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Review Article

Pathogenesis of Human Immunodeficiency Virus, Effective Treatment and Prevention Strategy

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ABSTRACT

The HIV-1 pandemic is a complicated multiplex of diverse epidemics belonging to nations and regions of the globe, and is positively the describing public-health disaster of our time. Research has magnified our concept of the viral replications, manipulations, and hides in an infected person. While pathogenesis and transmission dynamics has become fine and prevention strategies have diversified, a cure or preventive vaccine remains evasive. Antiretroviral treatment has transformed AIDS from an unavoidably fatal condition to a chronic, viable disease in some situations. This transformation has yet to be realized in those global parts that continue to support a disproportionate burden of new HIV-1 infections and increasing mortality.

INTRODUCTION

An estimated 40 million people live with HIV-1 worldwide, while about 25 million have died already. In 2005 alone, there were 4 million new HIV-1 infections and 3 million AIDS deaths. These estimates mask the dynamic nature of this evolving epidemic in relation to temporal changes, geographic distribution, magnitude, viral diversity, and mode of transmission. Now, there is no part of the globe infected through this pandemic (Fig. 1). Heterosexual transmission is the dominant path of transmission and reasons for about 85 % of all HIV-1 infections. Southern Africa remains the epicenter of the pandemic and continues to have high rates of new HIV-1 infections [1]. The rapid spread of HIV-1 in these regions through injecting drug use is of importance, since it is a bridge for rapid establishment of more generalized epidemics. A defining characteristic of the pandemic in the present decade is the raising burden of HIV-1 infections in women, which has extra indications for mother to fetus transmission. Women now make up about 42 % of those infected worldwide, whereas 70 % of whom live in sub-Saharan Africa. HIV-1 infection rates are 3 to 6 times higher in female adolescents than in their male counterparts,

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and this difference is attributed to sexual coupling patterns of young women with older men [2].

Fig. 1. Global distribution of HIV-1 infections, transmission approach, and its subtypes

Population prevalence of HIV-1 infection, concurrent sexual relationships, partner change, sexual practices, the presence of other sexually transmitted diseases, and population mobility patterns for economic rise the efficacy of HIV-1 acquisition. Although sub-Saharan Africa continues to bear a disproportionate burden of HIV-1 infections, there is now an increasing number of countries reporting stabilization or declines in prevalence. There is some evidence to attribute these reductions to effective changes in sexual behavior, such as postponement of sexual debut, reduction in casual relationships, and more consistent condom use in casual relationships [3]. While the relative contribution of cell-free virus compared to cell-associated virus in HIV-1 infection remains uncertain, there is progressive proof that viral load is chance of infection risk. The increase levels of viraemia are shown during acute infection and advanced HIV-1 progression. Further, co-infections with other sexually transmitted diseases in asymptomatic HIV-1 infected people can increase viral shedding to levels similar to those seen during acute infection. Thus, sexually transmitted diseases could boost HIV-1 infection to rates equivalent to those shown during primary infection [4]. Hence, exploration and medication of early infected people is a significant means to lower infection. However, most people are unaware of their HIV-1 conditions during these critical first months of infection. further screening methods based on laboratory testing and clinical algorithms are being build-up and investigated for effective examination of early infection before antibody advancement. Additionally, a more aggressive management of sexually transmitted infections in settings with generalized epidemics has the potential to affect current epidemic trajectories [5]. Based on their genetic make-up, HIV-1 viruses are divided into three groups (Fig. 2) and HIV-2 likely outcome from different cross-species transmission events. Pandemic HIV-1 has diversified into at least 9 subtypes (Fig. 1 and 2), also several circulating recombinant forms, which encode genetic structures from 2 or more subtypes. The continuously evolving HIV-1 viral diversity create an immense challenge to the development of

further preventive or therapeutic interruption. In terms of viral diversity, subtype C viruses continue to dominate and account for 55-60 % of all HIV-1 infections worldwide (Fig. 1) [6].

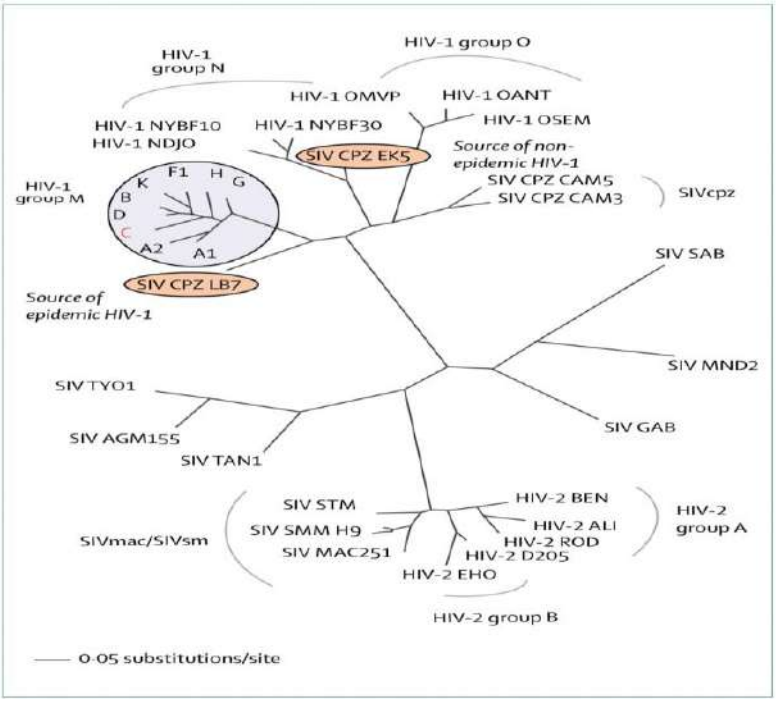

Fig. 2. Phylogenetic tree of lentiviruses in human and non-human primates

Non-subtype B isolates might differ in their virological characteristics from the subtype B isolates (viral load, chemokine co-receptor, transcriptional activation in specific bio-compartments). Infection with 2 or more genetically different viruses could shows to new recombinant viruses. Recombination takes place at a higher rate than primarily forecasted, and spreading recombinant forms account for nearly 20 % of infections in several regions [7]. Superinfections in which periods of virus acquisition are months to years beside have been demonstrated, while at a much decrease efficiency than co-infections. These findings challenge the postulate that HIV-1 acquisition occurs only once with a singular viral strain and the infected individual is protected from consecutive infections. This lack of immunization has substantial implications for vaccine development. Arising proof concludes that clinical progress to AIDS might be quicker in individuals with dual infections, and motivating secure sex practices in viremic HIV-1 infected people might be suitable to keep recurrent exposure to new viral strains minimal [8].

Pathogenesis of HIV-1

The global spread of HIV-1 shows that the virus efficiently counteracts innate and adapted immunity. Despite its modest genome size (<10 kb) and its few genes (Fig. 3), HIV-1 excels in taking advantage of cellular pathways while neutralizing and hiding from the different components of the immune system. The HIV-1 life cycle is complex (Fig. 3) and its time and result is dependent on target cell type and cell activation. In the primarily steps, HIV-1 gets access to cells without leading instant harmful destructions but the entry process may active intracellular signal cascades, which is take might facilitate viral replication [9]. The 2 molecules on the HIV-1

envelope, the glycoprotein gp120 and gp41, shape the spikes on the virion's surface. During the entry process, gp120 attaches to the cell membrane by first binding to the CD4+ receptor. Subsequent interactions between virus and chemokine co-receptors (CCR5 and CXCR4) trigger irreversible conformational changes. The actual fusion event takes place within minutes by pore formation, and releases the viral core into the cell cytoplasm [10].

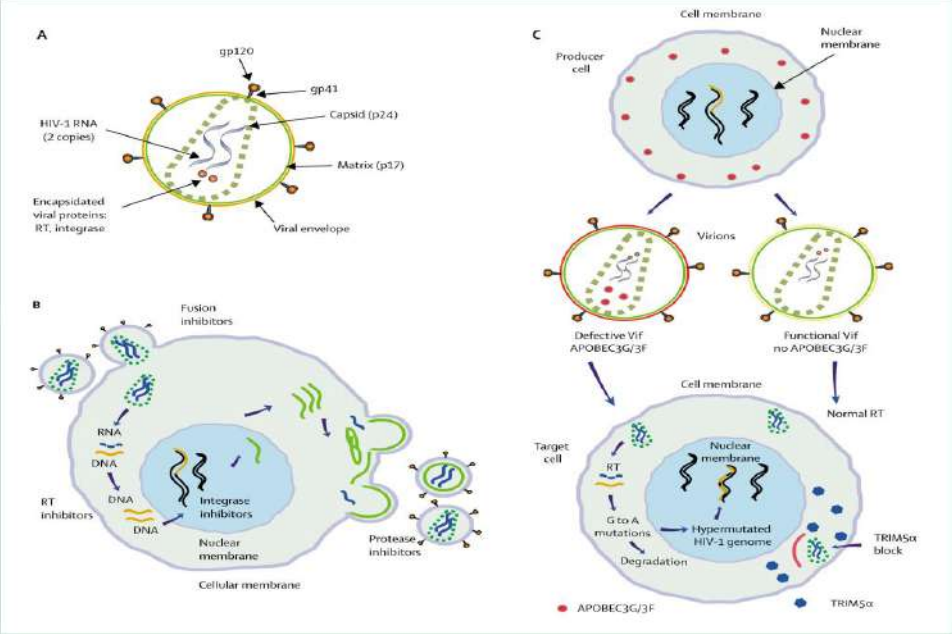

Fig. 3. HIV-1 retrovirus that encodes 3 structural genes (Gag, Pol, and Env)

Once a core disassembles, after that the viral genome is reverse transcribed into DNA through the virus' own reverse transcriptase. At the center of infection, the viral protein integrase in combination with host DNA repair enzymes inserts the viral genome into gene-rich, transcriptionally active domains of the host's chromosomal DNA. An integrase binding host factor (LEDGF/p75), facilitates integration, which marks the turning point by irreversibly transforming the cell into a potential virus producer. In the delay steps, assembly of viral particles requires host driven as well as virus driven transcription [11]. Viral proteins are shifted to and assemble in close to the cell membrane. Virus egress from the cell is not lytic and takes advantage of the vesicular sorting pathway, which normally mediates the budding of endosomes into multivesicular bodies. Cleavage of the Gag-Pol poly-protein by the viral protease produces mature infectious virions. Cytoplasmic molecules and components from producer cell surface lipid bilayer are comprised into the new viral particle, virions show characteristics of the cells in which they were developed [12]. Independently of the transmission route, most new infections are established by viral variants that rely on CCR5 usage. CXCR4 tropic viruses generally appear in late stages of infection and have been associated with increased pathogenicity and disease progression. Potential pathways for virus transmission involve endocytosis, transcytosis, and virus attachment to mannose C-type lectin receptors located on dendritic cells and macrophages. The initial replication takes place in the regional lymph organs and is composed of few viral variants, and leads to modest primary amplification [13]. With relocation of infected T-cells or virions into the bloodstream, secondary amplification in the gastrointestinal tract, spleen, and bone marrow leads in enormous infection of exposed cells. In close temporal relation with the

resulting peak of viraemia (106 to 107 copies per mL plasma), clinical symptoms can be manifest during primary HIV-1 infection (Fig. 4). The level of viraemia feature for the chronic phase of infection in an individual (viral set point) varies from the peak viraemia through 1 or more orders of magnitude [14].

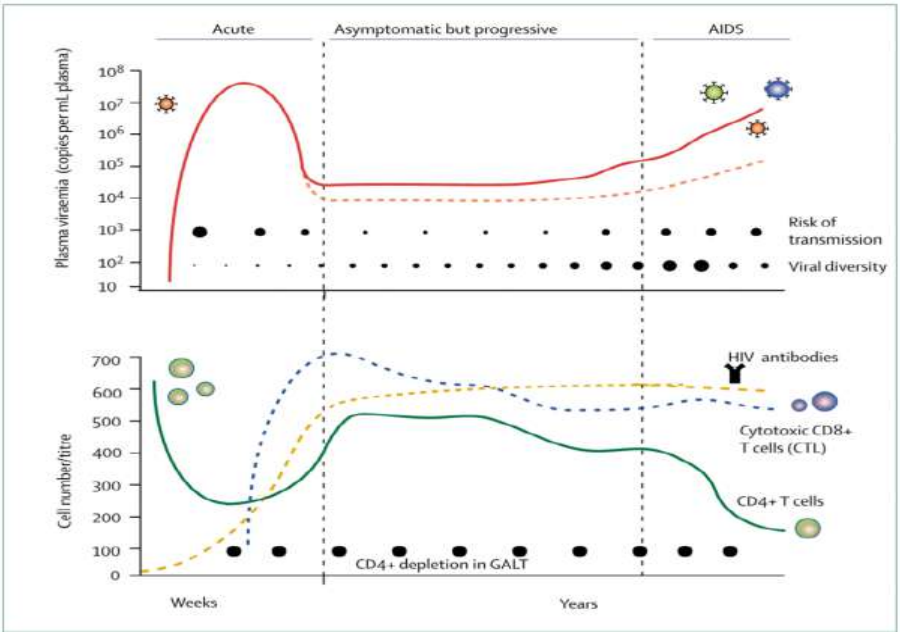

Fig. 4. The HIV-1 infection route clarified through the level of viral replication

The viral population is most homogeneous early after transmission, but as viral quasi-species diversify in distinct biological compartments, mutant viruses that are resistant to antibody neutralization, cytotoxic T-cells, or antiretroviral drugs are generated and archived in long-lived cells (viral reservoirs). A pronounced depletion of activated as well as memory CD4+ T-cells located in the gut-associated lymphoid tissues has been seen in individuals identified early after infection. A gradual destruction of the naive and memory CD4+ T-lymphocyte populations is the hallmark of HIV-1 infection, with AIDS being the last disease stage (Fig. 4) [15]. Although the often absence of signs during early and chronic phase, HIV-1 replication is dynamic throughout the disease. The half-life period of an individual virion is so short that half the entire plasma virus population is replaced in less than 30 minutes. The turnover rates of lymphocyte populations are upregulated many folds during HIV-1 infection, whereas cell proliferation decreases once viral replication is reduced by antiretroviral treatment [16]. Different depletion mechanisms have been proposed, with an emerging consensus favoring generalized immune activation as cause for constant depletion of the CD4+ cell reservoir. Immune activation predicts disease progression, therefore, seems to be a central characteristic of pathogenic HIV-1 infections. HIV-1 Nef contradicts to suppress T-cell activation, probably leading to the high degree of immune activation seen in infected people. 2 groups - long-term non-progressors and highly exposed persistently seronegative alone, have been investigated broadly to recognize innate and acquired protective determinants [17]. Host resistance factors including autoantibodies, human leucocyte antigen (HLA) haplotypes, mutations in the promoter regions, and coding regions of the co-receptors CCR5/CCR2, and up-regulation of chemokine production (Table 1). Cytotoxic T-cell responses, helper T-cell functions, and humoral responses are some of the acquired factors that

modulate the risk of transmission in highly exposed persistently seronegative individuals, and could also contribute to spontaneous control of replication in long-term non-progressors. HIV-1's ability to circumvent these defenses is as impressive as its efficiency to exploit the cellular machinery [18].

Table 1. Several host factors affecting vulnerability to HIV-1 infection

Innate	Genetic	Acquired	Intrinsic
Autoantibodies	HLA haplotype	Cytotoxic T-cell activity	APOBEC3G/3F
Chemokines	CCR5 gene/promoter	Helper T-cell function	TRIM5α
Cytokines	CCR5 gene/promoter	Neutralizing antibodies	N/A

Biomedical Diagnosis of HIV-1

The detection of HIV-1 infection is based on the diagnosis of particular antibodies or/and antigens, as well as several commercial kits are available. Serological tests are generally used for screening. A significant advance has been the availability of rapid HIV-1 antibody investigations. These assays are easy to do and provide results in 20 minutes, enabling specimen collection and proper diagnosis at the same visit. Rapid tests are important tools for surveillance, screening, and diagnosis, and can be reliably done on plasma, serum, whole blood, or saliva by clinical providers with little laboratory expertise [19]. The drawbacks of these serological examinations are diagnosis of infection during early infection when antibodies are absent or infants younger than 18 months who might express maternal HIV-1 antibodies. In these instances, direct virus detection is the only option (quantification of viral RNA or p24 antigen in heat denatured serum). For staging purposes, measurement of CD4+ cells and viraemia is required. Plasma viral load is broadly implemented to observe therapeutic success to antiretroviral. Further commercially available tests give sensitive quantification of plasma HIV-1 RNA copies [20]. The advance versions of the Amplicor and Quantiplex (Roche, USA, and Bayer Diagnostics, USA) assays have overcome primarily suboptimum performance for non-B subtypes. While the viral load determines the rate of destruction of the immune system, the number of CD4+ cells reveal the degree of immunodeficiency and since used to assess the stage of infection. CD4+ cell counts together with clinical manifestations are key criteria for HIV-1 disease classification. Flow cytometry analysis is the standard method for CD4+ cells quantification [21]. Standard methods for quantifying viral load and CD4+ cell counts need advanced laboratory infrastructures, and assays require a specimen to be tested within a short time of collection. Dried blood spot sample has resolved some of the issues related with specimens' transportation required for virological assessments. Measurement of reverse transcriptase activity in plasma samples, simplification of gene amplification methods (Taqman), and paper-strip quantification (dipstick) might provide cost-effective alternatives for the future. Similarly, microcapilliary flow-based systems, CD4+ chips, or total white counts (pan leucocyte gating) provide alternatives for establishment of the level of immunodeficiency in resource-limited settings [22].

Antiretroviral Treatment

Antiretroviral treatment is the best option for long-lasting and subsequently viral suppression and for reduction of morbidity and mortality. However, present drugs do not eliminate HIV-1 infection and lifelong treatment might be required.

Antiretroviral drugs recently authorized through the United States FDA target the viral reverse transcriptase or protease (Table 2). 8 nucleoside/nucleotide analogues and 3 non-nucleoside reverse transcriptase inhibitors block viral replication after cell entry but before integration [23]. Fixed-dose combine tablets clarify treatment regimens through lowering the daily pill burden, and drugs with long half-lives permit once/twice daily dosing. 8 protease blockers inhibit the maturation of virions leading in assembly of non-infectious particles. The presently authorized darunavir is the first of its group that maintains activity to viruses with lowered susceptibility to protease blockers. Enfuvirtide inhibits a gp41 region of the viral envelope and blocks the fusion event before the cell infected [24].

Table 2. Antiretroviral drugs recently authorized through US FDA

Tablets	Entry	Reverse transcriptase	Protease
Single compound tablets	Enfuvirtide	• Abacavir, Tenofovir, Delaviridine • Didanosine, Efavirenz • Emtricitabine, Nevirapine • Lamivudine • Stavudine • Zalcitabine • Zidovudine	• Amprenavir • Atazanavir • Darunavir • Indinavir • Nelfinavir • Ritonavir • Saquinavir
Fixed-dose combination tablets		• Abacavir/lamivudine • Zidovudine/lamivudine • Tenofovir/emtricitabine • Abacavir/lamivudine/zidovudine • Tenofovir/emtricitabine/efavirenz	Lopinavir/ritonavir

This drug requires to be injected 2 times daily and its use is retained for treatment of heavily drug-experienced patients, hence, it may assist overcome existing drug resistance. Production of advance antiretrovirals outlines on molecules that inhibit entry, reverse transcription, integration, or maturation. Compounds that have been designed to inhibit resistant viruses are urgently needed since many patients treated during the past decades harbor viral strains with reduced susceptibilities to many if not all available drugs (Table 3) [25]. The aim of antiretroviral treatment is to lower the morbidity and mortality that is commonly linked with HIV-1 infection. A combine of 3 or several active drugs is required to approach this goal in most patients. Effective treatment returns to near normal the turnover rates of both CD4+ and CD8+ T-cell populations. Effective but well accepted drugs with long half-lives and clarified regimens boost the strategies for first and second-line chemotherapeutic interferences [26].

Table 3. Antiretrovirals currently in phase II/III of clinical enhancement

	Drug	Mechanism	PI and RT resistant action
Maraviroc	MVC	CCR5 inhibitor	Yes, but not X4 variants
Vicriviroc	SCH D	N/A	Yes, but not X4 variants
Etravirine	TMC-125	Non-nucleoside reverse transcriptase inhibitor	Yes, also NNRTI-resistant strains
N/A	MK-0518	Integrase strand transfer inhibitor	Yes

N/A	GS-9137	N/A	Yes

Combined Antiretroviral Treatment

The combine of further effective antiretroviral agents, viral replication is suppressed at low levels that appearance of drug resistant HIV-1 variants was, not prevented but delayed. From this, CD4+ T-cell numbers increase, leading to a degree of immune reconstitution that is sufficient to reverse clinically apparent immunodeficiency. Widespread introduction of HAART in industrialized countries resulted in a striking decrease in morbidity and mortality [27], putting forward the hope that HIV-1 infection can be transformed into a treatable chronic disease. A criterion derived of plasma viraemia concentration, absolute or relative CD4+ cell counts, and clinical indications, is used to suggest initiation of HAART. The benefits of treatment clearly outweigh the potential side-effects in patients with clinical signs of immunodeficiency (AIDS defining illnesses) or with CD4+ numbers less than 200 per μL [28]. However, the best time point to begin treatment remains controversial in asymptomatic patients with modest depletion of CD4+ T-cells (>350 per/μL) and modest levels of viraemia (<100,000 copies/mL). Early depletion of gut CD4+ T-lymphocytes, increasing viral diversity, and the poor regenerative abilities of key populations of the immune system provide arguments for beginning treatment as early as possible. Toxicities, metabolic changes, and immune reconstitution disease are some of the long-term problems that complicate decade-long HAART [29]. One strategy directing life-long daily adherence to HAART has been organized treatment disruptions. If possible, this strategy could limit drug toxicity and lower treatment costs. Although preliminary findings for this strategy were mixed in terms of benefits, the recent early closure of the SMART trial was based on increased morbidity and mortality in the treatment interruption arm. Hence, in the absence of clinical significance, most researchers strongly discourage treatment interferences except as required to address treatment intolerance [30].

Resistance to Drug

Emergence of drug resistance is the most common reason for treatment failure. Inadequate consent, drug side-effects, or drug-drug interactions may cause to suboptimum drug concentrations, leading in viral rebound. Viral resistance has been illustrated to every antiretroviral drug and since poses a serious clinical or public-health issue. HIV-1 subtypes differ in the sequence of mutations leading to drug resistance, and some naturally occurring polymorphisms might actually modulate resistance. Drug-resistant HIV-1 is transmissible and can be detected in up to 20 % of newly infected individuals in countries with broad access to antiretrovirals [31]. The frequency of drug resistance in the untreated population show reduce in locations with poor approach to treatment. Short-term antiretroviral-based interruptions are significant in prevention of mother-to-child transmission. Hence, these interruptions could outcome in drug resistant viral variants in the mother and/or baby. Around half the women who received one dose of nevirapine to prevent mother-to-child transmission harbor viruses resistant to non-nucleoside reverse transcriptase inhibitors (NNRTI). These resistant viruses replicate efficiently and can be transmitted by breast milk, and minor resistant populations present long after the intervention can possibly decrease the effectiveness of subsequent NNRTI-based treatment regimens [32].

Viral Reservoirs

Viral reservoirs compose of anatomical sanctuaries and a small pool of infected long-lived memory T-cells. HIV-1 latency in long-lived cell populations (memory T-cells, macrophages) poses

an obstacle to eradication because current antiviral combination treatments fail to eliminate integrated proviruses from resting cells. Various methods, involving immune-modulatory molecules (IL 2, anti-CD3 monoclonal antibody, IL 7), have been employed to reactivate resting cells in the setting of HAART [33]. Histone deacetylase-1 blockers, such as valproic acid, liberate an inherent transcriptional inhibit and through doing so accelerate viral long terminal repeat-driven expression. Augmenting standard antiretroviral treatment with enfuviridine and valproic acid reduced the number of latently infected CD4+ T-cells (29-84 %), but to establish the relative contribution of each drug with respect to the final outcome is difficult [34].

Prevention Strategies

Mother-to-child transmission

Prevention of mother-to-child transmission has seen advances in both industrialized and resource-constrained settings. Intrapartum transmission has been lowered through rising permit to interference like single dose of nevirapine to mother and newborn. analyses regard drug-resistant viral strains have caused to many tests with combine treatments to lower transmission during the intrapartum period. Elective transport through caesarean section may lower HIV-1 transmission during the intrapartum period, but the advantages of the interruption could be countered through post-partum sepsis and rising maternal mortality [35]. Poor access to clean running water precludes, however, the use of formula feeding under these circumstances, and exclusive breastfeeding with abrupt weaning is one option for reducing transmission. A probable novel interruption still being trialed is the regular use of antiretrovirals during feeding. More attention is starting to focus on the pregnant mother, especially initiation of antiretroviral therapy in mothers with low CD4+ counts during pregnancy and thereafter. In a European cohort of exposed-uninfected children, no serious clinical manifestations were apparent, at least in the short term to medium term [36].

Sexual transmission

Decrease of heterosexual transmission is beneficial for management of the epidemic in several regions of the globe. Prevention is approached by lower in the number of discordant sexual acts or lower of the efficiency of HIV-1 transmission in discordant sexual events. The primarily may be obtained by abstinence and sex between concordantly seronegative individuals. Further interruptions pointed at reducing the risk of transmission per discordant sexual event are in the process of clinical trial [37]. Male and female condoms provide (or abstinence) a proven and affordable prevention option. Other biomedical prevention interventions include male circumcision, antiretrovirals for prevention (pre or post exposure), chemoprophylactic treatment of herpes simplex virus-2 (HSV-2), microbicides, and vaccines. Suitability of searching data, behavior variation after circumcision, surgical issue rates, and logistics of initiating the strategies before policy formulation as a prevention method [38]. Prevention strategies required to be supplied that may be implemented through women independently of their male sexual partner's understanding or attention. However, rectifying these disparities is a long-term challenge, further preventive interruptions may be used in the interim on the base of our incomplete knowledge at a biological status of HIV-1 risk for women. For example, there seems to be a correlation between levels of sexual hormones (progesterone) and transmission risk [39]. Moreover, rising access to female condoms and treatment of outside sexually transmitted infections, tests are underway to assess the use of several barrier strategies like cervical caps, invisible condoms, diaphragms, and diaphragms combined with microbicides. The control of vaginal infections is a probably significant method for lowering HIV-1 acquisition

that has yet to be trialed. Periodic presumptive medication for vaginal infections is being investigated as an HIV-1 prevention strategy [40].

Microbicides

Microbicides are a supplemental significant interfering biomedical products that is private and under women's control. These vital therapeutics probably could be implemented to prevent rectal and vaginal transmission of HIV-1. While the 3 phase III test outcomes of the first microbicidal product done between 80s to 90s did not explore preventive effects, they have expressed the clinical understanding in terms of selection of product, clinical testing, and safety issues. Beginning of 5 years have shown important developments in investment and product [41]. Early clinical trials of several products involving the launch of updated clinical tests for 5 various products is ongoing (Table 4). The improvement of antiretroviral gels raised these 3rd generation microbicides specificity in relation to surfactants, vaginal boosters, or entry blockers that have controlled the product pipeline (Fig. 5). The first antiretroviral gel to going for earlier trial is tenofovir gel, and the resulting in terms of precaution profile, tolerance, and low systemic absorption are encouraging. Further challenges are adherence to product use, absence of a surrogate marker, and the high rates of pregnancy in trial participants [42].

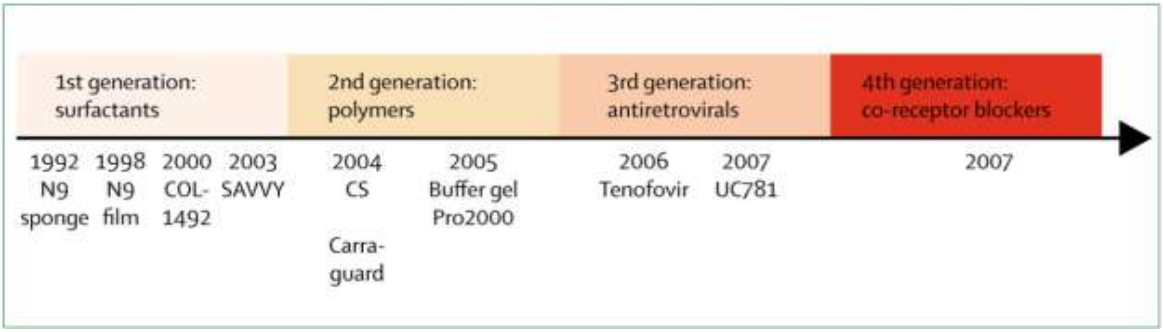

Fig. 5. Agenda of microbicide progress of various product generations

Table 4. Synopsis of microbicides recently ongoing modern clinical trials

	Phase	Mode of action	Effective against
Carraguard	III	Seaweed polymer, entry inhibitor	HIV-1/HIV-2, human papilloma virus, herpes simplex virus
Cellulose sulphate	III	Entry inhibitor	Broad range of sexually transmitted diseases; also active as contraceptive
PRO2000	III	Entry inhibitor	HIV-1/HIV-2, human papillomavirus, chlamydia
Savvy (C31G)	III	Surfactant	Broad range of sexually transmitted diseases; also active as contraceptive
Tenofovir gel	IIb	Nucleotide reverse transcriptase inhibitor	HIV-1/HIV-2
Buffer gel+PRO2000	Ib/III	Natural vaginal defense/entry inhibitor	Broad range of sexually transmitted diseases; also active as contraceptive
Tenofovir gel+oral	II	Nucleotide reverse transcriptase inhibitor	HIV-1/HIV-2

Vaccines

A safe, protective, and inexpensive vaccine would be the most effective and probably the only strategy to restrict the HIV pandemic. Safety analyses prevent the use of live virus as immunogen. Initially, efforts were focused on generating neutralizing antibodies with recombinant monomeric envelope gp120 as immunogen. This vaccine did not induce neutralizing antibodies and, not unexpectedly, the phase III trials failed to show protection. Antibody mediated HIV-1 neutralization is complicated by the high genetic diversity of the variable Envelope regions, epitopes masked by a carbohydrate shield (glycosylation), and conformational or energetic constraints [43]. Therefore, CD8 T-cell responses prohibit to further extent viral replication in-vivo, current vaccine improvement has marked on eliciting cellular immune responses. Overcoming pre-existing immunity against replication incompetent immunogenic vectors (recombinant adenovirus 5) is one of the challenges. Precautions and immunogenicity investigations via replication defective vaccine vectors are ongoing after primary examinations in non-human primates remarked safety. However, the general belief is that approaches aimed at eliciting both humoral and cell mediated immunity are most promising to prevent or control retroviral infection [44].

CONCLUSIONS

A significant strategy to both prevention and attention is knowledge of HIV-1 status. As approach to antiretroviral indications (mother-to-child inhibition, antiretroviral treatment) rises, the chances for HIV-1 testing will increase and develop chances for a prevention-care continuing, with the voluntary guidance and testing furtherance as an entry point [45]. These variations will lead in a shift in prohibiting struggles from a mark on individuals uninfected with HIV-1 to a more probable continuing of prevention. It involves uninfected, currently infected, infected, and asymptomatic people, or those with expressing HIV disease and on antiretroviral therapy. HIV/AIDS is an unexpected epidemic that demands an unusual response [46]. Much improvement has been made in a limited time space, although several scientific and programmatic challenges (Fig. 6). In the absence of a preventive vaccine or a cure, protection and lead to antiretroviral treatments are the significant strategies to slow down the HIV-1 pandemic. Actually, HIV-1 is primarily sexually transmitted and asymmetric effects on populations that are already socially or economically marginalized [47].

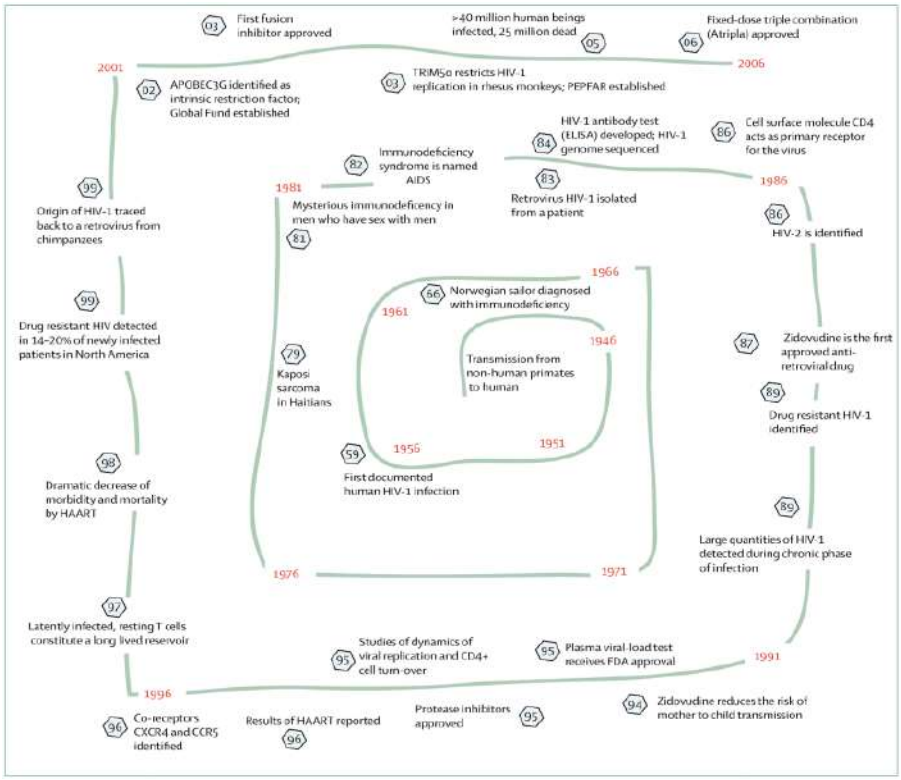

Fig. 6. Preferred investigations, scientific progress, and treatment strategies relevant to HIV-1/AIDS

In view of the immediacy of the problem, and the fact that both research and programs are mainly funded by the public sector, there is a greater demand from civil society for research and accountability partnership for use of public funds. The most affected countries face many other economic, political, and development challenges, which have raised issues in undertaking multicenter and multi-country research [48]. Research addressing women-particular topics (sexual hormones, transmission and disease progression, viral diversity, and antiretroviral potency) and women-particular prevention indications involving microbicides is significant [49]. There is definitely more attention being directed to HIV-1, more resources (panel), more civil society mobilization, more governments speaking up, more possibilities for treatment, and more evidence about what protection and treatment potions will work than in early decades. The relentless growth of the pandemic shows us that present strategies are insufficient. Therefore, we required to do research differently, although rising the scale and magnitude of present strategies in withhold with the disaster [50].

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CONFLICT OF INTEREST

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