MINI REVIEW
Volume 9:3, 2021

Journal of General Practice

ISSN: 2329-9126 Open Access

HIV- The Idiosyncratic Virus of Modern Era

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Abstract

The cardiovascular system is the first system to develop and to function. It supplies tissues and organs with oxygen, nutrients, hormones, immune competent cells and others and deliberates them from waste products and metabolic heat. Many attempts were made to gain insights into its three-dimensional structure by injecting air, liquids, waxes or hardening substances.

Keywords: **Hormones • Arteries • Veins • Blood vascular system • Capillaries**

About the Study

Human beings are the products of Psychological and Cosmological arrows of time. Inspite of assisting in the creation of human race, these arrows of time have also evolved flabbergasting screenplays in the form of life and death. The voyage of mankind to the future has always been trammeled by various types of scenarios and HIV is one of them.

This virus of RNA Retro viruses group causes AIDS, which by definition is CD4+ T Cell count of <200/µL. The most common cause of HIV disease throughout the world is HIV-1, which comprises several subtypes i-e HIV (M, N, O, P). The main structure of HIV virus is Lipid Bilayer Bubble that is purloined from the host cell. The Lipid Bilayer consists of Transmembrane Protein gp41 and docking protein gp120. The unified structure of gp41 and gp120 is called gp160 protein. The virus loves to infect CD4+ cells. The CD4+ molecule is found predominantly on T-Helper Cells but it is also expressed on the surface of monocytes/ macrophages, microglia, Langerhans cells under the skin and Follicular Dendritic cells in the spleen and Lymph nodes. After primary attachment between gp120 and CD4+ receptors, the gp120 undergoes a conformational change that facilitates its binding with one of the two major co-receptors. The two major co-receptors for HIV-1 are CCR5 and CXCR4. The CCR5 is expressed by Macrophages while CXCR4 is expressed by T-Helper Cells. Some of the Dendritic Cells express DC-SIGN receptor on their surface, that also binds with high affinity to the gp120 envelope protein, allowing the dendritic cell to facilitate the binding of virus to the CD4+ T Cell upon engagement of dendritic cells with CD4+ T Cells. The gp41 starts hooking the target cell after primary and secondary attachments between gp120 and CD4+ receptor plus co-receptor. Following fusion, the Preintegration complex, composed of viral RNA and viral enzymes that are surrounded by a Capsid Protein Coat, is released into the cytoplasm of the target cell. That is why, gp41 is also called Fusion molecule. Enfuvirtide is a fusion inhibitor that stops the expression of gp41. The capsid of the HIV contains three enzymes namely Reverse Transcriptase Enzyme, Integrase enzyme and Protease enzyme. The proteins that make the capsid are called P24 proteins. As soon as, the Preintegration complex reaches the nucleus of human cell, the viral reverse transcriptase enzyme catalyzes the Reverse Transcription of the genomic RNA into DNA, and the Protein coat opens to release the resulting double-strand proviral HIV-DNA. The viral DNA is integrated into the host cell chromosomes through the action of viral enzyme Integrase. Cellular activation plays an important role in the replication cycle of HIV and is critical to the pathogenesis of HIV disease. When the DNA of HIV is transcribed into HIV's mRNA, the mRNA of HIV is translated into proteins that undergo modification through Glycosylation, Myristoylation, Phosphorylation and Clevage. The viral particle is formed by the assembly of HIV proteins, enzymes and genomic RNA at the plasma membrane of the cells. HIV employs at least three mechanisms to evade neutralizing response of antibodies that are Hypervariability in the primary sequence of the envelope, Extensive Glycosylation of the envelope & Conformational masking of Neutralizing Epitopes. The diagnosis of HIV leading to AIDS can be confirmed by ELISA, western blot test, p24 Antigen capture assay, HIV RNA by PCR, HIV RNA by bDNA, HIV RNA by NASBA and CD4+ T Cell count.

The eradication of purgatory scenes produced by HIV needs the galvanization of efforts worldwide. Research should be carried out to ferret out potential CD4+ Receptor Blockers for therapeutic purposes. Scientists should also explore arenas to discover CCR5 Blockers and CXCR4 Blockers. Maraviroc is the CCR5 blocker known to date. Studies should also be conducted for finding a selective Cyclophilin A inhibitor. Cyclopholin A is implicated in blocking the activity of TRIM-α protein. Quest should

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Received: January 7, 2021; **Accepted**: January 21, 2021**; Published**: January 28, 2021

also be initiated to devise the tools for inhibition of Viral vif protein that targets APOBEC for proteasomal degradation. Search should be carried out for the inhibition/blocking or destroying the Lipid Rafts where the core acquires its external envelope. The discovery of drugs that should inhibit the expression of viral genes like gag, pol, env and six other regulatory genes will be a quantum leap in therapeutic arena. This can be achieved either at Transcriptional stage or at translational level. Remedies should also be ferreted out to inhibit/block the activity of pro-inflammatory cytokines TNF-α, IL-1β and IL-6 that induce HIV expression. The pharmaceutical companies should be tasked with the synthetic production of Interferon α & β, IL-32 and IL-27 that are helpful in the suppression of HIV replication. The availability of the preparations of T-regs that are helpful in lowering viral loads and high CD4+/CD8+ T Cell ratios would be a great leap forward in therapeutic arena. CD8+ T cells secrete a variety of soluble factors that inhibit HIV replication. These soluble factors include CC-Chemokines RANTES (CCL5), MIP-1α (CCL3), and MIP-1β (CCL4). Synthetic production or preparations of these factors for availability in the market may bring a new aurora of hope and blessings to the victims of HIV.

To arrest the extremities and dreads of HIV, Zidovudine, Lamivudine and Vitamin A should be included in the essential drugs list of third world countries that reduce the risk of transmission from mother to infant during pregnancy. Deworming, Anti-malaria and anti-tuberculosis campaigns should be made prodigious affairs throughout the globe. A paradigm of male circumcision should be initiated around the planet, which is associated with low risk of HIV infection among heterosexual men.1 A campaign against Bacha Bazi (Child Sexual Abuse) in Afghanistan and Pakistan would be a great leap forward in beating the perils of HIV.2,3 According to Asian Epidemic Modelling (AEM), conducted in 2015, the primary mode of HIV transmission in Pakistan is the use of contaminated injection equipment among people who inject drugs (PWID). Therefore, countries like Pakistan need to implement programs to control an expanding HIV epidemic among IDUs.4,5 Another group which contributes to the HIV epidemic in Pakistan is that of HIV+ returned migrant workers from Gulf states especially from UAE.6 Hence, the countries with HIV+ returned migrant workers shall undertake an exercise of screening their citizens for timely deduction of the virus and isolation of the affected individuals.

The continuous pummeling of HIV also needs the pains of Medical Physicists and mechano-biologists. Physics tells us that the very existence of living creatures is the confirmation of Grand Unification Theories. In my opinion, the medical physicists should devise tools or an environment where the very existence of all the forces between matter particles come to standstill or in other words absent/nil. In such scenario, no virus formation like that of HIV will take place due to absence of Grand Unification and gravity. The invention of tools by Medical physicists and bio-medical engineers that can disturb particle/anti-particle pairs phenomena inside HIV virus can also help in the downfall of viruses like HIV. Every dawn of tomorrow brings the incantations of optimism and the hope lies in the immanence of God.

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How to cite this article: Ali, Faisal."HIV- The Idiosyncratic Virus of Modern Era" *J Gen Pract* 9(2021): 387.