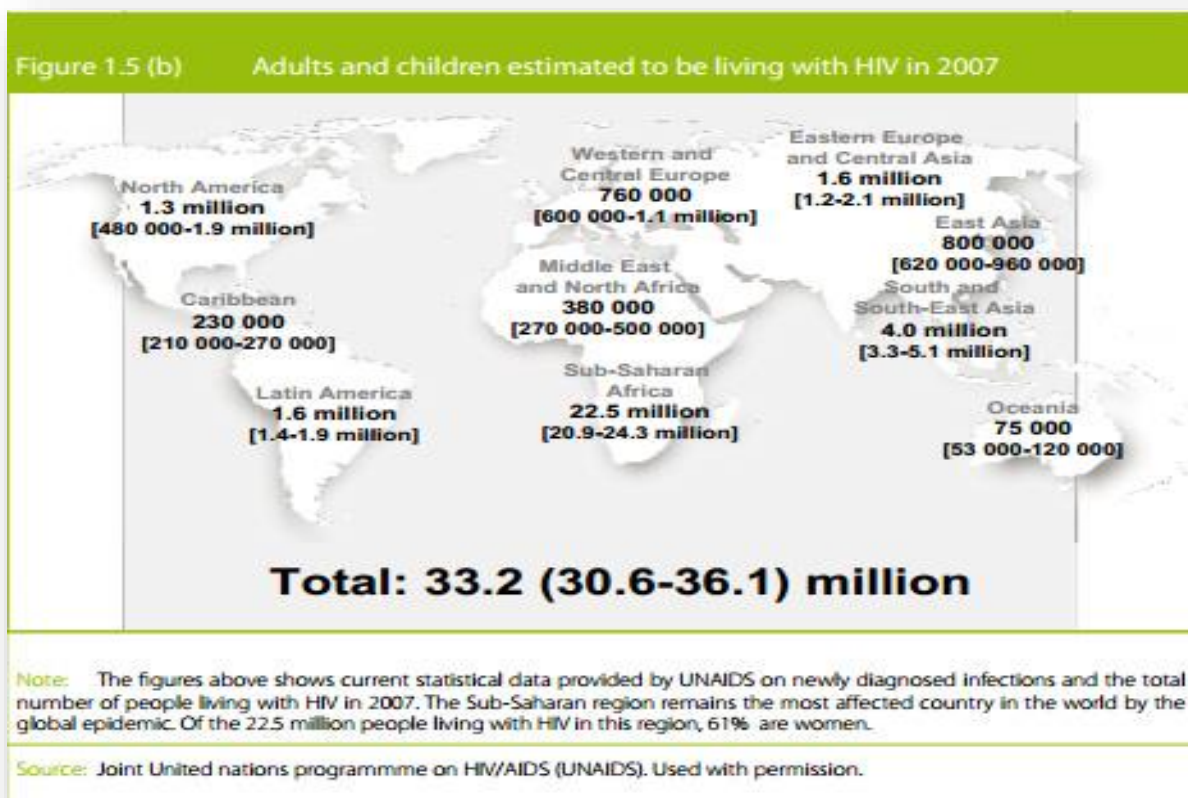
Former names of the virus include:

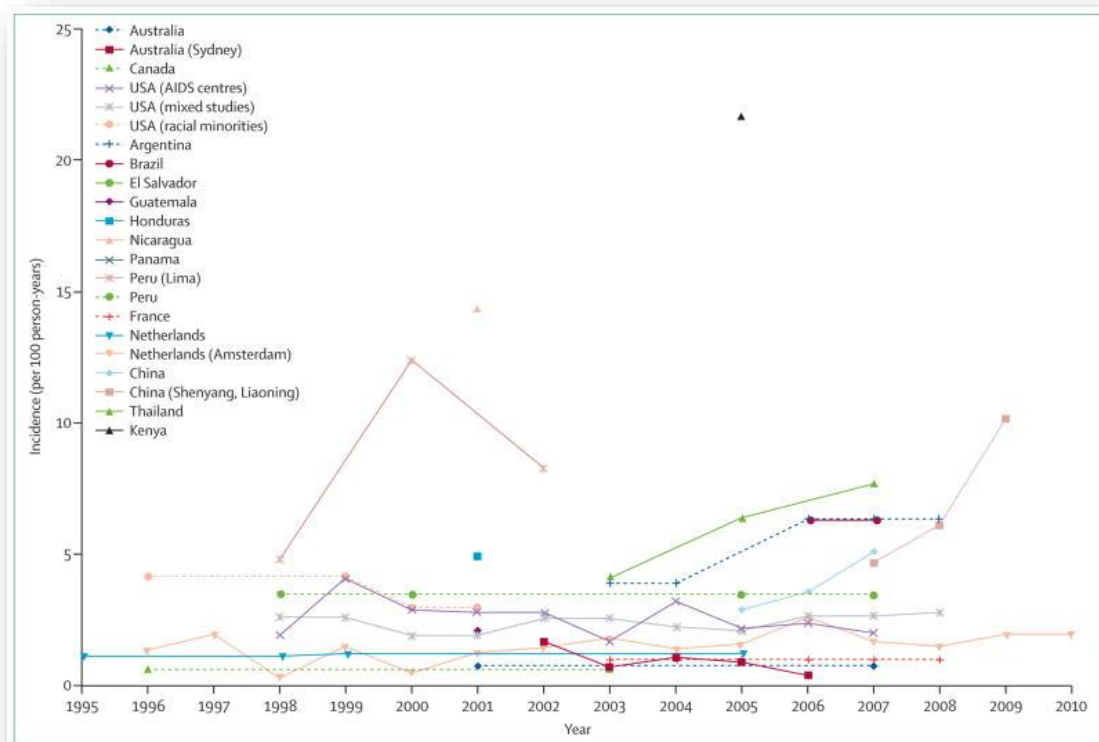
- 1-Human T cell lymphotropic virus (HTLV-III)
- 2- Lymphadenopathy associated virus (LAV)
- 3- AIDS associated retrovirus (ARV)

The first cases of acquired immunodeficiency syndrome (AIDS) were reported in Los Angeles in the United States in the spring of 1981. Injection drug use (IDU) was identified as a direct route of HIV infection and transmission among injection drug users. The largest group of early AIDS cases comprised gay and bisexual men (referred to as men who have sex with men(or MSMs). The virus is transmitted primarily through the exchange of blood using needles, syringes, or other IDU equipment (e.g., cookers, rinse water, cotton) that were previously used by an HIV-infected person

EPIDEMIOLOGY

Despite the improved access to antiretroviral treatment, the implementation of prevention programs and development of low cost testing for early detection, the HIV epidemic is on the rise in many countries. More than 2.6 million more people were living with HIV in 2006 than in 2004. The total number of individuals with the infection in 2006 reached 39.5 million of which 17.7 million were women and 2.3 million were children under the age of 15 years. Sadly, the number of children with HIV infection accounted for 40% of the overall number of newly diagnosed people in 2006. The 2007 statistics show that this number has remained almost steady.





AIDS was first recognized in 1981 and is caused by HIV in Los Angeles in USA.

In 1995, the virus exist in Nerthland.After one year (1996) USA has first place in epidemic with this virus, and enter to Canada and Amesterdam in Nerthland.For two years (1997-1998) the epidemiology was stable.

In 1999 the virus highly spread in Peru(Lima), and USA (ratial minorities) has same percentage of infection with this virus befor two years, and increase in USA (AIDS center) and Nerthland (Amesterdam).In 2000, the infection decrease in whole world.

In (2001-2002), it's increase in Nerthland (Amesterdam) and USA, decrease in Peru and was stable but enter to Australia (Sydney).

In 2003, the infection of the virus was low compared with several years, but it appear in Thailand and Argentina in high level and France in low level.

After 2003 to 2005 the percentage was stable and increase in Thailand.

In 2005, the virus enter to Chaina and spread highly in Argentina.

The first infection in Barazil At 2006, in this year the virus in Australia (Sydney) was stop.

In 2007, the spread of this virus stop in many countries

(Chaina,Thailand,USA,Barazil,Australia,Peru) but it also complete in other contries and enter to Shenyang,Liaoning in Chaina.

At 2008,2009 the virus disappear in Argentina and Chaina (Shenyang,Liaoning).

To 2010, the virus exist in Nerthland (Amesterdam) and disappear in almost all contries.

Classification of HIV :

HIV IS CLASSIFIED IN THE:

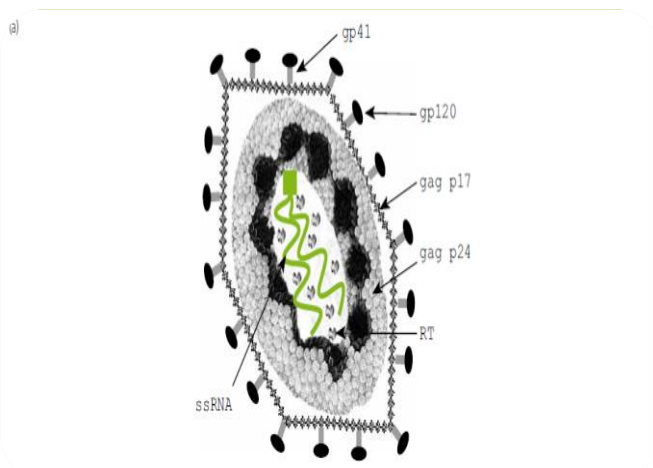
Family	Retroviridae
Subfamily	Lentivirinae,
Genus	Lentivirus

characterizes and structure of viros genome :

The structure of HIV follows the typical pattern of the retrovirus family, comprising a single stranded , positive-sense ribonucleic acid (RNA) genome of about 9.7 kilobases. There are two strands of HIV RNA and each strand has a copy of the virus's nine genes (Figure 1.1a).

The RNA is surrounded by a cone-shaped capsid which consists of approximately 2000 copies of the p24 viral protein. Surrounding the capsid is the viral envelope. The viral envelope is composed of a lipid bilayer membrane, formed from the cellular membrane of the host cell during budding of the newly formed virus particle. Host-cell proteins, such as the major histocompatibility complex (MHC) antigens and actin, remain embedded within the viral envelope, along with the viral envelope protein.

Each envelope subunit consists of two non-covalently linked membrane proteins: glycoprotein (gp) 120, the outer envelope protein, and gp41, the transmembrane protein that anchors the glycoprotein complex to the surface of the virion. The envelope protein is the most variable component of HIV, although gp120 itself is structurally divided into highly variable (V) and more constant (C) regions. The variability of V regions may be a product of envelope functionality, as has been especially well described in V3, where amino acid changes alter coreceptor use. The variability of the HIV envelope also confers a uniquely complex antigenic diversity.

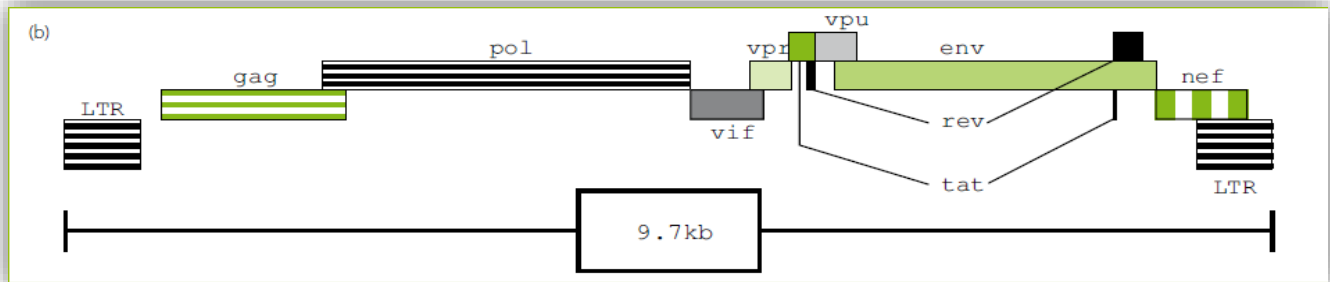


(Figure 1.1a)

HIV virion structure highlighting envelope (gp120, gp41) and structural (gag p17, gag p24) proteins. RT = reverse transcriptase; ssRNA = single-stranded RNA.

GENOME OF HIV :

The genomic organisation of HIV is extremely efficient. Use of all three reading frames (the triplet codes) of the genetic sequence permits overlapping of gene-coding regions. There are nine genes of HIV (Figure 1.1b).



(b) The single-stranded RNA genome of HIV efficiently encodes nine major structural and catalytic proteins by using overlapping parts of the genome. Additionally, the nucleic acid secondary and tertiary structure performs functions independent of translation. LTR = long-terminal repeat

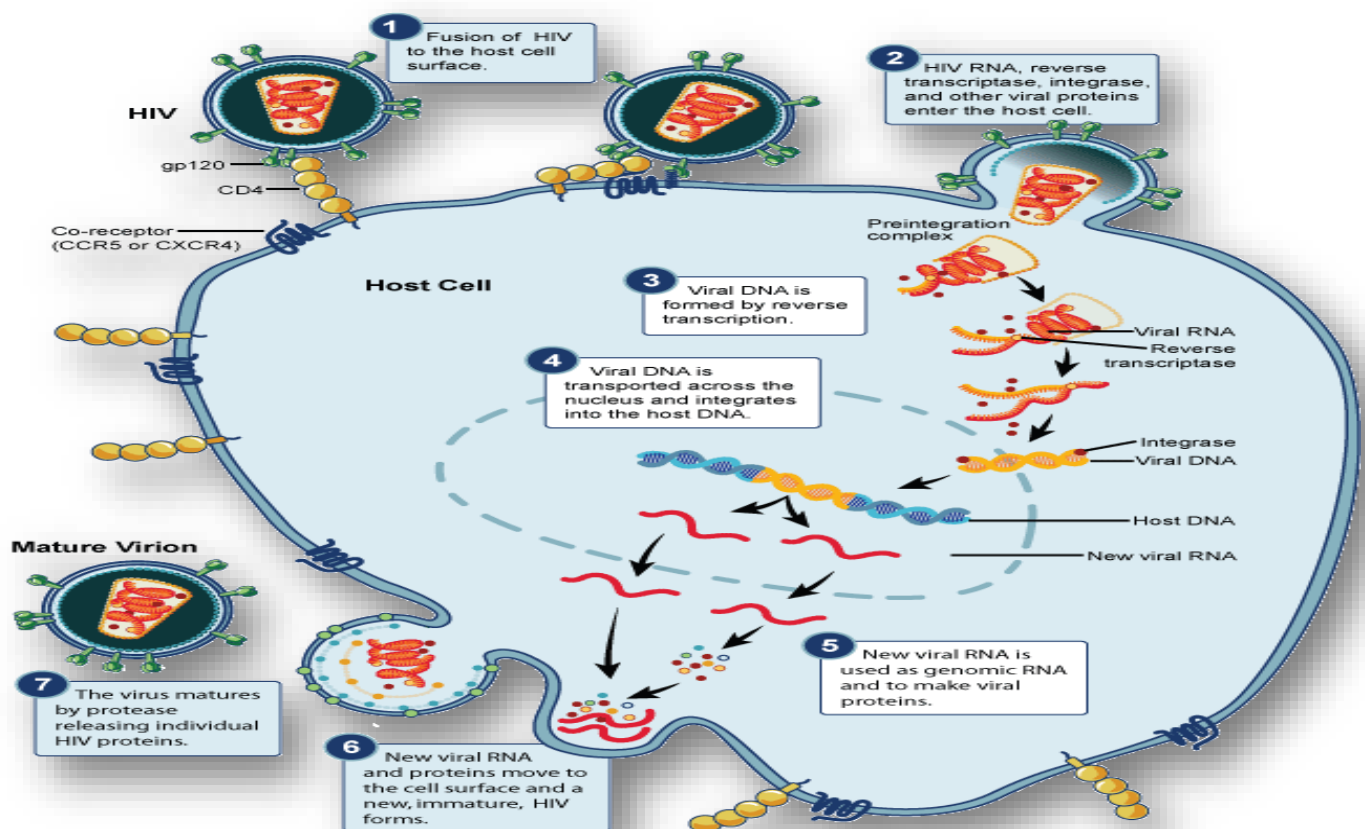
THE TARGETED ORGAN :

The AIDS virus that enters through sexual organs spreads to the lymph nodes and damages the immune system of the body {as the lymph helps fight diseases or provide immunity to the body }

HIV Replication Cycle

STEPS IN THE HIV REPLICATION CYCLE

1. Fusion of the HIV cell to the host cell surface.
2. HIV RNA, reverse transcriptase, integrase, and other viral proteins enter the host cell.
3. Viral DNA is formed by reverse transcription.
4. Viral DNA is transported across the nucleus and integrates into the host DNA.
5. New viral RNA is used as genomic RNA and to make viral proteins.
6. New viral RNA and proteins move to cell surface and a new, immature, HIV virus forms.
7. The virus matures by protease releasing individual HIV proteins.



HIV REPLICATION CYCLE GLOSSARY:

CD4: a large glycoprotein that is found on the surface of helper T cells, regulatory T cells, monocytes, and dendritic cells. Its natural function is as a co-receptor that assists the T cell receptor (TCR) to activate its T cell following an interaction with an antigen presenting cell. CD4 is a primary receptor used by HIV-1 to gain entry into host T cells.

CO-RECEPTOR (CCR5 OR CXCR4): protein molecules on the surface of lymphocytes or monocytes that bind to the gp120 protein of HIV and facilitate, usually with CD4, entry of viral nucleic acid and proteins into the cell.

DNA (DEOXYRIBONUCLEIC ACID): is a nucleic acid that contains the molecular basis of heredity for all known living organisms and some viruses and is found in the nuclei and mitochondria of eukaryotes. Chemically DNA consists of two polymer strands of units called nucleotides made up of one of four possible bases plus sugar and phosphate groups. The polymers are joined at the bases by hydrogen bonds to form a double helix structure.

FUSION OF VIRUS AND CELL MEMBRANES: a merging of cell and virus membranes that permits HIV proteins and nucleic acids to enter the host cell.

GENOMIC RNA: the nucleic acid that contains all of the hereditary information of a virus, and is found in a mature virion.

GP120: an HIV glycoprotein having a molecular weight of 120 that protrudes from the outer surface of the virion. This glycoprotein binds to a CD4 receptor on a T cell to facilitate entry of viral nucleic acid and proteins into the cell.

HIV (HUMAN IMMUNODEFICIENCY VIRUS): is a lentivirus and a member of the retrovirus family. HIV infects and destroys helper T cells of the immune system causing a marked reduction in their numbers. Loss of CD4 cells leads to generalized failure of the immune system and susceptibility to life threatening opportunistic infections.

INTEGRASE: An enzyme found in retroviruses including HIV that permits the viral DNA to be integrated into the DNA of the infected cell.

PREINTEGRATION COMPLEX (PIC): It is composed of viral RNA and proteins (nucleocapsid, p6, Vpr, integrase, and matrix) as well as some host proteins. It functions to reverse transcribe genomic RNA into double stranded DNA prior to integration into the host genomic DNA.

PROTEASE: an enzyme that hydrolyzes or cuts proteins and is important in the final steps of HIV maturation.

NUCLEUS: a membrane enclosed cellular organelle of eukaryotes that functions to contain the genomic DNA and to regulate gene expression.

REVERSE TRANSCRIPTASE : an enzyme found in HIV that creates double stranded DNA using viral RNA as a template and host tRNA as primers.

RNA (RIBONUCLEIC ACID) : a nucleic acid that differs from DNA in that it contains ribose and uracil as structural components.

RNA VIRUS : a virus that uses RNA as its genetic material and belongs to either Group III, IV, or V of the Baltimore Classification System of Viruses. HIV belongs to Group III, double stranded RNA viruses.

VIRION: a single and complete extracellular infective form of a virus that consists of an RNA

Pathology and clinical feature

HOW IS HIV TRANSMITTED ?

HIV CAN BE TRANSMITTED FROM AN INFECTED PERSON TO ANOTHER THROUGH:

- Blood (including menstrual blood)
- Vaginal secretions
- Breast milk

Blood contains the highest concentration of the virus, followed by semen, followed by vaginal fluids, followed by breast milk.

ACTIVITIES THAT ALLOW HIV TRANSMISSION:

- Unprotected sexual contact
- Direct blood contact, including injection drug needles, blood transfusions, accidents in health care settings or certain blood products
- Mother to baby (before or during birth, or through breast milk)

Sexual intercourse: In the genitals and the rectum, HIV may infect the mucous membranes directly or enter through cuts and sores caused during intercourse (many of which would be unnoticed). Vaginal and anal intercourse is a high-risk practice.



Sharing injection needles: An injection needle can pass blood directly from one person's blood stream to another. It is a very efficient way to transmit a blood-borne virus. Sharing needles is considered a high-risk practice.

Mother to Child: It is possible for an HIV-infected mother to pass the virus directly before or during birth, or through breast milk. Breast milk contains HIV, and while small amounts of breast milk do not pose significant threat of infection to adults, it is a viable means of transmission to infants.



THE FOLLOWING "BODILY FLUIDS" ARE NOT INFECTIOUS:

- Saliva
- Tears
- Sweat
- Feces
- Urine

HIV IS NOT SPREAD BY:

- Shaking hands
- Work together
- Eat together
- Hugging

WHAT IS THE HIV SYMPTOMS ?

Natural Course Of HIV/Aids :

STAGE 1 – PRIMARY:

- Short, flu-like illness - occurs one to six weeks after infection
- Mild symptoms
- Infected person can infect other people

STAGE 2 – ASYMPTOMATIC:

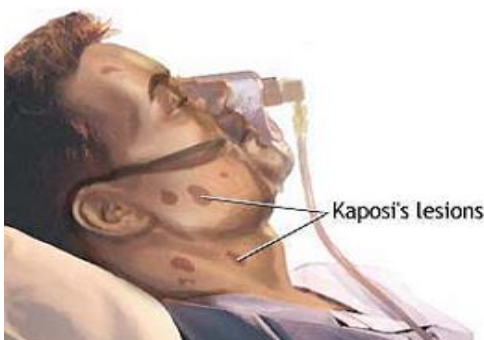
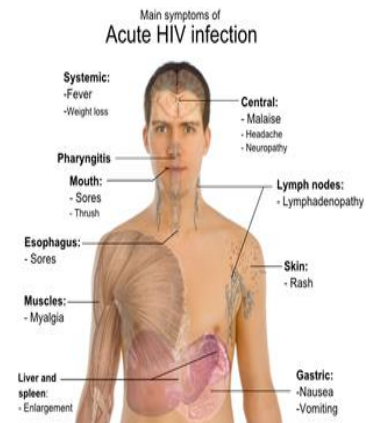
- Lasts for an average of ten years
- This stage is free from symptoms
- There may be swollen glands
- The level of HIV in the blood drops to low levels
- HIV antibodies are detectable in the blood

STAGE 3 – SYMPTOMATIC :

- The symptoms are mild
- The immune system deteriorates
- Emergence of opportunistic infections and cancers

STAGE 4 - HIV ⇒ AIDS:

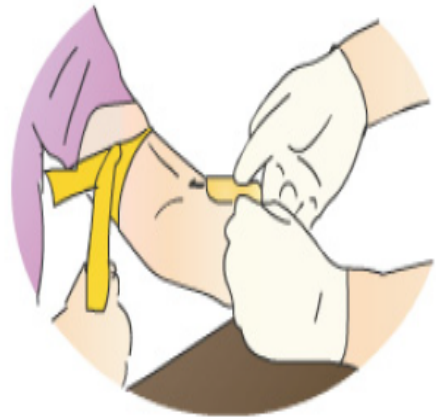
- The immune system weakens
- The illnesses become more severe leading to an AIDS diagnosis



DIAGNOSIS OF HIV :

If you think you may have HIV, you can easily get tested to find out if you have it.

The screening test for HIV checks for HIV antibodies in the blood. The body makes HIV antibodies to fight the virus. Since it usually takes 6 to 12 weeks for the body to make these antibodies, the test cannot be positive if done earlier than 6 weeks after an infection.



If an HIV test is positive, it is repeated. If the second test is also positive, there is another test that checks for HIV proteins in the blood. If that test is positive, a person is then diagnosed with HIV.

After diagnosing a person with HIV, the doctor uses a test to measure the amount of HIV in the blood. This is called a viral load. The higher the viral load is, the faster AIDS will probably develop. Viral load determines the suggested treatment.

If you engage in high risk behavior, such as unprotected sex or sharing needles for intravenous drug use, get tested for HIV every 3 to 6 months. Your test can be confidential or anonymous.

Most states require that you sign a consent form before having an HIV test. This guarantees that nobody can check you for HIV without you knowing.

A confidential test means that if you test positive, the results will be reported to your state health department, but will not be given to anyone else without your permission. An anonymous test is where your name is not recorded and no one besides you can ever learn the test result. Not all states have anonymous tests, but most provide confidential tests.

If you are pregnant, you may want to get tested even if you think you are not at risk. If you are HIV positive, treatment with antiretroviral drugs during your pregnancy could greatly reduce the chances of you passing the infection to your baby.

TREATMENT OF HIV:

Right now there is no cure for AIDS. However, treatment is available to slow its progression and improve the quality of life. Thanks to advanced medical treatment AIDS patient can live long productive lives. Doctors have however noticed that these same patients are at a higher risk for developing lung problems, rectal cancer, diabetes, kidney failure, and severe depression. It is not known whether these medical problems are because of the HIV virus or potentially because of the treatment itself.

The treatment for AIDS focuses on suppressing the growth of the virus and improving the patient's quality of life. This is called Highly Active Antiretroviral Therapy, or HAART. This is usually a combination of 3 or more drugs.

AIDS treatment is based on the levels of HIV in the blood, called the viral load. Viral loads are tested at the beginning of treatment and then every 3 to 4 months during treatment. In some cases viral loads are tested even more often.

Drugs used for treatment include antiretroviral drugs and fusion inhibitors. Antiretroviral drugs slow down the growth and reproduction of HIV. Fusion inhibitors stop the virus from reproducing by preventing its membrane from fusing with the membrane of the CD4 lymphocytes.

Laboratory diagnosis of HIV viruses

Tests for HIV differ in methodology as well as testing purpose. Generally, tests are done for three reasons: individual diagnosis, protection of blood or tissue products safety, and public health surveillance. According to the objective of testing, the most appropriate test is chosen based on convenience, test characteristics, and the population to whom the testing subject belongs.

1-SEROLOGY:

By ELISA : three months after HIV infection the ELISA/Western Blot Test is a series of blood screenings are performed to test for HIV. The enzyme-linked immuno assay (ELISA or EIA) . ELISA and the Western blot test detect HIV antibodies in your blood. Antibodies are proteins your immune system produces in response to the presence of foreign substances such as viruses. If you test positive for HIV on the ELISA test, your provider will order the Western blot test to confirm HIV infection..

2- MOLECULAR:

- 1-The reverse transcription polymerase chain reaction
- 2-nucleic acid sequence amplification.(NASBA)
- 3-Branched chain bDNA

1-SPECIFIC TESTS FOR HIV INFECTION:

• 1-ANTIGEN DETECTION:P24 ANTIGEN

After a single massive infection viral antigen p24 and RT may be detected in blood about 2 weeks.

• 2-VIRUS ISOLATION

The viruses present in circulation and body fluids within lymphocytes or free cells virus titres parallel p24 titres being high soon after infection low and antibody bound during the asymptomatic period and again high towards the end.

The infectivity being highest in the early phase and when the person becomes terminally ill. The virus is present in many parts of the body and can be isolated from the peripheral lymphocytes by the technique of co- cultivation of patients lymphocytes with the uninfected lymphocytes in the presence of interleukin-2. viral replication can be detected by RT.

• 3-DETECTION OF VIRAL NUCLEIC ACID

As the most sensitive and specific test, PCR has become the gold standard for diagnosis in all stages of HIV. PCR:DNA PCR -RNA PCR.

A related test, HIV RNA PCR be used for can diagnosis as well as for monitoring the level of viremia.

• 4-ANTIBODY DETECTION

The 24 weeks to months for the antibodies to appear after infection and during part of this period, the individual may be highly infectious known as the window period. infection can be detected during the window period by the p24 assay. Antibody testing will have to be done after 2. 6 months to ascertain whether infection has occurred or not. IgM antibodies disappear in 8-10 weeks while IgG antibodies remain throughout.

2-NON SPECIFIC TESTS FOR HIV:

- 1-total and differential leucocyte count.
- 2- T-lymphocyte subset assays
- 3-platelet count
- 4-IgG and IgG levels
- 5- skin tests for CMI

***SCREENING TEST:**

ELISA – Rapid test – Simple test

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