Review Article on HIV-An Epidemic

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ABSTRACT

HIV (Human Immunodeficiency Virus) is a virus of Lentivirus genus. It is being discovered as a causative organism of AIDS (Acquired Immune Deficiency Syndrome). The main reason for transmission is the exchange of body fluids that can be directly injected into another person's bloodstream. This virus can't survive outside the body and hence somehow can't be spread via touch or close contact so the negative attitudes causing stigmatisation and discrimination should reduce. With the advancement in diagnosis and research as well as treatment methods like ART, HAART, Gene therapy we can control the viral load and prolong the time of progression to AIDS which results in near-normal life expectancy. But still, modern medicines are unable to completely cure the disease and it has placed HIV as one of the most dreaded pathogens of the 21st century. Since millions of people are infected it can even be called 'medical apocalypse' and undoubtedly defines the public-health crisis of our time. Symptoms vary from person to person and some people may have many unpredictable symptoms or may not have any symptoms for years. The ongoing research efforts help us provide opportunities for the development of novel treatment or preventive strategies. This review article focuses on transmitting and non-transmitting factors, diagnosis procedures and challenges, epidemiological data, treatment methods including gene therapy, ART, HAART, PI+NNRTIs treatments drugs and injections briefing, vaccines detailing, preventive strategies by public health sectors, risk assessment of HIV worldwide.

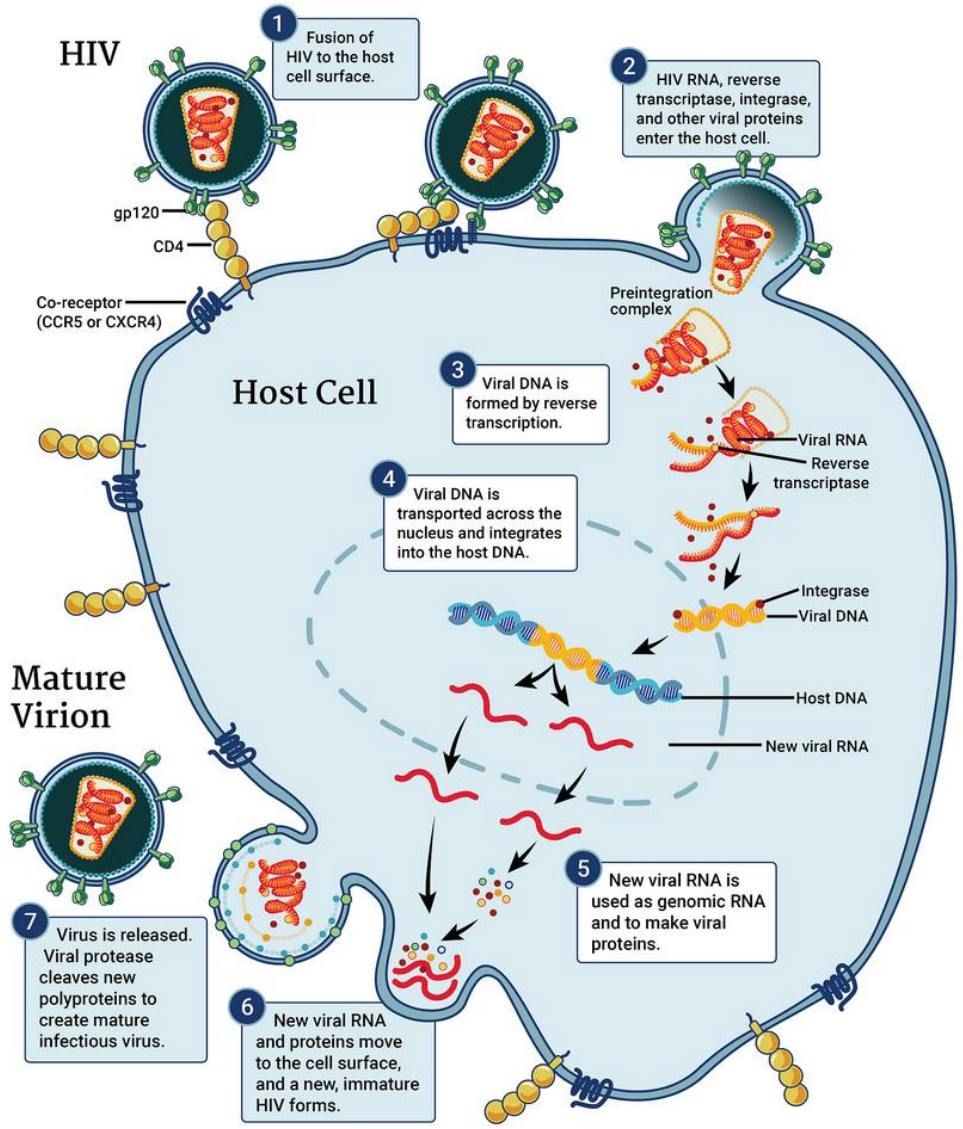
Keywords- AIDS, ART, HAART, PI+NNRTIs, Gene Therapy, stigmatisation, preventive strategies.

INTRODUCTION

HIV (human immune deficiency virus) is a virus of reteroviridae family has genus lentivirus. It attacks on immune cells of human and make the person unsafe and undefensive to other infections and diseases [1]. HIV has RNA as genetic material. It is different in structure from other retroviruses. There are 2 main groups of HIV; HIV group 1 and HIV group 2. HIV group 1 is around 95% of all infections of HIV. HIV group 2 is approximately 55% genetically different from HIV group1. HIV group 1 is classified into 4 subgroups: group M, group N, group O, group P in which group M is further classified [2]. The main reason of transmission of HIV is unsafe sex but it can be transmitted through non sexual methods also. AIDS (Acquired Immuno Deficiency Syndrome) is the final stage of HIV infection. It happens when almost all the immune system is weak [3].

Life cycle - There are 7 stages of HIV life cycle in human body.

In 1st stage HIV binds to the receptor surface of CD4+ cells. In 2nd step the HIV envelope and CD4+ cell's membrane get fused and HIV RNA reverse transcriptase and other HIV proteins enter into the host cell. The 3rd step is REVERSE TRANSCRIPTION in which viral DNA is formed. In the next stage viral DNA moves towards the nucleus of host cell and incorporate with the DNA of host cell. Now the new DNA forms new viral RNA. In the very next stage which is 5th new viral RNA makes viral protein. In 6th stage new viral RNA and protein moves towards the cell membrane and forms new immature HIV. In the very next and last stage which is 7th the immature HIV pulls itself from the host cell and becomes the new maturing HIV. [4]



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HOW HIV SPREADS (*Which body fluids can transmit HIV?)*

Blood, Semen (cum), Pre-seminal fluid (pre-cum), Rectal fluids, Vaginal fluids, Breast milk.

These fluids can come directly in contact with mucous membrane which are found inside the rectum, vagina, penis and mouth of human or any damaged tissue or wound or can be directly injected into the bloodstream (via needle or syringe) that can cause transmission.

Transmission through blood transfusions

a) From mother to her baby
b) From anal sex-
c) From vaginal sex
d) From sharing needles, syringes or other drug injection equipment

Some rare ways through which HIV can be transmitted

a) Oral sex
b) Workplace
c) Medical care
d) Pre-chewed food
e) Biting
f) Deep, open-mouth kissing
g) Tattoos and body piercings
h) female-to-female [6]

Ways HIV is not transmitted

HIV does not survive long outside the human body (such as on surfaces), and it cannot reproduce outside a human host. It is not transmitted by these ways-:

Sharing dishes, through the air, saliva, sharing toilet seats, tears, closed mouth kissing, sweat, hugging, shaking hands, mosquitoes, ticks or other insects.

Prevention of transmission from pregnant women to her child.

Women who are pregnant or planning pregnancy should get tested for HIV as early as possible. If one has HIV, the most important thing one can do is to take ART every day, exactly as prescribed. Women in their third trimester should be tested again if they engage in behaviours that put them at risk for HIV. If one is HIV-negative and they have an HIV-positive partner, they should talk to doctor about taking pre-exposure prophylaxis (PrEP) to help keep you from getting HIV. People with HIV who take HIV medicine as prescribed and get and keep an undetectable viral load have effectively no risk of transmitting HIV to an HIV-negative partner through sex. After birth, babies born to a mother with HIV are given ART right away for 4 to 6 weeks. If one is treated for HIV early in their pregnancy, the risk of transmitting HIV to your baby can be 1% or less. Breast milk can have HIV in it. So, after delivery, one can prevent giving HIV to their baby by not breastfeeding [6].

HIV DIAGNOSIS

HIV tests are done for 3 different purposes: for public health surveillance, for individual diagnosis, protection of blood or tissue products safety [7]. HIV can be diagnosing by these primary tests.

1. **ELISA test:** ELISA stands for, enzyme-linked immunosorbent assay. If your ELISA test is positive then for confirmation for HIV infection usually Western Bloat Test is

done. ELISA test can be negative in primary infection. If you have any doubt of HIV infection then you should be tested in 3-4 months again.

2. **Home tests:**This test kit is approved by U.S. food and drug administration. By using this kit the particular one can diagnose HIV infection at home.
3. **Saliva test:**In this test your saliva is tested in laboratory. This test is cross checked by testing of your blood sample.
4. **Viral load test:**This test measures the quantity of HIV in your blood. For this there are 3 techniques: reverse transcription polymerase chain reaction (RT-PCR), branched DNA (bDNA) and nucleic acid sequence-based amplification assay (NASBA). The basic principles of these 3 techniques are same [8]
5. **Western Blot test:** In this test a small blood sample is taken and it confirms HIV infection by separating blood proteins. These tests are 99.99% accurate [9]

Challenges for HIV diagnosis-

It is very difficult to identify HIV infected person in terms of behavioural and biological manner. Blood test (in which antibody count is done called antibody test) is the basic test which is done at broad spectrum for confirming HIV infection [10].

HIV SUPERINFECTION

When a person with HIV gets another type, or strain, or mutant of the virus it is called HIV superinfection.

- The new strain of HIV can replace the original strain or may be remain along with the original strain.
- Superinfection may cause some people to get sicker faster because the new strain of the virus is resistant to the medicine (antiretroviral therapy or ART) they're taking to treat the original strain.
- Hard-to-treat superinfection is rare.
- Medicines taken to treat HIV can help protect someone from getting a superinfection.
- If you and your partner have HIV and keep an undetectable viral load, there is effectively no risk of transmitting HIV to the other through sex [11].

DRUG RESISTANCE

A. Innovative HIV drugs: HIV drugs are known as antiviral drugs or antiretroviral drugs (ARVs) because HIV is a type of virus and AIDS is caused by this virus [12]. Some ARVs are:

1. **Nucleoside reverse transcriptase inhibitors (NRTIs):**This type of drugs improves the ability of body to fight against the infection by increased the number of immune cells like CD4+ cells. Some of the NRTIs suppress the number of HIV virus replicating. Some NRTIs drugs are;

zidovudine or tenofovir; Lamivudine or emtricitabine; Efavirenz or nevirapine.

2. **Non-nucleoside reverse transcriptase inhibitors (NNRTIs):**They are structurally similar to NRTIs. They bind to the different sites of virus and inhibit its activity. Some examples of NNRTIs are:

Nevirapine (e.g. viramune XR), Rilpivirine (e.g. edurant), Efavirenz (e.g. stocrin), Etravirine(e.g. intelence)

3. **Protease inhibitors (PIs):** WHO recommends PIs should be used as second line treatments for treating HIV. PIs inhibit the activity of other viral enzyme, HIV protease which is required to unite HIV particles. Some examples of PIs are:

Saquinavir (e.g. Invirase); Indinavir (e.g. Crixivan); Ritonavir (e.g. Norvir); Amprenavir (e.g. Agenerase); Fosamprenavir (e.g. Telzir); Lopinavir (e.g. Kaletra); Atazanavir (e.g. Reyataz); Tipranavir (e.g. Aptivus); and Darunavir (e.g. Prezista).

4. **New antiretroviral:** these drugs use different mechanism to seize HIV replication cycle. These drugs interrupt HIV entry into human cells. It attaches to human cellular receptors like CCR5 & CXCR4 to prevent entry. Some drugs in this category are still under trial [13].
5. **Fusion inhibitors:** this drug blocks the HIV to entering into the T-cells, whom HIV uses as host cell. There is only one fusion inhibitor known which is: enfuvirtide (e.g.Fuzeon)
6. **Post attachment inhibitors:**this type of drug inhibits the entry of HIV in certain immune cells. In 2018 FDA approves a drug in this category. This is: ibalizumab-uiyk (Trogarzo)
7. **Chemokine coreceptor antagonists (CCR5 antagonists):** this drug is mainly used in US. These drugs inhibitos or block the entry of HIV into cells. Example of this drug which is currently available is: maraviroc (Selzentry)
8. **Entry inhibitors:** These types of drugs inhibit the entry of HIV into healthy T-cells. Examples of entry inhibitor are:

enfuvirtide (Fuzeon); ibalizumab-uiyk (Trogarzo); maraviroc (Selzentry)

9. **Combination drugs:** in this type multiple drugs are combined and form one single drug which is used in medication.The following combination drugs only include **a PI and a CYPA3A inhibitor:**

atazanavir and cobicistat (Evotaz), darunavir and cobicistat (Prezcobix), lopinavir and ritonavir (Kaletra)

The following combination drugs only include **NRTIs:**

- abacavir, lamivudine, and zidovudine (Trizivir),
- abacavir and lamivudine (Epzicom),
- emtricitabine and tenofovir alafenamide fumarate (descovy),

- emtricitabine and tenofovir disoproxil fumarate (truvada),
- lamivudine and tenofovir disoproxil fumarate (Cimduo, Temixys),
- lamivudine and zidovudine (Combivir) [14].

Eight approved NRTIs are: zidovudine (AZT), didanosine, zalcitabine , stavudine ,lamivudine , abacavir , emcitrabine and Tenofovir.

B. HAART

HAART is a therapy given at the time of treatment of HIV. It is also called ART or cART (combination antiretroviral therapy). It is generally combination of 3 or more antiretroviral drugs. Base of HAART is to co-manage of different type of antiviral drugs that inhibits replication of virus by different mechanisms [15,16,17,18].

The goals of HAART in patients with HIV infections include:

- Reduce morbidity and mortality (AIDS and non-AIDS associated causes)
- Improve the quality of life
- Reduce plasma viral RNA load
- Prevent transmission to others (sex partners, needle-sharing partners, mother to infant)
- Prevent drug resistance
- Improve immune function [19]

C. Injection practices in recent years

For treatment of HIV/AIDS two major trials were conducted which shows positive results and hence presently used for treatment. The ATLAS study recruited people presently on treatment with conventional therapy, while the FLAIR study evaluated starting people on therapy with a combination of ***cabotegravir and rilpivirine.*** In both cases, the injectable showed equivalent results in keeping the levels of HIV in the body low when compared with the oral regimen.

This injectable combination has been approved by regulators in the European Union, the United States and Canada. These two trials conducted, caused no serious problems and is safe. It shows some common reactions like pain at the site of injection and minor irritations. People infected with HIV can have this injectables once in a month and another study, the ATLAS-2M showed the potential of administering the drug every two months. It was still effective at reducing viral load in patient's body [20]

The standard treatment for HIV-1 infection is a combination of ARV medicines from at least two different classes that need to be taken daily to suppress viral replication, increase number of CD4 cells (i.e. white blood cells that are important in helping to fight infections), and stop disease progression[21].

TREATMENT

1. **ART (Antiviral therapy)** : the treatment for HIV is known as ART [22]. It was recognised by FDA in 1987[23,24,25,28]. In this procedure combination of drugs will be taken by the particular one. The main goal of ART treatment is to decrees the viral load in a person's body [26]. Govt. of INDIA launched ART programme on 1st April 2004[27].

   List of the currently FDA-approved anti-HIV drug

Combination	Components	Date of FDA approval
Combivir	Zidovudine (300 mg),lamivudine (150 mg)	September 27,1997
Trizivir	Abacavir (300 mg), lamivudine (150 mg) zidovudine (300 mg)	November 14, 2000
Epizicom	Abacavir (600 mg), lamivudine (300 mg)	August 2, 2004
Truvada	Tenofovir disoproxil fumarate (300 mg), emtricitabine (200 mg)	August 2, 2004
Atripla	TDF (300 mg), emtricitabine (200 mg), efavirent (600 mg)	July 12, 2006

[29]

There are some side effects of these drugs which can be seen over 5-35% people. Common side effects are headache, constipation, rashes, osteoporosis, cough, pain, depression, nausea, fatigue, dizziness, mania, abdominal pain etc. [13]

2. **Gene Therapy-** Currently, HIV is treated via a therapy in which a combination of antiviral drugs is given to the patients, this is often called HAART. Due to this decrease in mortality rate by HIV/AIDS is observed. By HAART the quality of life of a patient is increased but along with that some side effects of this therapy are also seen and for suppressing this virus, lifelong treatment is required and this is very expensive too [30].

   According to an announcement from the ***Keck School of Medicine at USC***, the goal is to develop a therapy that "prepares patients for a **stem cell transplantation** using their cells with little to no toxicity, engineers or researchers use their stem cells to fight HIV and stimulates those cells to quickly produce new and engineered immune cells once they're reintroduced into the patient." [31]. Cell and gene therapies help in preventing progressive HIV infection by interfering with HIV replication in the absence of chronic antiviral therapy. Individuals homozygous for a deletion in the **CCR5** gene **(CCR5Δ32)** are largely resistant to infection from R5-topic HIV-1 strains, which are most commonly transmitted [32].

   The gene therapy strategy has been inspired by three cases where Leukemia patients who also had HIV received blood stem cell transplants from donors who also carried a mutation that confers immunity to HIV. The mutation was in the **CCR5** gene, which encodes a receptor that HIV uses to infect immune cells and is present in about 1 percent of the population, USC said.[31]. Gene therapy in humans has not been easy to implement. Genes inserted into complex human cells have triggered serious unintended consequences and have often proven to be short-lived. Yet perseverance may be paying off.

   Di Giusto et al. report a step toward workable gene therapy in the form of stable expression of a lentiviral vector encoding anti-HIV RNAs in blood stem cells transplanted into AIDS patients. None of these patients is cured, but the vector seems to stably express the potentially therapeutic RNAs. Putting exogenous gene sequences into humans is risky, and review boards are appropriately conservative. But Di Giusto et al. took advantage of a clinical situation to design a trial that minimized extra risk to the subjects [33].

What if I delay treatment?

HIV will continue to harm your immune system. This will put you at higher risk for developing AIDS. This will also put you at higher risk for transmitting HIV to your sexual and injection partners.[34]

EPIDEMIOLOGY

year	No. of people living with HIV	People newly infected with HIV	AIDS deaths	References
2014	36.9 million	2.0 million	1.2 million	[35]
2015	35.6 million	1.2 million	2.1 million	[36]
2016	36.4 million	2.4 million	1 million	[36]
2017	37.2 million	1.7 million	954,000	[36]
2018	37.9 million	1.7 million	770,000	[36]
2019	38 million	1.7 million	690,000	[37,38]

HIV SYMPTOMS

HIV destroys CD4+ cells in human body which are critical to immune system. So that many symptoms occurs during HIV infection. Symptoms vary person to person and some people may not have symptoms for years and some have very unpredictable symptoms. There are 4 stages of HIV [39]

- **Accute primary Infection**- in this stage primary symptoms shows which are like a normal flu and some people don't have any symptom. And they cannot even detect a HIV infection without doing a test.[40]
- **Asymptomatic** -No infection is seen for a few years after infection, the person lives his normal life (10-15years).
- **Symptomatic**-by coming to this stage, the immune system of that persons becomes very weak and he or she starts having many severe disease like severe diarrhea, fever, persistent cough, mouth and skin problems, regular infections, night sweats, weight loss, PCP, toxoplasmosis, TB and Kaposi sarcoma [40], increase the risk of lung cancer and high BP, high BP can cause PAH (Pulmonary arterial hypertension) [41] etc.
- **AIDS/ Progression of HIV to AIDS-**as the result of this persistent infection the particular one said to have AIDS. There is no particular one test for AIDS. Doctors do many tests for this, in which one also has count of CD4+ cells. With the correct treatment a person can overcome the severe infection of AIDS [40].
  HIV also causes some neurological complications name as: HIV-associated dementia (HAD) , this is the most severe form of HIV-induced neurocognitive disorders [42].

HIV VACCINES

There is a lot of pressure on the scientist to make the HIV vaccine. The HIV vaccine is being worked on. Some vaccines based on plant and animal models are under investigation. HIV-1 infection is major challenging thing in the path of vaccines [43,44]. Broadly neutralizing antibodies (bNAbs) specific for conserved epitopes on the HIV-1 envelope (Env) are believed to be essential for

protection against multiple HIV-1 clades. However, vaccines capable of stimulating the production of bNAbs remain a major challenge. Given that poly reactivity and autoreactivity are considered important characteristics of anti-HIV bNAbs, we designed an HIV vaccine incorporating the molecular adjuvants BAFF (B cell activating factor) and APRIL (a proliferation-inducing ligand) with the potential the maturation of polyreactive and autoreactive B cells as well as to enhance the affinity and/or avidity of Env- specific antibodies [45,46,47].

Side effects of vaccines-HIV medicine can cause side effects in some people. However, not everyone experiences side effects. The most common side effects are-Nausea and vomiting, Diarrhea, Difficulty, sleeping, Dry mouth, Headache, Rash, Dizziness, Fatigue, and Pain.

Talk to your health care provider if your treatment makes you sick. Your health care provider may prescribe medicines to help manage the side effects or may change your treatment plan [34].HIV vaccines or medicines do not cause any hormonal changes.

STIGMATISATION AND DISCRIMATION

The negative attitudes and beliefs about HIV/AIDS are known as HIV stigma. Some assumptions regarding HIV are not socially acceptable like-

- it can be spread among some particular group of people.
- Feelings that some people deserve AIDS because of their choices.
- Some moral judgments about people who take precautionary steps for HIV.
- Myths and misinformation increase the stigma and discrimination surrounding HIV and AIDS.
- Adopting a human rights approach to HIV and AIDS is in the best interests of public health and is key to eradicating stigma and discrimination.

Discrimination is the behaviour that is actually the result of those negative attitude or beliefs. This can cause misunderstandings and can even lead the patient to face depression [48,49].

Bad behaviours-

- A health care professional refusing to provide care or services to a person living with HIV
- Refusing casual contact with someone living with HIV
- Harassment and abuse
- Poor health services, access and uptake
- Socially isolating a member of a community because they are HIV positive
- Referring to people as HIVers or Positives [48,49]

Effects caused-This stigmatisation and discrimination can affect the emotional well-being and mental health of people living with HIV. This can even create negative self-image in the people living with HIV. This is often called “internalized stigma” or” self-stigma”. this can lead to feeling of shame, fear of disclosure, isolation and despair. These feelings can keep people from getting tested and treated for HIV.

This is one of the major reason why most of the population is not even tested for HIV/AIDS and facing issues because of not getting proper treatment at proper time.[48]

This can also cause poverty due to poor social and emotional wellbeing. It can even lead patient to face risky situations and behaviours.

Cure to stigmatisation and discrimination-

- Talk about HIV- it provides opportunities to correct misconceptions and help others to learn more about HIV.
- It can also increase awareness among youngsters and aged people as well.
- Words and actions can make a major change in our everyday lives.
- This can even lead others with your supportive behaviours.
- Anti-discrimination laws, decriminalisation, Awareness camps, websites, blogs, social media channels can help in spreading awareness [48,49,50].

HIV PREVENTIONS

- Screening of HIV during pregnancy.
- By using HIV prevention medicine.
- Not to share needles, syringes, injecting equipment such as spoons and swabs, or the actual drugs or liquids used to dilute them.
- Use of lubricant during sex is also preventing HIV infection. Use condom. It is the most effective thing to prevent HIV which is transmitting during sex [51,52,53,54].

FACTORS THAT INCREASE HIV RISK

1) **Viral load**

   - The amount of HIV in the blood who has HIV.
   - Its highest during acute phase of HIV, and without HIV treatment.
   - Taking medicines can reduce this load upto a great extent that it can even can't be detected easily (called an undetectable viral load)
   - People with HIV who keep an undetectable viral load (or stay virally suppressed) can live healthy long lives.
   - Having undetectable viral load can also prevents transmitting the virus to other via sex, sharing needles, other injections equipment, mother to child during pregnancy, and breastfeeding.

2) **Sexually transmitted diseases (STDs)**
   - In case, you have another STD, you may more likely to get or transmit HIV
   - Getting tested and treated for STDs can lower the risk of getting or transmitting.
   - If you have HIV and get an undetectable viral load, getting an STD doesn't appear to increase the risk of transmitting HIV. But STDs can cause other problems.
   - Using condoms and other protection methods can reduce the risk of getting or transmitting HIV, gonorrhoea, chlamydia or other STDs transmitted through genital fluids. But condoms are less effective at preventing STDs that transmits through sores or cuts or the skin like human papillomavirus, genital herpes, and syphilis.
   - If you are sexually active, you and your partners should get tested for STDs, even if you don't have symptoms.
3) **Alcohol and drug use**
   - If you're drunk or high, you're more likely to engage in risky sexual behaviours like having sex without protection (such as condoms or medicines to prevent or treat HIV).
   - Drinking alcohol, particularly binge drinking, and using "club drugs" can alter your judgment, lower your inhibitions, and impair your decisions about sex or drug use.

- You may be more likely to have unplanned sex (vaginal and anal sex can increase more risk), without protection or not properly used protections every time, or have more sexual partners, or use other drugs [55,56].

PEOPLE WHO ARE AT MOST RISK

- People with a current or previous partner with HIV
- Men who have unprotected sex with men
- Women who have unprotected sex with men who have sex with men
- People who inject drugs and share equipment
- People who have unprotected sex with somebody who has injected drugs and shared equipment
- People who share sex toys with someone infected with HIV.
- People who have multiple sexual partners
- People who have been raped (an assault involving penetration of the vagina, anus or mouth)
- People who have received a blood transfusion, transplant or other risk-prone procedures in countries which do not have strong screening for HIV
- Babies with mothers who have untreated HIV-before or during or by breastfeeding [57]

STRATEGIES BY WHO

International community has declared AIDS as an epidemic and targets to finish it till 2030. This proposal has been accepted by United Nations Assembly in September 2015 [58,61]. Some strategies had been used to control HIV which shows extraordinary effects and leads to great achievements which hence lead WHO to make a special programme in 1986 [59,61]. Global health sector strategy on HIV/AIDS 2011-2015 [60,61] helped in revert and controlling the deaths caused by HIV/AIDS.17 million people has undergone this Antiviral treatment and new HIV infections is reduced to a good limit. From most of the Countries transmission from mother to her child has been eliminated. And approximately 43% reduction is been shown in deaths caused by HIV since 2003.

The 5 major strategy components are-

1. **Setting the scene** –reviews the current status of HIV epidemics and responses, identifies opportunities and challenges for the future, and argues the case for adequate investment in the health sector response to HIV.
2. **Framing the strategy** –describes the three organizing frameworks for the strategy (universal health coverage, the continuum of HIV services and the public health approach);
3. **Presenting a global vision and setting global goals and targets** –presents a set of impact and service coverage targets for 2020 and 2030 to drive the response;
4. **Recommending priority actions** –recommends fast-track actions to be taken by both countries and WHO under each of five strategic directions;
5. **Guiding implementation** –outlines key elements of strategy implementation, including strategic partnerships, monitoring and evaluation, and costing [61].

Strategy -***Monitoring and Evaluation***

1) **Vision-** zero new infections, deaths, discrimination in world where people living with HIV are able to live long and healthy lives.
2) **Goal-**end of the AIDS epidemic as a public health threat by 2030
3) **2020 Targets-** reduce new cases to 5 lakh, zero new infections among infants, reduced HIV-related deaths to below 5lakh, 90% people living with HIV tested, 90% treated, 90% virally suppressed.

4) **Frameworks for action-**
strategic direction1- information for focused action
Strategic direction2- interventions for impact
Strategic direction3- delivering for equity
Strategic direction4- financing for sustainability
Strategic directions5- innovation for acceleration
5) **Strategy implementation-** leadership,partnership, accountability, monitoring and evaluation
6) **Country action, WHO action HQ, regions and countries**

Challenges for strategy

Although health area infected with HIV has shown very major responses to this epidemic but still it faces some important and major challenges.

1. **Not enough and not fast enough**-Currently the strategy which is being using has shown good results till now but its working rate in terms of time is very slow which cannot achieve global level target completely in coming times. As per data, about 17 million people out of 37 million people don't know about the status of their HIV infection and 22 million people has not received Antiviral therapy yet.[61,62]
2. **Major inequities persist & populations are being left behind**-Increment of new infected people of HIV is not getting deserved importance and attention in some countries due to which it is being increasing rapidly in girls and women as compared to that of boys and men. Due to Human rights violation, myths about the infection, stigmatisation, gender discrimination. The access of public health services is hindered. This is the major drawback because children, adolescents, young men and women are the major part of population [61,63].
3. **Middle-income countries requires specific focus**- According to a estimate 70% population of the world is living in the middle income countries. So that global success is depending upon these Countries acceleration.
4**. Fragile communities & mobile population**- Natural disaster, economic crisis, climate changes and many other challenges gives rise to move people from one country to another ,this is very challenging for public health services to access these people.
5. **Ensuring and maintaining the quality**-Spreading these HIV programmes without any surity can also increase the risk. As the negative effects or points is just being assumed by it, no proper knowledge is been known yet.
6. **increasing burden of coinfections and other comorbidities**-AIDS deaths are declining by the expandation of ART, but investments in treatments are being challenged due to increased morbidity and mortality associated with coinfections, such as hepatitis B and hepatitis C, and other comorbities, including cancer, cardiovascular disease, diabetes and other noncommunicable diseases, and mental health and substance use disorders.
7. **doing more of the same is not enough**- proceeding at current pace will not be enough to end an epidemic that is constantly evolving.

The action outlined in this strategy involve accelerating the development and implementation of comprehensive, high impact HIV prevention and treatment interventions, using rights-based and people- centered approaches, identifying sustainable financing for HIV programmes into the future and ensuring progressive integration of the HIV response into broader health programmes and services.

HIV strategy (2016-2020) is 3rd in the series of public sector strategy. This strategy aims for end of viral hepatitis, epidemic, sexually transmitted diseases (STDs)/infections. These strategies use a common structure, drawing on three organising frameworks

1-universal health coverage
2- The continum of health services
3-the public health approach

The main target of HIV strategy is "end of AIDS". Some other strategies are also associated with this strategy like -"end of TB strategy" [63]. And UnAIDS strategy & other HIV strategy acts as a partner in these strategies.

“Key populations, or key populations at higher risk, are groups of people who are more likely to be exposed to HIV or to transmit it and whose engagement is critical to a successful HIV response. In all countries, key populations include people living with HIV. In most settings, men who have sex with men, transgender people, people who inject drugs, sex workers and their clients and prisoners are at higher risk of exposure to HIV than other groups. However, each country should define the specific populations that are key to their epidemic and response based on the epidemiological and social context.

REFERENCES

1. What are HIV & AIDS from HIV.gov; last updated: June 05, 2020. **https://www.hiv.gov/hiv-basics/overview/about-hiv-and-aids/what-are-hiv-and-aids**
2. HIV strains and type https://www.avert.org/professionals/hiv-science/types-strains#footnote5_1yagjxd
3. Medilineplus ;HIV/AIDS https://medlineplus.gov/
4. **https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-life-cycle#:~:text=The%20seven%20stages%20of%20the%20HIV%20life%20cycle%20are%3A%201,imagine%20what%20HIV%20looks%20like.**
5. **https://www.niaid.nih.gov/diseases-conditions/hiv-replication-cycle**
6. https://www.hiv.gov/hiv-basics/hiv-prevention/reducing-mother-to-child-risk/preventing-mother-to-child-transmission-of-hiv#:~:text=After%20birth%2C%20babies%20born%20to,your%20baby%20by%20not%20breastfeeding.
   Content Source: CDC's HIV Basics
   Date last updated: December 19, 2018
7. https://www.cdc.gov/hiv/basics/hiv-transmission/hiv-superinfection.html
   Page last reviewed: October 28, 2020Content source: Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention
8. AIDS diagnosis by university of California https://www.ucsfhealth.org/conditions/aids/diagnosis
9. Western Blot Test by Stanford health care https://stanfordhealthcare.org/medical-conditions/sexual-and-reproductive-health/hiv-aids/diagnosis/western-blot-test.html#:~:text=The%20Western%20blot%20test%20separates,combined%20tests%20are%2099.9%25%20accurate.
10. Schito, M. L., D'Souza, M. P., Owen, S. M., & Busch, M. P. (2010). Challenges for rapid molecular HIV diagnostics. The Journal of infectious diseases, 201 Suppl 1(Suppl 1), S1–S6. https://doi.org/10.1086/650394
11. https://www.cdc.gov/hiv/basics/hiv-transmission/hiv-superinfection.html
12. **https://i-base.info/guides/starting/what-is-art**
13. **Antiretroviral therapy (anti-HIV) by health engine 19 march 2007**

Medically reviewed by Thomas Dean Chiampas, PharmD, BCPS, AAHIVP — Written by the Healthline Editorial Team — Updated on April 24, 2020.

14. **https://healthengine.com.au/info/antiretroviral-therapy-anti-hiv-drugs**
15. Shafer RW, Vuitton DA. Highly active antiretroviral therapy (HAART) for the treatment of infection with human immunodeficiency virus type 1. Biomed Pharmacother. 1999 Mar;53(2):73-86. [Abstract: 10337461]
16. Kitahata MM, Koepsell TD, Deyo RA, Maxwell CL, Dodge WT, Wagner EH. Physicians' experience with the acquired immunodeficiency syndrome as a factor in patients' survival. N Engl J Med. 1996 Mar 14;334(11):701-6. [Abstract: 8594430]
17.]. Cunningham WE, Tisnado DM, Lui HH, Nakazono TT, Carlisle DM. The effect of hospital experience on mortality among patients hospitalized with acquired immunodeficiency syndrome in California. Am J Med. 1999 Aug;107(2):137-43. [Abstract: 10460044]
18. Rackal JM, Tynan AM, Handford CD, Rzeznikiewiz D, Agha A, Glazier R. Provider training and experience for people living with HIV/AIDS. Cochrane Database Syst Rev. 2011 Jun 15;(6):CD003938. [Abstract: 21678344]
19. Highly Active Antiretroviral Therapy (HAART)
    Eggleton JS1, Nagalli S2 Author information Book from StatPearls Publishing, Treasure Island (FL), 03 Mar 2020 PMID: 32119420

20. **What do we know about injectable HIV medication?**
    Pascal AkahomeJanuary 2021
    https://www.aidsmap.com/about-hiv/what-do-we-know-about-injectable-hiv-medication

21. First long-acting injectable antiretroviral therapy for HIV recommended for approval
    News 16/10/2020

    https://www.ema.europa.eu/en/news/first-long-acting-injectable-antiretroviral-therapy-hiv-recommended-approval

22. **https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-treatment-basics#:~:text=treatment%20for%20HIV%3F-,The%20treatment%20for%20HIV%20is%20called%20antiretroviral%20therapy%20(ART).,HIV%20live%20longer%2C%20healthier%20lives.**
23. **HIV Antiretroviral Therapy**
    Tyler R. Kemnic; Peter G. Gulick. Author InformationLast Update: June 23, 2020
24. **https://smartsexresource.com/topics/highly-active-antiretroviral-therapy-haart**
25. Antiretroviral therapy of HIV infection in infants and children: towards universal accesshttps://www.who.int/hiv/pub/guidelines/art/en/
26. **https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-treatment-basics**
27. **http://naco.gov.in/sites/default/files/Antiretroviral%20Therapy%20Guidelines%20for%20HIV-Infected%20Adults%20and%20Adolescents%20May%202013%281%29_0.pdf**

28. Decreases in Community Viral Load Are Accompanied by Reductions in New HIV Infections in San Francisco
    MoupaliDas ,Priscilla Lee Chu,Glenn-Milo Santos,SusanScheer,EricVittinghoff,WilliMcFarland,Grant N. ColfaxPublished: June 10, 2010https://doi.org/10.1371/journal.pone.0011068

29. **Anti-HIV Drug Discovery, Development and Synthesis of Delavirdine:**

30. Scott G. Kitchen, Saki Shimizu, Dong Sung An,Stem cell-based anti-HIV gene therapy, Virology,Volume 411, Issue 2,2011,Pages 260-272,ISSN 0042-6822,https://doi.org/10.1016/j.virol.2010.12.039.
31. New HIV Gene Therapy, CAR-T Treatments Could be on the Horizon for PatientsPublished: Sep 03, 2020 By Alex Keown available at https://www.biospace.com/article/new-hiv-gene-therapy-car-t-treatments-could-be-on-the-horizon-for-patients/
32. Hoxie, J. A., & June, C. H. (2012). Novel cell and gene therapies for HIV. Cold Spring Harbor perspectives in medicine, 2(10), a007179. http://perspectivesinmedicine.cshlp.org/content/2/10/a007179
33. D. L. DiGiusto, A. Krishnan, L. Li, H. Li, S. Li, A. Rao, S. Mi, P. Yam, S. Stinson, M. Kalos, J. Alvarnas, S. F. Lacey, J.-K. Yee, M. Li, L. Couture, D. Hsu, S. J. Forman, J. J. Rossi, J. A. Zaia, RNA-Based Gene Therapy for HIV with Lentiviral Vector–Modified CD34+ Cells in Patients Undergoing Transplantation for AIDS-Related Lymphoma. Sci. Transl. Med. 2, 36ra43 (2010).
34. https://www.cdc.gov/hiv/basics/livingwithhiv/treatment.html
35. Current Scenario of HIV/AIDS, Treatment Options, and Major Challenges with Compliance to Antiretroviral TherapyMonitoring Editor: Alexander Muacevic and John R AdlerAdnan Bashir Bhatti,[1] Muhammad Usman,[2] and Venkataramana Kandi[3]Published online 2016 Mar 1. doi: 10.7759/cureus.515PMCID: PMC4818110PMID: 27054050 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4818110/
36. https://www.avert.org/global-hiv-and-aids-statistics
Last updated:18 February 2020**Last full review:**25 September 2018**full review:**25 September 2019
37. https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/data-use/hiv-data-and-statistics
38. **https://aidsinfo.unaids.org/**
39. **https://www.hivireland.ie/hiv/stages-of-infection/**
40. **https://www.avert.org/about-hiv-aids/symptoms-stages**
41. **https://www.healthline.com/authors/ann-pietrangelo**
42. **Variable progression of HIV-associated dementia**
F. H. Bouwman, R. L. Skolasky, D. Hes, O. A. Selnes, J. D. Glass, T. E. Nance Sproson, W. Royal, G. J. Dal Pan, J. C. McArthur
Neurology Jun 1998, 50 (6) 1814-1820; DOI: 10.1212/WNL.50.6.1814
43. J Neurovirol. 2008 Aug;14(4):292-300. doi: 10.1080/13550280802074539.Nonhuman primate models of NeuroAIDS
Rachel Williams, Sirosh Bokhari, Peter Silverstein, David Pinson, Anil Kumar, Shilpa Buch
Affiliations expand
PMID: **18780230**PMCID: PMC2715277DOI: 10.1080/13550280802074539CurrOpinBiotechnol. 2020 Feb;61:209216
44. doi:10.1016/j.copbio.2020.01.004. Epub 2020 Feb 12.Plant-made HIV vaccines and potential candidates
JocelyneTremouillauxGuiller, KhaledMoustafa , KathleenHefferon, GoabaoneGaobotse , AbdullahMakhzoum
45. AIDS Rev. Apr-Jun 2015;17(2):107-13.Catch Me If You Can--The Race Between HIV and Neutralizing AntibodiesYvonneGeiß[1], Ursula Dietrich[1]
Affiliations expand PMID: **26035168**

46. J Virol. 2015 Apr;89(8):4158-69. doi: 10.1128/JVI.02904-14. Epub 2015 Jan 28.DNA vaccine molecular adjuvants SP-D-BAFF and SP-D-APRIL enhance anti-gp120 immune response and increase HIV-1 neutralizing antibody titers
Sachin Gupta, Emily S Clark, James M Termini, Justin Boucher, Saravana Kanagavelu, Celia C LeBranche, Sakhi Abraham, David C Montefiori, Wasif N Khan, GeoffreyWStone
Affiliations expandPMID: **25631080**PMCID: PMC4442371DOI: 10.1128/JVI.02904-14
47. Kim, J. H., Rerks-Ngarm, S., Excler, J. L., & Michael, N. L. (2010). HIV vaccines: lessons learned and the way forward. *Current opinion in HIV and AIDS*, *5*(5), 428–434. https://doi.org/10.1097/COH.0b013e32833d17ac
48. https://www.cdc.gov/hiv/basics/hiv-stigma/index.html
49. https://www.avert.org/professionals/hiv-social-issues/stigma-discriminationStigma in the HIV/AIDS epidemic: A review of the literature and recommendations for the way forward
Anish P. Mahajan, Jennifer N. Sayles, Vishal A. Patel, Robert H. Remien, Daniel Ortiz
50. https://www.researchgate.net/publication/271597092_DNA_vaccine_molecular_adjuvants_SP-D-BAFF_and_SP-D-APRIL_enhance_anti-gp120_immune_response_and_increase_HIV-1_neutralizing_antibody_titers
51. https://www.who.int/news-room/q-a-detail/vaccines-and-immunization-what-is-vaccination?adgroupsurvey={adgroupsurvey}&gclid=CjwKCAiAouD_BRBIEiwALhJH6IrBUqeBIUxSLvHmGcJrSCSqXlU7Kc_38cdTYjA9822LBKA8YOMMJhoCE0AQAvD_BwE
52. https://www.nhs.uk/conditions/hiv-and-aids/prevention/
53. https://www.cdc.gov/hiv/basics/prevention.html
54. https://www.cdc.gov/hiv/risk/estimates/riskfactors.html
55. https://www.winchesterhospital.org/health-library/article?id=19029
56. HIV: Sexual Transmission, Risk Factors, & Prevention
by Nicole Telfer, Science Content Producer— November 30, 2018
https://helloclue.com/articles/sex/hiv-sexual-transmission-risk-factors-and-prevention
57. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1497195/
Joshua Schechtel, MD, Thomas Coates, PhD, Kenneth Mayer, MD, and Harvey Makadon, MD
58. In March 1987, WHO published the "Special Programme on AIDS: strategies and structure projected needs", which is available athttp://apps.who.int/iris/bitstream/10665/62299/1/WHO_SPA_GEN_87.1.pdf (accessed 15 March 2016). In addition, the Global
59. The global health sector strategy on HIV/AIDS 2011–2015http://apps.who.int/iris/
60. GLOBAL HEALTH SECTOR STRATEGY ON HIV 2016–2021 TOWARDS ENDING AIDShttps://www.who.int/hiv/strategy2016-2021/ghss-hiv/en/
61. Global AIDS Update 2016, UNAIDS http://www.unaids.org/en/resources/documents/2016/Global-AIDS-update-2016
62. The present strategy on HIV uses the definition of "key populations" presented in the UNAIDS Strategy 2016–2021, available athttp://www.unaids.org/en/resources/documents/2015/UNAIDS_PCB37_15-18 (accessed 15 March 2016):
63. End TB Strategy, see http://www.who.int/tb/strategy/en/ (accessed 15 March 2016).