

HIV: ETIOLOGY, DIAGNOSIS, TREATMENT AND ALTERNATIVE THERAPIES

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Summary

HIV – infection has alarmed the population of the world for its severity of infection. Attempts in developing a novel vaccine, medicine are continuous and are under progress. In the present review we have highlighted the detailed knowledge, information regarding the diagnosis, its treatment and precaution in controlling the AIDS.

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Introduction

Human immunodeficiency virus (HIV) is a lentivirus (a member of the retrovirus family) that causes *acquired immunodeficiency syndrome* (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells. The four major routes of transmission are unsafe sex, contaminated needles, breast milk, and transmission from an infected mother to her baby at birth (perinatal transmission). Screening of blood products for HIV has largely eliminated transmission through blood transfusions or infected blood products in the developed world.^{1,2}

HIV infects primarily vital cells in the human immune system such as helper T cells (specifically CD4⁺ T cells), macrophages, and dendritic cells. HIV infection leads to low levels of CD4⁺ T cells through three main mechanisms: First, direct viral killing of infected cells; second, increased rates of apoptosis in infected cells; and third, killing of infected CD4⁺ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When CD4⁺ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections.³

DIAGNOSIS

Laboratory tests employed for the diagnosis of HIV infection may be classified into the following groups⁴

Antibody based tests

Screening tests

ELISA (Enzyme-linked immunosorbent assay)

Rapid tests

Supplemental or confirmatory

Immunofluorescent assay (IFA)

Western blot

Other tests

p24 antigen

Polymerase chain reaction (PCR)

Alternative to classical tests

Oral fluid (saliva) HIV tests

Urine tests

Screening tests

ELISA (Enzyme-linked immunosorbent assay)

Standard screening tests for HIV include detection of anti-HIV antibodies in blood by enzyme immunoassays (EIA/ELISA). These tests use virus antigens (proteins) to detect the circulating antibodies. The bound antibodies are detected by a colorimetric reaction. These tests become positive 3-12 weeks after infection and have more than 99% sensitivity and greater than 95% specificity. The tests can detect infection with HIV-1 and HIV-2. However, false positives may occur in people with multiple blood transfusions, malignancies, alcoholic hepatitis etc. False negatives can occur very early in the infection or in patients who do not produce enough detectable antibodies or very late in the infection.

Generations

1. First generation - whole viral lysates
2. Second generation - recombinant antigen
3. Third generation - synthetic peptide
4. Fourth generation - antigen + antibody (Simultaneous detection of HIV antigen and antibody) - HIV duo

Rapid tests:

Apart from the ELISA tests which take two to three hours to perform and require specialised equipment, several rapid tests are available which give the result within half an hour. Rapid tests give a visual reaction and include dot-blot tests and particle agglutination. The rapid tests detect HIV-1 and 2 and do not require specialised equipment and can be easily done in smaller laboratories. However, specificity of these tests is lower than ELISA. These tests may not detect infection when the antibody level is very low.

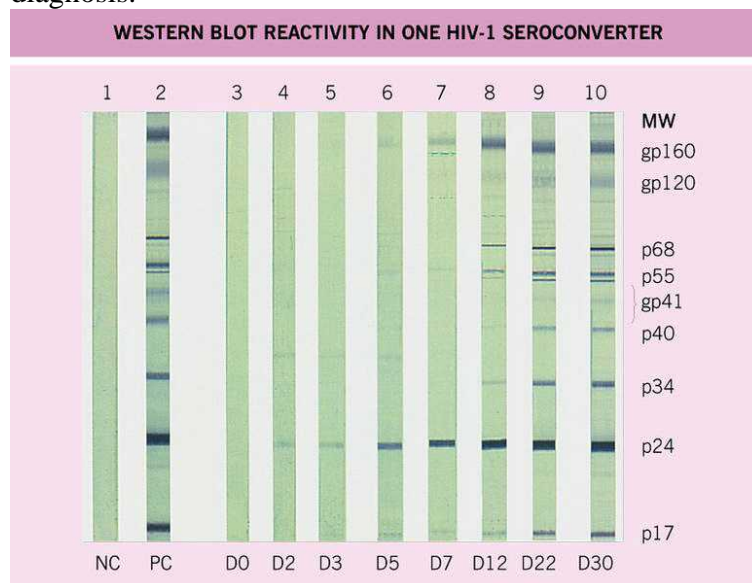
Supplemental or confirmatory

Western Blot Tests: It illustrate the Window Period

In the Western Blot (WB) test, viral antigens are separated and transferred on a nitrocellulose paper. The specific antibodies bind to the different antigens and give a band.

Below are some photographs of Western Blot tests. On the left side of the image there are two columns to be used as points of comparison. The column marked "NC" is an HIV-negative test result and the column marked "PC" is an HIV-positive test result. Columns 3 to 10 show a series of tests on an individual person who became infected with HIV to illustrate how an HIV test result can change during the window period from HIV-negative to HIV-positive. Each column is one Western Blot test. These tests were performed on a single person beginning with the day the person was first infected with HIV (Column 3, Day 0) to when the person had a conclusive HIV infection (Column 10, Day 30). Each black or dark grey horizontal stripe is representative of the presence of a different antibody against a protein found in HIV. To be conclusive (HIV-positive), a Western Blot must have 5 horizontal stripes. An HIV infection is not the same as an AIDS

diagnosis.



Western Blot (WB) tests were initially used as the gold standard and confirmatory test for HIV but now it is used for resolving discordant screening results. WB tests are highly specific as they detect HIV antibodies to specific HIV proteins. But they are more laborious to perform and expensive.

Other tests

P24 ANTIGEN

The antigen test detects HIV free antigen (p24) in the serum.

This test is useful:

- During window period.
- To detect HIV infection in newborn because diagnosis is difficult due to presence of maternal antibodies.
- During late disease when patient is symptomatic.

Unfortunately, this test has a low sensitivity and not routinely recommended. The reason for the lack of sensitivity of this test is that the free antigen (p24) in serum may be complexed with p24 antibody. Antigens although transient can appear as early as two weeks after infection and lasts 3-5 months, so this method can shorten the window period by one week.

PCR/Viral Load Testing:

A PCR (Polymerase Chain Reaction) test, also known as a "viral load," is used to measure the amount of HIV in an HIV-positive person's blood. Because this test looks for HIV directly in a

person's blood instead of detecting antibodies (the body's reaction to HIV), it may detect an HIV infection about a week after an exposure. Therefore the PCR test is used by researchers and health care providers to identify infections during the window period. Three different techniques namely RT-PCR, nucleic acid sequence based amplification (NASBA) and branched-DNA (b-DNA) assay have been employed to develop commercial kits. These kits shorten the window period between infection and detectability to about 12 days. Role in post exposure prophylaxis (PEP) Both these tests (p24 and PCR) are not routinely recommended in case of occupational exposure because of its low positive predictive value. Hence, negative test must not be a ground to discontinue PEP.

Alternative to classical test

Orasure-(saliva)HIV Tests

Noninvasively collected specimens of oral fluids are used, although generally referred to as saliva; the fluid used for testing is actually oral mucosal transudate. This system obtains antibodies that are comparable to or exceed those from serum samples.

This test first employs ELISA, and then WB.



Oraquick Advance rapid HIV Test

This test was approved in 2004. It provides results in 20 min. The blood, plasma, or oral fluid is mixed in a vial with developing solution and the results are read from a stick-like testing device.

Urine Tests

Intact IgG antibodies are found in urine, but their exact origin is unknown. The collection of urine is simple, noninvasive, and inexpensive. The use of urine is appropriate for physicians, officers, health clinics, and developing countries where healthcare personnel may not be trained professionally or where clean needles to withdraw blood may not be available.

Major disadvantage

There is no approved urine-based confirmatory assay, necessitating collection of blood when results are reactive. The USA FDA has approved an ELISA and WB for use to test urine for antibodies to HIV-1.

Nucleic Acid Amplification Testing (NAAT)

Although standard tests that measure antibody response to the HIV virus have become increasingly sensitive, cases of HIV are occasionally missed because individuals can have negative antibody tests during the early stages of infection. Also, a few people with long-term HIV infection may have false negative antibody tests or may be chronic carriers who are clinically asymptomatic. The NAAT test helps avoid these problems as it amplifies the HIV viral RNA and detects viral genes instead of viral antibodies or antigens. Adding this new HIV screening method, to standard HIV testing, researchers were able to uncover six percent more cases of HIV infection in urban STD and drug treatment clinics and HIV testing sites in Atlanta than with standard HIV antibody tests alone.

TREATMENT

Approved antiretroviral drugs

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs):^{5,6}

Abbreviation	Generic name	Brand name
3TC	lamivudine	Epivir
ABC	abacavir	Ziagen
AZT or ZDV	zidovudine	Retrovir
d4T	stavudine	Zerit
ddI	didanosine	Videx EC
FTC	emtricitabine	Emtriva
TDF	tenofovir	Viread

Combined NRTIs:^{5,6}

Combination	Brand name
ABC + 3TC	Epzicom (US)
	Kivexa (Europe)
ABC + AZT + 3TC	Trizivir
AZT + 3TC	Combivir
TDF + FTC	Truvada

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):^{5,6}

Abbreviation	Generic name	Brand name
DLV	delavirdine	Rescriptor
EFV	efavirenz	Sustiva (US)
		Stocrin (Europe)
ETR	etravirine	Intelence
NVP	nevirapine	Viramune

Protease Inhibitors (PIs):⁷

Abbreviation	Generic name	Brand name
APV	amprenavir	Agenerase
FOS-APV	fosamprenavir	Lexiva (US)
		Telzir (Europe)
ATV	atazanavir	Reyataz
DRV	darunavir	Prezista
IDV	indinavir	Crixivan
LPV/RTV	lopinavir + ritonavir	Kaletra
		Aluvia (developing world)
NFV	nelfinavir	Viracept
RTV	ritonavir	Norvir
SQV	saquinavir	Invirase (hard gel capsule)
TPV	tipranavir	Aptivus

Fusion or Entry Inhibitors:

Abbreviation	Generic name	Brand Name
T-20	enfuvirtide	Fuzeon
MVC	maraviroc	Celsentri (Europe)
		Selzentry (US)

Herbal Remedy For HIV Infection

Name of the Plant	Family	Target	Isolated active molecule
<i>Xanthoceras sorbifolia</i>		HIV-1-protease	29-hydroxy-3-oxitirucalla,7,24-diene-4-oic acid. Epigallocatechin[4P-8,2b-0-7] epicatechidiene-21-oic acid.
<i>Maclura tinctoria</i>	Moraceae	HIV inhibitory activity	Xanthones such as Maclura-Xanthone B,C Alvaxanthone Flavonoids such as Dihydrocudraylavone B.
<i>Monotes africanus</i>	Dipterocarpaceae	HIV inhibitory activity	Flavonol 6,8, diprenylkaempferol
<i>Tripterygium hypoglaucum</i>	Celatraceae	HIV inhibitory activity	Alkaloids such as Peritassine A, Hypoglaunine C, Triptonines A and B, Wifordinines A,B,C.
<i>Syzygium claviflorum</i>	Myrtaceae	HIV-Inhibitors	3-O-acyl-betalinic acid and Oleanolic acid.
<i>Rosa woodsii</i>	Rosaceae	HIV-Inhibitors	3-O-(3,3-dimethyl)-succinyl betulinic acid

<i>Prosopis glandalosa</i>	Leguminosae	HIV-Inhibitors	3-O-(3,3-dimethyl)-succinyl betulinic acid
<i>Phoradendron juniperinum</i>	Loranthaceae		3-O-Glutaryl ursolic acid.
<i>Syzygium claviform</i>	Myrtaceae		3-O-Isovalalanyl ursolic acid
<i>Ternstroemia gymmanthera</i>	Theaceae		
<i>Palicourea condensate</i>	Rubiaceae	Anti-HIV	Macrocyclic peptide palicourein
<i>Chassalia parvifolia</i>	Rubiaceae		Circulines A-F
<i>Psychotria longipes</i>	Rubiaceae		Cyclopsychotride A
<i>Oldenlandia offinis</i>	Rubiaceae		Kalatia B1 Cycloviolins A-D
<i>Viola spices</i>	Violaceae	Anti-HIV	Violapeptide I and Varus A-H1
<i>Viola arvensis</i>	Violaceae		

COMPLEMENTARY AND ALTERNATIVE THERAPIES

List of common complementary and alternative therapies^{14, 15, 16, 17}

Complementary and alternative therapies can be divided into five main categories. The list below contains a few of the most popular examples.

Whole medical systems

- Naturopathic medicine (mostly practised in the West; includes diet modification, herbal medicine, acupuncture and massage)
- Traditional Chinese medicine (includes herbal medicine, acupuncture and massage)
- Ayurveda (ancient Indian healing system; includes diet modification, herbal medicine, cleansing therapies, massage, meditation and yoga)

- Homeopathy (most commonly prescribes extremely diluted solutions of natural substances)

Mind-body medicine

- Relaxation techniques, meditation and visualization
- Spirituality and prayer
- Yoga (may incorporate spirituality, meditation and body postures)
- Tai Chi (a Chinese martial art incorporating meditation and breathing exercises)
- Qi gong (includes meditation, body postures and breathing exercises)
- Aromatherapy (uses remedies derived from plants that are inhaled, applied to the skin or used internally)

Biologically based practices

- Vitamins and minerals
- Herbal remedies
- Animal-derived extracts
- Prebiotics and probiotics (aim to encourage the growth of beneficial microbes)

Manipulative and body-based practices

- Massage
- Chiropody (invented in America; manipulates the spine)
- Osteopathy (invented in America; manipulates the spine, joints and muscles; American osteopathic physicians are also trained in conventional medicine)
- Shiatsu (traditional form of Japanese massage therapy)
- Reflexology (invented in America; applies pressure to the feet, hands or ears)
- Rolfing (named after American Ida Pauline Rolf; manipulates soft tissue)

Energy medicine

- Acupuncture (involves inserting fine needles into the body)
- Reiki (practitioners claim to channel healing energy through their palms)
- Therapeutic touch and distant healing (practitioners claim to manipulate energy “biofields” with their hands)
- Bioelectromagnetic-based therapies (involve unconventional use of sound, light, magnetism, and other forms of electromagnetic radiation)

PREVENTION

SAFE SEX:The only safe sex is ‘no sex’; all other practices like masturbation, cuddling, hugging, rubbing, sticking to one partner or using condom if one cannot avoid multiple partners are safer sex practices.

SAFE BLOOD:Judicious use of blood and use only pretested HIV free blood or blood product.

SAFE NEEDLES:Insist your doctors and nurses to use sterile or disposable needles and instruments.

SAFE MOTHERHOOD:Before taking any major step in life like marriage or having child ascertain that you are HIV free.

SAFE RAZOR AND BLADE:

Never share your shaving blades with anyone and also ask your barber to use properly cleansed razor and new blade during shaving or hair cut. (Although the risk of getting infection from a saloon is minimal)

Conclusion

The review explains the various methods for diagnosis of the HIV infection, and current management strategies including movement away from ZDV monotherapy, institution of combination therapy earlier in the disease. New classes of antiretroviral such as protease inhibitor are considered to be the most potent therapeutic agents for the treatment of HIV infection to date.

The protease inhibitor and other novel therapeutic strategies and future generation of drugs under active development have recently provided potent new weapons against HIV.

Future generations of drugs under active development will probably provide HIV infected patients, a new ray of hope in life.

Acknowledgement

We acknowledge sincere thanks to Honorable Padmabhushan Balasaheb Vikhe Patil, ex. Minister, Govt. of India, Chairman Pravara Rural Education Society, Pravaranagar for his kind encouragement. We also thank Honorable Radhakruhsna Vikhe Patil, Minister, Govt. of Maharashtra, & Shri.Rajendra VikhePatil,Managing trustee PRES for their co-operation Encouragement,and support.

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