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Review Article

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A Review on: HIV and FDA-Approved Anti-HIV Medications

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Abstract

Acquired immune deficiency syndrome. AIDS is the most advanced stage of HIV infection. AIDS is diagnosed when a person infected with HIV has a CD4 count of less than 200 cells/mm3 or has an AIDS-defining condition. Any one of several illnesses that can lead to a diagnosis of AIDS in a person infected with HIV. AIDS is the most advanced stage of HIV infection. FDA-Approved Anti–HIV Medication-Non-nucleoside Reverse Transcriptase Inhibitors, Nucleoside Reverse Transcriptase Inhibitors, Protease Inhibitors, Protease Inhibitors (PIs), continued, Fusion Inhibitors, CCR5 Antagonists, Integrase Inhibitors, Fixed-Dose Combination for example Nevirapine, Lamivudine, Indinavir, Ritonavir, Zidovudine. The conclusion of this review article is to desicription of HIV, symptoms, types and last but not least enlists the medication which is approved by the U.S. Food and Drug Administration (FDA) for treatment of HIV in the United States.

Keywords: HIV, FDA-Approved Anti–HIV Medication

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1. Introduction

Human immunodeficiency virus infection / acquired immunodeficiency syndrome (HIV/AIDS) is a disease of the human immune system caused by infection with human immunodeficiency virus (HIV).[1] During the initial infection, a person may experience a brief period of influenza-like illness. This is typically followed by a prolonged period without symptoms. As the illness progresses, it interferes more and more with the immune system, making the person much more likely to get infections, including opportunistic infections and tumors that do not usually affect people who have working immune systems. HIV is transmitted primarily via unprotected sexual intercourse (including anal and even oral sex), contaminated blood transfusions, hypodermic needles, and from mother to child during pregnancy, delivery or breastfeeding.[2] Some bodily fluids, such as Saliva and tears, do not transmit HIV.[3] Prevention of HIV infection, primarily through safe sex and needle-exchange programs, is a key strategy to control the spread of the disease. There is no cure or vaccine; however, antiretroviral treatment can slow the course of the disease and may lead to a near-normal life expectancy. While antiretroviral treatment reduces the risk of death and complications from the disease, these medications are expensive and may be associated with side effects.

Genetic research indicates that HIV originated in west-central Africa during the early twentieth century.[4] AIDS was first recognized by the Centers for Disease Control and Prevention (CDC) in 1981 and its cause HIV infection was identified in the early part of the decade.[5] Since its discovery, AIDS has caused an estimated 36 million deaths (as of 2012).[6] As of 2012, approximately 35.3 million people are living with HIV globally.[6] AIDS is considered a pandemic a disease outbreak which is present over a large area and is actively spreading.[7] HIV/AIDS has had a great impact on society, both as an illness and as a source of discrimination. The disease also has significant economic impacts. There are many misconceptions about HIV/AIDS such as the belief that it can be transmitted by casual non-sexual contact.

The disease has also become subject to many controversies involving religion. It has attracted international medical and political attention as well as large-scale funding since it was identified in the 1980s.[8]HIV gradually destroys the immune system by attacking and killing CD4 cells. CD4 cells are a type of white blood cell that plays a major role in protecting the body from infection. HIV uses the machinery of the CD4 cells to multiply (make copies of it) and spread throughout the body. This process is called the HIV life cycle. HIV medicines protect the immune system by blocking HIV at different stages of the HIV life cycle. Antiretroviral therapy (ART) involves taking a combination of HIV medicines from at least two different HIV drug classes every day. Because HIV medicines in different drug classes block HIV at different stages of the HIV life cycle, ART is highly effective in reducing the amount of HIV in a person's body (HIV viral load). ART also reduces the risk of HIV resistance. ART can't cure HIV, but it does protect the immune system, which helps people with HIV live longer, healthier lives. (Figure 1)

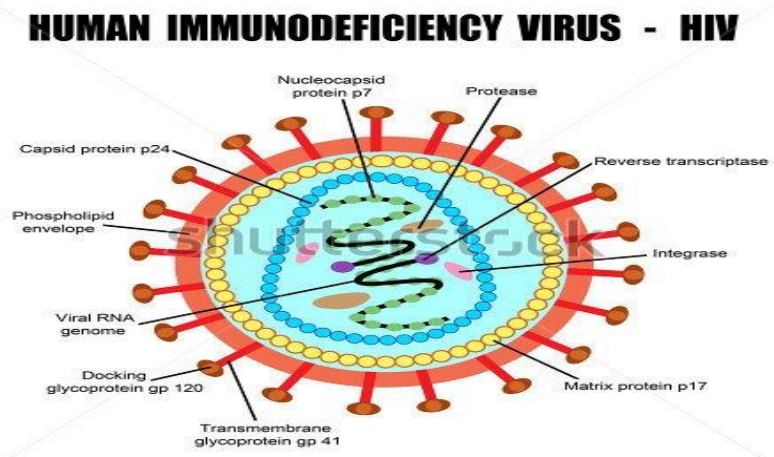

Figure 1. Structure of HIV virus

1.1 Connection between HIV medicines and the HIV life cycle:

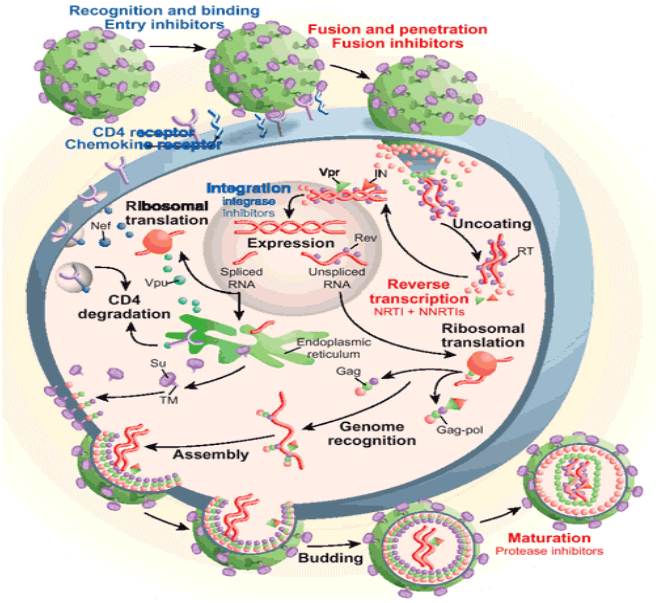

Figure 2. Life Cycle of HIV virus

Without treatment, HIV infection gradually destroys the immune system and advances to AIDS. HIV medicines protect the immune system by blocking HIV at different stages of the HIV life cycle. HIV medicines are grouped into different drug classes according to how they fight HIV. Each class of drugs attacks HIV at a different stage of the HIV life cycle. Standard HIV treatment (also called antiretroviral therapy or ART) involves taking a combination of HIV medicines from at least two different HIV drug classes every day. Because HIV medicines in different drug classes block HIV at different stages of the HIV life cycle, ART is highly effective in reducing the amount of HIV in a person's body (HIV viral load). ART also reduces the risk of HIV drug resistance. (Figure 2)

1.2 Types of HIV /AIDS

Two major types of HIV have been identified such as,

1.2.1 HIV 1: It is the cause of worldwide epidemic and is most commonly referred to as HIV. It is a highly variably virus, which mutate readily. There are many different strains of HIV-1, which can be classified according to groups and subtypes; M and O. Within group M, there are currently known to be at least ten genetically distinct subtypes which are A to J.

1.2.2 HIV 2: In addition, Group contain another distinct group of heterogeneous viruses.HIV -2 is less pathogenic and rarely, it is found mostly in West Africa.[10]

1.3 HIV Infection Mechanism:

HIV begins its infection by the CD4 receptor on the host cell.CD4 is present on the surface of many lymphocytes. Which are a critical parts of the body's immune system. It is now known that a co-receptor is needed for HIV to enter the cell. Following fusion of the virus with the host cell, HIV enters the cell. The genetic material of the virus, which is RNA, is released and undergoes reverse transcription into DNA .An enzyme in HIV called reverse transcriptase is necessary to catalyze this conversion of viral RNA into DNA enters the host cell nucleus where it can be integrate into the genetic material of the cell. The enzyme Integrasecatalyses this process. Once the viral DNA is integrated into the genetic material of the host .It is possible that HIV may persist in a Latent state for many years. This ability of HIV to persist in certain latently infected cells is the major barriers to eradication or cure of HIV.[11]

1.4 Symptoms of HIV/AIDS:

These symptoms usually disappear within a week to a month and are often mistaken for another viral infection, such as flu. However, during this period people are highly infectious because HIV is present in large quantities in genital fluids and blood. Some people infected with HIV may have more severe symptoms at first or symptoms that last a long time, while others may have no symptoms for 12 years or more. (Table1)

Table 1. Symptoms of HIV

Early Symptoms	Later Symptoms
In the first stages of HIV infection, most people will have very few, if any, symptoms. Within a month or two after infection, they may experience a flu-like illness, including:	During the late stages of HIV infection, the virus severely weakens the immune system, and people infected with the virus may have the following symptoms
Fever Headache Tiredness Enlarged lymph nodes in the neck and groin area	Rapid weight loss Recurring fever or profuse night sweats Extreme and unexplained tiredness Prolonged swelling of the lymph glands in the armpits, groin, or neck Diarrhea that lasts for more than a week Sores of the mouth, anus, or genitals Pneumonia Red, brown, pink, or purplish blotches on or under the skin or inside the mouth, nose, or eyelids Memory loss, depression, and other neurologic disorders.

2. FDA-Approved ANTI –HIV Medication

There are six major types of drugs used to treat HIV/AIDS. Called antiretrovirals because they act against the retrovirus HIV, these drugs are grouped by how they interfere with steps in HIV replication (PDF).

2.1 Entry Inhibitors interfere with the virus' ability to bind to receptors on the outer surface of the cell it tries to enter. When receptor binding fails, HIV cannot infect the cell.

2.2 Fusion Inhibitors interfere with the virus's ability to fuse with a cellular membrane, preventing HIV from entering a cell.

2.3 Reverse Transcriptase Inhibitors prevent the HIV enzyme reverse transcriptase (RT) from converting single-stranded HIV RNA into double-stranded HIV DNA a process called reverse transcription. There are two types of RT inhibitors:
Nucleoside/nucleotide RT inhibitors (NRTIs) are faulty DNA building blocks. When one of these faulty building blocks is added to a growing HIV DNA chain, no further correct DNA building blocks can be added on, halting HIV DNA synthesis.
Non-nucleoside RT inhibitors (NNRTIs) bind to RT, interfering with its ability to convert HIV RNA into HIV DNA
2.4 Integrase Inhibitors block the HIV enzyme integrase, which the virus uses to integrate its genetic material into the DNA of the cell it has infected.
2.5 Protease Inhibitors interfere with the HIV enzyme called protease, which normally cuts long chains of HIV proteins into smaller individual proteins. When protease does not work properly, new virus particles cannot be assembled.
2.6 Multi-class Combination Products combine HIV drugs from two or more classes, or types, into a single product. human history, it has provided important insights into Creutzfeldt–Jacobs Disease (CJD) in humans and Bovine Spongiform Encephalopathy (BSE) in cattle [7].

The following table lists anti-HIV medications approved by the U.S. Food and Drug Administration (FDA) for treatment of HIV in the United States. The medications are presented by drug class and identified by generic name/acronym and brand name.[9, 10](Table2).

Table 2. FDA approved medications

Drug Class	Generic Name (Acronym)	Brand Name	Manufacturer	FDA Approval Date
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
NNRTIs bind to and alter reverse transcriptase, an enzyme HIV needs to make copies of itself.	Delavirdine (DLV)	Rescriptor	Pfizer	April 4, 1997
	Efavirenz (EFV)	Sustiva	Bristol-Myers Squibb	Sept. 17, 1998
	Etravirine (ETR)	Intelence	Tibotec	Jan. 18, 2008
	Nevirapine (NVP)	Viramune	BoehringerIngelheim	June 21, 1996
	Rilpivirine (RPV)	Edurant	Janssen Pharmaceuticals, Inc.	May 20, 2011
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
NRTIs block reverse transcriptase, an enzyme HIV needs to make copies of itself.	Abacavir (ABC)	Ziagen	GlaxoSmithKline	Dec. 17, 1998
	Didanosine (ddl)	VidexVidex EC (enteric-coated)	Bristol-Myers Squibb Bristol-Myers Squibb	Oct. 9, 1991 Oct. 31, 2000
	Emtricitabine (FTC)	Emtriva	Gilead Sciences	July 2, 2003
	Lamivudine (3TC)	Epivir	GlaxoSmithKline	Nov. 17, 1995
	Stavudine (d4T)	Zerit	Bristol-Myers Squibb	June 24, 1994
	Tenofovir DF (TDF)	Viread	Gilead Sciences	Oct. 26, 2001
	Zidovudine (ZDV, AZT)	Retrovir	GlaxoSmithKline	March 19, 1987
Protease Inhibitors (PIs)				
PIs block HIV protease, an enzyme HIV needs to make copies of itself	Atazanavir (ATV)	Reyataz	Bristol-Myers Squibb	June 20, 2003
	Darunavir (DRV)	Prezista	Janssen Pharmaceuticals, Inc.	June 23, 2006
	Fosamprenavir (FPV)	Lexiva	GlaxoSmithKline	Oct. 20, 2003
	Indinavir (IDV)	Crixivan	Merck	March 13, 1996
	Nelfinavir (NFV)	Viracept	Agouron Pharmaceuticals	March 14, 1997 This
Protease Inhibitors (PIs), continued				
PIs block HIV protease, an enzyme HIV needs to make copies of	Ritonavir (RTV)	Norvir	Abbott Laboratories	March 1, 1996
	Saquinavir (SQV)	Invirase	Hoffmann-La Roche	Dec. 6, 1995
	Tipranavir (TPV)	Aptivus	BoehringerIngelheim	June 20, 2005
Fusion Inhibitors				
PIs block HIV protease, an enzyme	Enfuvirtide (T-20)	Fuzeon	Hoffmann-La Roche, Trimeris	March 13, 2003

HIV needs to make copies of				
CCR5 Antagonists				
CCR5 entry inhibitors block CCR5, a protein on the CD4 cells that HIV needs to enter the cells	Maraviroc (MVC)	Selzentry	Pfizer	Aug. 6, 2007
Integrase Inhibitors				
Integrase inhibitors block HIV Integrase, an enzyme HIV needs to make copies of it.	Raltegravir (RAL)	Isentress	Merck	Oct. 12, 2007
Fixed-Dose Combination				
Fixed-dose combination tablets contain two or more anti-HIV medications from one or more drug classes.	Abacavir, Lamivudine	Epzicom	GlaxoSmithKline	Aug. 2, 2004
	Abacavir, Lamivudine, Zidovudine	Trizivir	GlaxoSmithKline	Nov. 14, 2000
	Efavirenz, Emtricitabine, Tenofovir DF	Atripla	Bristol-Myers Squibb, Gilead Sciences	July 12, 2006
	Elvitegravir, Cobicistat , Emtricitabine, Tenofovir DF	Stribild	Gilead Sciences	Aug. 27, 2012
	Emtricitabine, Rilpivirine, Tenofovir DF	Complera	Gilead Sciences	Aug. 10, 2011
	Emtricitabine, Tenofovir DF	Truvada	Gilead Sciences	Aug. 2, 2004
	Lamivudine, Zidovudine	Combivir	GlaxoSmithKline	Sept. 27, 1997
	Lopinavir, Ritonavir	Kaletra	Abbott Laboratories	Sept. 15, 2000

3. Conclusion

The human immunodeficiency virus, or HIV, is the virus that causes HIV infection. During HIV infection, the virus attacks and destroys the infection-fighting CD4 cells of the body's immune system. Loss of CD4 cells makes it difficult for the immune system to fight infections. Acquired immunodeficiency syndrome, or AIDS, is the most advanced stage of HIV infection. Antiretroviral therapy (ART): The recommended treatment for HIV. ART involves taking a combination of three or more anti-HIV medications from at least two different drug classes every day to control the virus. Many anti-HIV medicines which are approved by USFDA that inhibit HIV during various stages of cycles. To prevent strains of HIV from becoming resistant to a type of antiretroviral drug, healthcare providers recommend that people infected with HIV take a combination of antiretroviral drugs in an approach called highly active antiretroviral therapy (HAART). Developed by NIAID-supported researchers, HAART combines drugs from at least two different classes. So that the conclusion of this review article is to enlist the medication which is approved by the U.S. Food and Drug Administration (FDA) for treatment of HIV in the United States.

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