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A REVIEW ON HUMAN IMMUNODEFICIENCY VIRUS INFECTION AND RETROVIRUSES

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ABSTRACT: Human Immunodeficiency Virus or HIV is generally known, is a unique type of virus (retrovirus). HIV is a slow virus that causes acquired immunodeficiency syndrome, a human condition in which the progressive failure of the immune system allows opportunistic infections and life-threatening cancers to spread. Retroviruses are a single positive susceptible RNA virus with a DNA mediator and binding parasite targeting a host cell. Retroviruses have risen to prominence in human pathology through their recent association with leukemia and acquired immunodeficiency syndrome (AIDS). This virus infects species of vertebrates ranging from fish to primates and can cause various types of malignancies, homeopathy, immune diseases, and neurodegenerative diseases. Since the Peyton Rous experimented more than 70 years ago, animal retroviruses have served as models for viral carcinogenesis, with oncogenes being discovered for the first time. The central goals of retrovirology today are the treatment and prevention of human and non-human diseases and the use of this virus in research. Recent studies have shown that retroviruses can be used in several ways, such as as a model for biological research, understanding genetics, and molecular and cellular biology studies.

INTRODUCTION: The Human Immuno-deficiency Virus or HIV, as it is commonly known, is a unique type of virus (a retrovirus). The human immunodeficiency virus is a lentivirus that causes the acquired immunodeficiency syndrome, a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive.

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AIDS (acquired immune deficiency syndrome) is the final stage of HIV disease, which causes severe damage to the immune system [1]. HIV is the virus that causes AIDS. Disease limits the body's ability to fight infection due to markedly reduced helper T cells. Patients have a fragile immune system (defense mechanism). Patients predisposed to multiple opportunistic infections leading to death.

Epidemiology of HIV and AIDS in India: HIV/AIDS is an epidemic in India. The NACO estimated that 2.11 million people lived with HIV/AIDS in India in 2015. Despite being home to the world's third-largest population suffering from HIV/AIDS (as of 2018, with South Africa and Nigeria having more), the AIDS prevalence rate in

India is lower than in many other countries. In 2016, India's AIDS prevalence rate stood at approximately 0.30% - the 80th highest in the world. Treatment of HIV/AIDS is primarily *via* a "drug cocktail" of antiretroviral drugs and education programs to help people avoid infection [2]. A 2006 study published in the British medical journal "The Lancet" reported an approximately 30% decline in HIV infections among young women aged 15 to 24 years attending prenatal clinics in selected southern states of India from 2000 to 2004, where the epidemic is thought to be concentrated. In addition, recent studies suggest that many married women in India, despite practicing monogamy and having no other risk behaviors, acquire HIV from their husbands and HIV testing of married males can be an effective HIV prevention strategy for the general population.

In 2007, the third phase of the National AIDS Control Programme (NACP III) targeted the high-risk groups and conducted outreach programs. It also decentralized the effort to local levels and non-governmental organizations (NGOs) to provide welfare services to the affected. The US$ 2.5 billion National AIDS Control Plan III was set up by India in 2007 and received support from UNAIDS. The third stage dramatically increased targeted interventions, aiming to halt and reverse the epidemic by integrating prevention, care, support, and treatment programs. By the end of 2008, targeted interventions covered almost 932,000 of those most at risk, or 52% of the target groups (49% of FSWs, 65% of IDUs, and 66% of MSM).

Some efforts have been made to tailor educational literature to low literacy levels, mainly through local libraries. This is the most readily accessible locus of information for interested parties. In addition, increased awareness regarding the disease and citizen's related rights aligns with the Universal Declaration on Human Rights. In 2009, India established a National HIV and AIDS Policy and the World of Work, which sought to end discrimination against workers based on their actual or perceived HIV status. Under this policy, all enterprises in public, private, formal, and informal sectors are encouraged to establish workplace policies and programs based on non-discrimination principles, gender equity, health work environment, non-screening for employment confidentiality, prevention, and care and support. Researchers at the Overseas Development Institute have called for greater attention to migrant workers, whose concerns about their immigration status may exclude them from these policies and leave them particularly vulnerable.

No agency is tasked with enforcing a non-discrimination policy. Instead, a multi-sectoral approach has been developed involving awareness campaigns in the private sector. The AIDS Bhedbhav Virodhi Andolan (AIDS Anti-Discrimination Movement) had prepared many citizens' reports challenging discriminatory policies and filed a petition in the Delhi High Court regarding the proposed segregation of gay men in prisons. A play titled 'High Fidelity Transmission' by author Rajesh Talwar has focused on discrimination. The importance of the condom as compared with abstinence and illegal testing of vaccines. HIV/AIDS-related television shows and movies have appeared in the past few years, mostly to appeal to the middle class. An important component of these programs is depicting HIV/AIDS-affected persons interacting with non-infected persons in everyday life. As per UNDP's 2010 report, India had 2.395 million people living with HIV at the end of 2009, up from 2.27 million in 2008. Adult prevalence also rose from 0.29% in 2008 to 0.31% in 2009. Setting up HIV screening centers was the first step taken by the government to screen its citizens and the blood bank.

The adult HIV prevalence in India is declining from an estimated level of 0.41% in 2000 through 0.36% in 2006 to 0.31% in 2009. Adult HIV prevalence at a national level has declined notably in many states, but variations still exist across the states. A decreasing trend is also evident in HIV prevalence among the young population of 15-24 years. A 2012 report described a need for youth HIV counseling. According to NACO data, India had demonstrated an overall reduction of 57 percent in estimated annual new HIV infections (among the adult population) from 0.274 million in 2000 to 0.116 million in 2011. The estimated number of people living with HIV was 2.08 million in 2011. According to NACO, the prevalence of AIDS in India in 2015 was 0.26%, down from 0.41% in 2002; in 2016, it had risen to 0.30%.

India is the second-most populous country in the world, with more than 880 million people in 1993. With less than 1% of the global landmass, India has more than 16% of the world's population, more than South America, Africa, and Australia combined.

The number of people will exceed one billion by 2000, surpassing even China. By then, India will have more new cases of HIV infection per year than any single country and probably the most significant number of HIV-infected people as well. Whatever happens in India will therefore have a substantial impact upon the global pandemic of HIV and AIDS.

The paper considers the history of the HIV epidemic in India, the probable routes of entry of HIV into India, trends in prevalence in population samples, the geographic distribution of HIV in India, AIDS in India, clinical problems in India, projections of HIV/AIDS cases and how to control HIV/AIDS. The HIV epidemic has grown silently in India over the past decade, with the virus spread mainly through heterosexual intercourse. However, all known routes of transmission are known in India, and increasing seroprevalence has been noted among prostitutes, STD clinic patients, blood donors, and IV drug users. Unfortunately, the population has been largely ignorant of the advance of HIV, with public officials and the media at a loss to inform the public about what is taking place adequately. More incredible energy and resources are now being devoted to the problem, but it may be too late to stop a significant epidemic. The authors reviewed all available published and unpublished data to present an overview of the epidemiology of HIV and AIDS in India. Transmission of HIV: HIV Transmitted by Sexual intercourse (anal and vaginal), contaminated blood and blood products, tissues and organs, contaminated needles, syringes and another piercing instrument, mother-to-child transmission (MTCT) [3].

HIV is not transmitted through shaking hands, hugging/kissing, coughing or sneezing, using a public phone, visiting a hospital, opening a door, sharing food, eating or drinking utensils, using toilets.

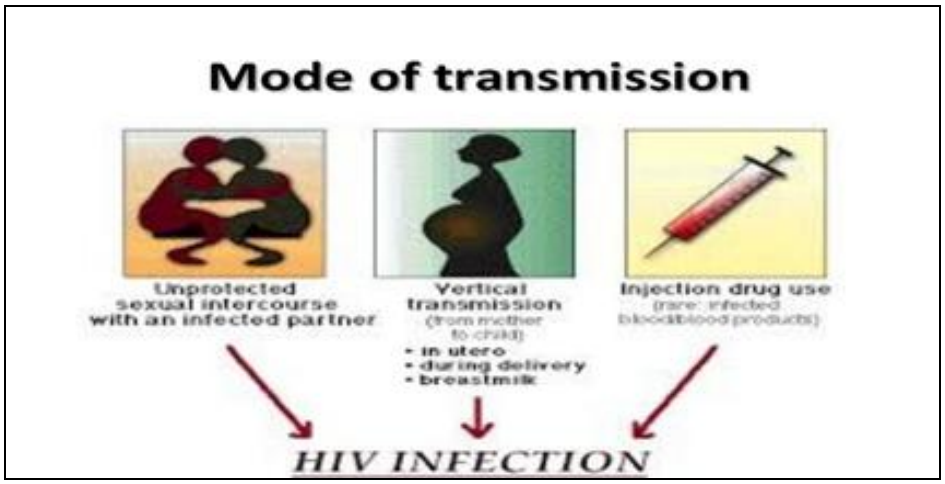

FIG. 1: MODES OF HIV TRANSMISSION

Retroviruses: A retrovirus is a single-stranded positive-sense RNA virus with a DNA intermediate and as an obligate parasite, targets a host cell. Once inside the host cell cytoplasm, the virus uses its reverse transcriptase enzyme to produce DNA from its RNA genome. The reverse of the usual pattern, thus retro (backward). This new DNA is then incorporated into the host cell genome by an integrase enzyme, at which point the retroviral DNA is referred to as a provirus. The host cell then treats the viral DNA as part of its genome, translating and transcribing the viral genes and the cell's genes, producing the proteins required to assemble new copies of the virus. It is difficult to detect the virus until it has infected the host. At that point, the infection will persist indefinitely [4].

Diseases Caused by a Retrovirus

Human: The human immunodeficiency virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes HIV infection and acquired immunodeficiency syndrome (AIDS). AIDS is a

condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. Without treatment, the average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype. Infection with HIV occurs by transferring 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 [5].

Retroviruses and Human Disease: Retroviruses have leaped into prominence in human pathology through their recent association with leukemia and the acquired immune deficiency syndrome (AIDS). This family of viruses infects vertebrate species ranging from fish to primates and can cause diverse types of malignancy, homeopathy, immune disease, and degenerative neural disease. Since Peyton Rous's experiments more than 70 years ago, animal retroviruses have served as models of viral carcinogenesis, and oncogenes were first discovered in them.

Retroviruses Are Classified Into Three Main Subfamilies: the RNA tumor viruses (oncovirinae), the "slow" viruses (lentiviral) and the "foamy" viruses (spumavirinae). These three groups are morphologically distinct and the oncovirus is further divided into those producing B type, C type, and D type virions. Retroviruses are so-called because there is a step "backward" in genetic information during their replication cycle. The virus particles contain genes in single-stranded RNA, which is converted into a double-stranded DNA "provirus" early in infection by the viral enzyme reverse transcriptase. The DNA provirus becomes inserted into the chromosomal DNA of the infected host cell and thus establishes a persistent infection. This may remain latent or be expressed and produce progeny virus. Proviral genomes have occasionally integrated into germline DNA to become Mendelian genetic traits of the host. Several endogenous proviral genetic elements have been identified and cloned from human DNA and seem to represent "fossil" retrovirus infections from earlier primate evolution. One such factor is expressed as antigen and occasional C-type particles in the syncytiotrophoblast of the human placenta and teratocarcinoma, but it is not associated with the disease. Until seven years ago, infectious human retroviruses were unknown; now, at least four human retroviral pathogens are recognized. Human T cell leukemia virus type 1 (HTLV-1, sometimes called ATLV) and type 2 (HTLV-2) belong to the oncovirus subfamily, whereas human immunodeficiency virus type 1 (HIV-1, alias LAV-1, HTLV-3, ARV) and type (HIV-2) are more closely related to the lentivirus subfamily. At least one serotype of the human foamy virus exists, known as the human syncytial virus. Simian foamy viruses are neurotropic, but how they affect man is still obscure. Human syncytial virus infection may be linked with de Quervain's sub-acute thyroiditis. It has been postulated that some forms of non-A, non-B. Retroviruses might cause hepatitis, but evidence for reverse transcriptase activity in the plasma of affected patients has not been upheld. Quite recently, preliminary proof of reverse transcriptase and putative retroviral particles was found in cells cultured from subjects with Kawasaki disease. HTLV-1 is also associated with spastic par paresis and a link with multiple sclerosis tropical has been suggested. Nevertheless, retroviruses are fashionable, especially for syndromes awaiting the discovery of etiological agents.

Molecular Biology and Pathogenesis of Retroviruses: Retrovirus has done an adequate amount of harm to human life during the past few decades and became a significant threat globally. These are the group of viruses that belong to the family Retroviridae and typically carry their genetic material in the form of ribonucleic acid (RNA), while the genetic material of their hosts is in the form of deoxyribonucleic acid (DNA).Retroviruses are named for an enzyme known as reverse transcriptase (RT), which was discovered independently in 1971 by American virologists Howard Temin and David Baltimore. They have received Nobel Prize in physiology and medicine in the year 1975. Retroviridae is a family of enveloped, obligate parasites with single-stranded positive-sense RNA (ssRNA) that replicate in a host cell through the process of reverse transcription. The activity of RT makes it feasible for genetic material from a retrovirus to become permanently integrated into the DNA genome (provirus) of an infected cell.

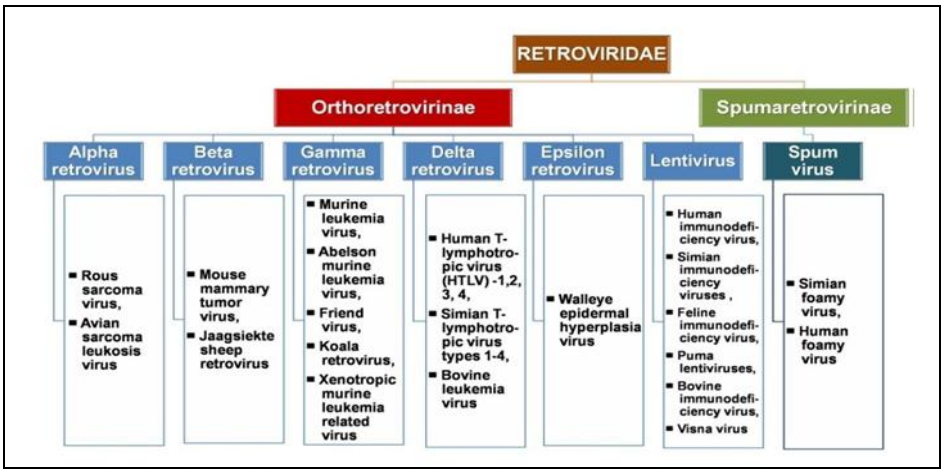

FIG. 2: CLASSIFICATION OF RETROVIRIDAE FAMILY OF VIRUSES

Retroviridae is subdivided into Orthoretrovirinae and Spumaretrovirinae **Fig. 2.** Under Ortho retrovirinae, the various genus is an Alpha retrovirus (Rous sarcoma virus, avian sarcoma Leukosis virus), Beta retrovirus (Mouse mammary tumor virus, Jaagsiekte sheep retrovirus), Gamma retrovirus (murine leukemia virus, Abelson murine leukemia virus, Friend virus, koala retrovirus, xenotropic murine leukemia-related virus), Delta retrovirus (Human T-lymph tropic virus (HTLV) types 1-4, simian T-lymph tropic virus types 1-4, Bovine leukemia virus), Epsilon retrovirus (Walleye epidermal hyperplasia virus) and Lentivirus (human immunodeficiency virus (HIV), simian immunodeficiency viruses (SIV), feline immunodeficiency virus, puma lentivirus, bovine immunodeficiency virus, caprine arthritis encephalitis virus, visna virus) are present. In contrast, under Spumaretrovirinae only one genus is present spumavirus (simian foamy virus, human foamy virus). The retroviruses host range includes humans, murine, feline (cat), avian (birds), and bovine (pig), and it is dependent upon the viral envelope, glycoproteins, and structural proteins involved in integration. Infections with several retroviruses can lead to severe conditions, such as AIDS, a range of malignancies, neurological diseases, and added clinical conditions. In addition, some retroviruses can even become integrated as DNA in the germline and passed as endogenous viruses from generation to generation. Using retrovirus in research has built up the need to advance the investigation detail regarding the viral particles and genomes, their modes of replication, integration and host immune evasion. The primary replication of retroviruses includes that **Fig. 3.** the ssRNA becomes double-stranded DNA (dsDNA) and gets into the host genetic material and employs host machinery to synthesize new virions.

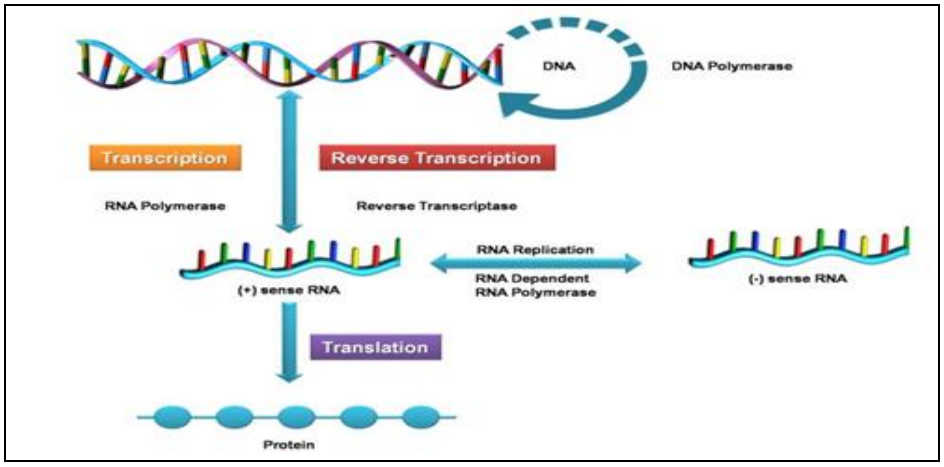

FIG. 3: THE REVERSE OF CRICKS' CENTRAL DOGMA THAT OCCURS IN RETROVIRUSES. THE RNA GENOME IS CONVERTED BY REVERSE TRANSCRIPTASE INTO DOUBLE-STRANDED DNA, FOLLOWED BY INTEGRATION INTO THE HOST GENOME, TRANSCRIPTION AND TRANSLATION OF VIRAL PROTEINS OCCUR ALONG WITH THE HOST

Interesting Points about Retroviruses:

- Retroviruses contain RNA as genetic material but have DNA-dependent steps in their replication.
- Replicates *via* reverse transcription because of the presence of reverse transcriptase enzyme.
- Integrase transfers the viral DNA into the cell nucleus and viral dsDNA is covalently and randomly integrated into the cell's genome.
- Retroviruses that can transform host cells at high rates contain gene sequences such as viral oncogenes and proto-oncogenes.
- Human retroviruses can cause immune deficiencies, cancer, and neurological diseases [6].

Retrovirus Structure, Genome and Proteins: The typical retrovirus structure is enveloped, spherical to pleomorphic in shape, and has a diameter of 80-100 nm. The other geniuses of retrovirus virions **Fig. 3.** have diverse morphology. Still, they have the sae mvirions component, including the outer envelope coat, two copies of the genetic material, and the viral proteins.

The envelope consists of lipids obtained from the host plasma membrane during the budding process and the glycoprotein such as gp120 and gp41 in HIV. The retroviral envelope serves three separate functions that include the outer lipid bilayer protects from the extracellular environment, it also aids in the entry and way out of host cells through endosomal membrane trafficking, and the facility to straightforwardly enter cells by fusing with their membranes [7].

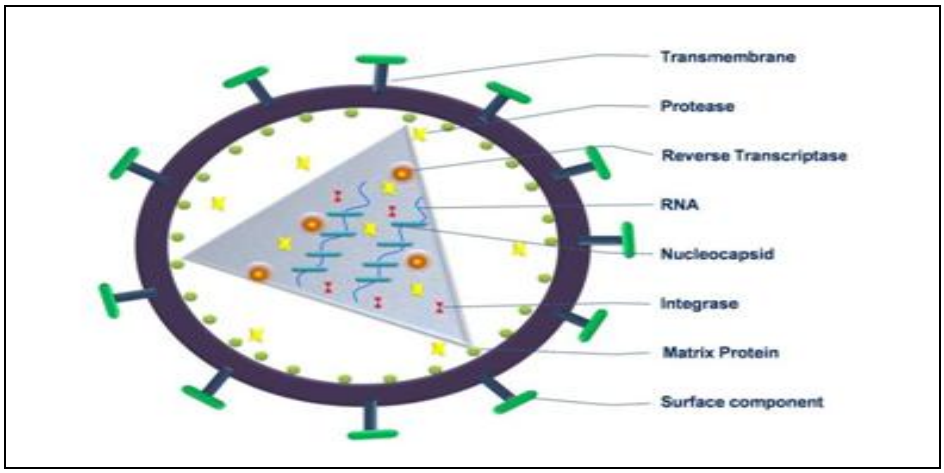

FIG. 4: A SCHEMATIC CROSS-SECTION THROUGH A RETROVIRAL PARTICLE: SHOWING RETROVIRUS COMPONENTS

A retrovirus genome is monopartite, linear, dimeric, ssRNA (+) of about 8–10 kb, with a 5'-cap and a 3'poly-A tail. The group-specific gene (gag), pol, pro, envelope (env) genes are flanked between the R regions. The 5'-long terminal repeats (LTRs) consist of U3 (unique sequence), R primer binding site (PBS), and U5 regions. The 3' end includes a polypurine tract (PPT), U3 and R regions. The R region is a short repeated sequence at each end of the genome used during the reverse transcription to ensure correct end-to-end transfer in the growing chain. U5, on the other hand, is an exceptional temporary arrangement in the middle of R and PBS. PBS consists of 18 bases corresponding to the 3' end of the tRNA primer. L region is an untranslated leader region that gives the sign for packaging of the genome RNA. The retroviral protein includes gag, protease, pol, and env proteins. The gag is the primary retroviral structural protein responsible for orchestrating the majority of steps in viral assembly. Most of these assembly steps occur through interactions with three gag sub-domains-matrix (MA), capsid (CA), and nucleocapsid (NC). The gag sub domains are structurally discrete but have functionally overlapping roles in the viral assembly process [8].

Replication of Retroviruses: Replication is a multistep process; each step is crucial for the virus entry and multiplies itself in the host cell. The study of retroviruses particle assembly, budding, and release has been especially rich in terms of the

exchange of concepts and techniques with related areas of cell biology. There are seven steps in the replication cycle of the retrovirus. The initial step is attachment, in which the retrovirus utilizes one of its glycoproteins to attach to one or more particular cell-surface receptors on the host cell. Some retroviruses likewise use an optional receptor, referred to as the co-receptor. The second and third steps are penetration and uncoating, individually. Retroviruses infiltrate the host cell by direct fusion of the virion's envelope with the host's plasma membrane. The fourth step is replication, which happens after the retrovirus undergoes partial uncoating, releasing its genome and three essential enzymes (RT, Integrase, and pol gene coding enzymes). At this stage, the RNA genome is converted by RT into double-stranded DNA, followed by integration into the host genome, transcription, and translation of viral proteins along with the host.

The fifth step is assembly, in which retrovirus capsid is assembled in an immature form. The sixth step is budding, in which the green viral particle acquires the host plasma membrane, and the final step is maturation and release. The gag and pol proteins of the retrovirus are cleared by the retroviral protease, thus forming the mature and infectious form of the virus. Retrovirus replication is well studied in the case of HIV. HIV replicates millions of times per day, destroying the host immune cells and eventually causing disease progression. During HIV replication, the virus recognizes host cells such as CD4+ T-lymphocytes. Entry of HIV into the cells requires certain substances on the cell surface, such as CD4 receptors and co-receptors such as CCR5 and CXCR4.

These receptors interact with protein complexes that are embedded in the viral envelope. The viral proteins consist of extracellular gp120 and transmembrane gp41 proteins. When HIV approaches the target cell, the gp120 binds with the cell surface receptor; this process is termed attachment. Following co-receptor binding results in a conformational change in gp120; this allows gp41 to unfold and extend its hydrophobic terminal into the cell membrane. Gp41 then folds back on itself; this causes the virus to move close toward the cell and facilitates the fusion of their membranes. The viral nucleocapsid then enters the cell and releasing two viral RNA strands and three essential replication enzymes; Integrase, protease, and RT. HIV RT is a heterodimer composed of two subunits (p66 and p51). At first, RT begins the reverse transcription of viral RNA; it consists of two catalytic domains-ribonuclease H active site and polymerase active site. In the polymerase active site, single-stranded viral RNA is transcribed into an RNA-DNA double helix.

These RNA-DNA hybrids are cleaved into individual stands by ribonuclease H. The polymerase then completes the remaining strand into a DNA double helix (dsDNA). After the formation of dsDNA, Integrase moves into action; it cleaves each dinucleotide from the 3' end of the DNA, creating two sticky ends. Integrase then transfers the viral DNA into the cell nucleus and viral dsDNA is covalently and randomly integrated into the cell's genome. The host cell genome now contains the genetic information of HIV.

Activation of the host cell induces the transcription of proviral DNA by Pol II produces viral spliced and unsliced messenger RNAs. This messenger RNA now migrates into the cytoplasm, where building blocks for a new virus were synthesized. Some of the building blocks have to be processed by the viral protease, where longer proteins are cleaved into small core proteins. The processing of viral proteins is crucial to create an infectious virus. Translation of unsliced viral RNAs produces env, gag, and gag-pol polyproteins.

The two viral RNA strands with three enzymes come together and core proteins assemble around them, forming a capsid, an immature virus particle. Capsid leaves the host cell by acquiring a new envelope of host and viral proteins (mature virus) such as gp120 and gp41; this process is known as budding. Recent reports suggest that clattering is recruited into the HIV particle with high specificity during this process of budding. These matured viruses become ready to infect the other cells. A critical aspect of viral replication is the assembly of virus particles, which are subsequently released as progeny viruses. While much attention has been focused on better understanding this phase of the viral lifecycle, many aspects of the molecular details remain poorly understood [8].

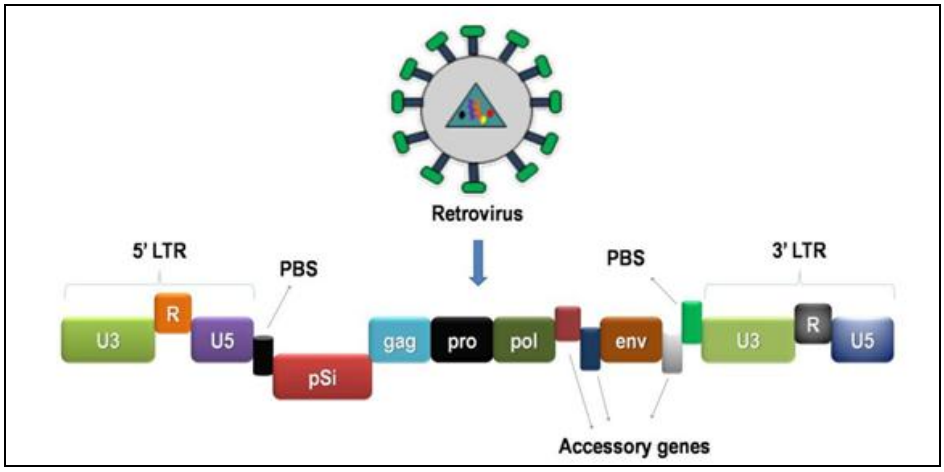

FIG. 5: RETROVIRUS STRUCTURE AND GENOME

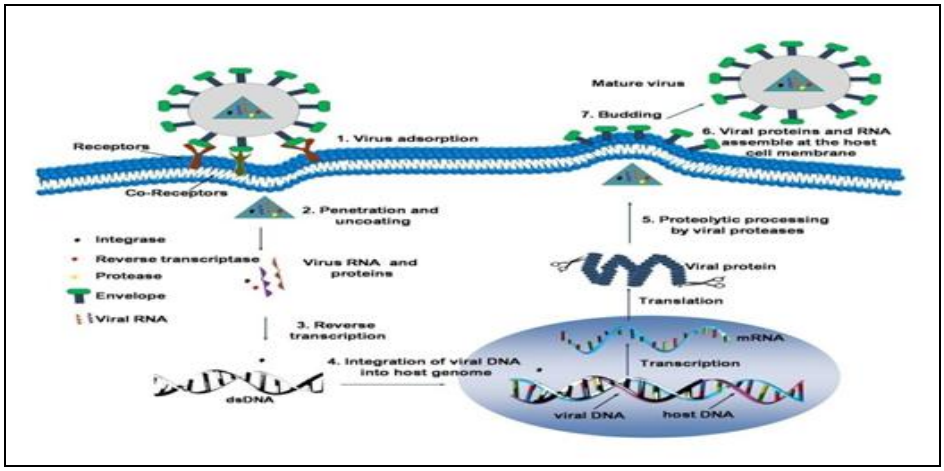

FIG. 6: REPLICATION OF RETROVIRUSES

Mode of Transmission: Most of the retrovirus's information occurs through the cell to cell, mother to fetus transmission, and biological fluids. Cell-to-cell transmission of retroviruses is much more efficient as compared with cell-free conditions, and as retroviruses reach through the tight cell-cell interface, they are out of reach of the immune system. However, retrovirus employs various mechanisms of immune evasion and can destroy the immune system or subvert it to enable successful transmission.

Antiretroviral Therapy: There are about 34 million HIV-1–infected people in the world, and this number plainly says that there is an urgent unmet need for investigation of antiretroviral therapy (ART), and management of this worldwide risk is highly desired. ART is the treatment of people infected with retroviruses using antiretroviral drugs. Antiretroviral therapy aims to reduce the amount of virus in an infected individual body (viral load) to a level that can no longer be detected with an ongoing treatment blood test. Considerable advances in ART have been made since the introduction of zidovudine (3'-azido-3'-deoxythymidine-AZT) in 1987. The regular treatment consists of a grouping of at least three drugs called highly active antiretroviral therapy (HAART) that hold back the viral replication within the host cell and thereby reduces the viral load. Six classes of antiretroviral agents currently exist (specifically towards HIV); they include the following [9].

1. Nucleoside reverse transcriptase inhibitors (NRTIs) such as abacavir, emtricitabine, and tenofovir takes action by interfering with the HIV replication cycle through competitive inhibition of reverse transcriptase enzyme, a key enzyme in replication, and thereby terminates the DNA formation. These can also remove the DNA formation by incorporating into the proviral DNA; the reason is that NRTIs are structurally similar to the DNA nucleotide bases.

2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) includes nevirapine, efavirenz and etravirine, which acts by non-competitive binding of NNRTIs at the hydrophobic pocket of the p66 subunit of the enzyme, results in a conformational change and alters the active site, and limits RT activity. The limitation of these drugs is that it has a low genetic barrier, *i.e.*, a single mutation in RT genome induces a high-level of phenotypic resistance and prevents its use.

3. Protease inhibitors (PIs) include indinavir, atazanavir, darunavir, and tipranavir. This retrovirus protease is a 99-amino-acid aspartic acid protein, which plays a vital role in the maturation of virus particles late in the viral life cycle. During or immediately after viral budding from an infected cell, proteases systematically cleaves individual proteins from the gag and gag-pol polypeptide precursors into functional subunits for viral capsid formation. Protease inhibitors act as competitive inhibitors that directly bind to protease and put off the subsequent cleavage of polypeptides. It has recently been suggested that PIs can directly inhibit lymphocyte apoptosis, and this effect may contribute to an immunologic benefit independently of an antiviral effect.

4. Integrase inhibitors (INSTIs) such as dolutegravir and raltegravir are used in combination with a protease inhibitor and target the strand transfer step of retroviral DNA integration. FDA approved these in 2007. Integration is essential for viral replication and is thus an attractive target for novel chemotherapy. The integrase enzyme is responsible for transferring virus-encoded DNA to the host cell chromosome, a necessary event in retrovirus replication INSTIs active against a wide range, including CCR5 co-receptor and CXCR4 co-receptor–using strains.

5. Fusion inhibitors (FIs) include enfuvirtide-act extracellularly to prevent the fusion. It is a peptide based on the gp41 sequence that specifically prevents membrane fusion by competitively binds to gp41 and preventing the conformational change of gp41 required to complete the final step in the fusion process. Chemokines receptor antagonist. This small molecule, such as maraviroc, selectively and reversibly binds the CCR5 co-receptor, blocking the V3 loop interaction and inhibiting fusion of the cellular membranes. Using these inhibitors individually or in combination, the virus replication process is slowed, and the retroviruses find it more challenging to overcome this combined attack. ART has the potential both to reduce mortality and morbidity rates among infected people and to improve their quality of life [10].

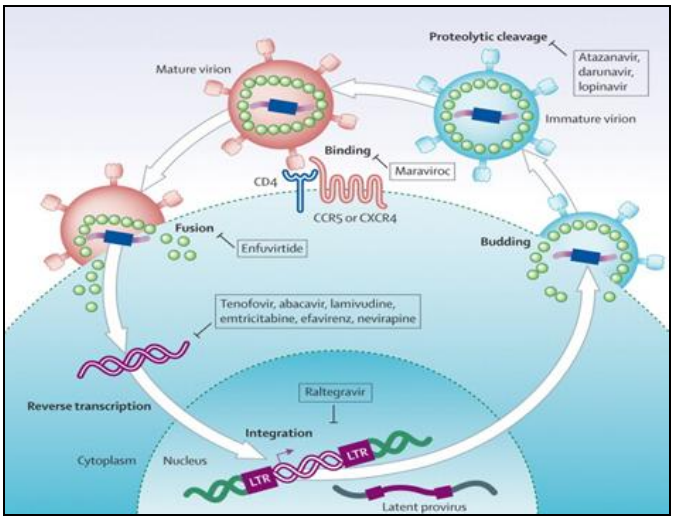

FIG. 7: ANTIRETROVIRAL THERAPY

TABLE 1: CLASSES OF ANTIRETROVIRAL AGENTS AND THEIR MODE OF ACTION

S. no.	Antiretroviral agents	Examples	Mode of action
1	Nucleoside reverse transcriptase inhibitors (NRTIs)	Abacavir, Emtricitabine	Competitive inhibition of reverse transcriptase enzyme a key enzyme in replication and thereby terminates the DNA formation
2	Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Niverapine, Efavirenz, Etravirine	Non-competitive binding of NNRTIs at the hydrophobic pocket of the p66 subunit of the reverse transcriptase enzyme results in a conformational change and alters the active site and limits enzyme activity
3	Protease inhibitors (PIs)	Indinavir, Atazanavir, Darunavir, Tipranavir	Act as competitive inhibitors that directly bind to protease and put off the subsequent cleavage of polypeptides, an essential step in viral maturation
4	Integrase inhibitors (INSTIs)	Dolutegravir, Raltegravir	Target the strand transfer step of retroviral DNA integration
5	Fusion inhibitors (FIs)	Enfuvirtide	Specifically prevents membrane fusion by competitively

			binding to gp41 and preventing the conformational change of gp41 required to complete the final step in the fusion process
6	Chemokines receptor antagonist	Maraviroc	It binds selectively and reversibly binds the CCR5 co-receptor, blocking the V3 loop interaction and inhibiting fusion of the cellular membranes

CONCLUSION: The central goals of retrovirology nowadays are the treatment and the prevention of human and non-human diseases and using this virus in research. Recent studies have shown that retroviruses can be used in several ways, such as models for biological research, for understanding of genes, molecular and cell biology studies. On the other hand, attention to these viruses extends beyond their disease-causing capabilities, the discovery of oncogenes, understanding of mechanisms that regulate eukaryotic gene expression was possible because of the study on retroviruses. The complete knowledge of retrovirus could help the researchers and clinicians use them in various fields of biology and medicine to develop new methodologies and techniques. Ongoing investigation on the application of retroviruses in gene therapy and anti-cancer agents makes these types a widely studying group.

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