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Review Article

Advances in HIV Prevention and Treatment: A Literature Review

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Abstract

Background: The last decade has witnessed several advances in the management of HIV/AIDS with the development of potent and safe antiretroviral drugs and new HIV prevention technologies.

Objective: This review summarizes the recent advances in the management of the HIV infection.

Methods: Medline via PubMed and Google search engine were searched for articles dealing with antiretroviral therapy and new prevention technologies.

Results: The understanding of the lifecycle of the HIV was a turning point that provided researchers with the knowledge and tools needed to prosecute drug discovery efforts focused on targeted inhibition with specific pharmacological agents. New prevention technologies continue to expand the current toolbox, transforming HIV/AIDS from an inevitable lethal disease into a manageable condition. The integration of behavioral, biomedical and structural interventions will likely reduce the incidence of HIV while promising new leads for an effective HIV vaccine keep the hope of a world free of HIV alive.

Conclusion: Although the fight against HIV has been long and arduous, many signs seem to suggest that ending HIV epidemic is not only possible; it is well in our reach.

Keywords: Antiretroviral Therapy; HIV/AIDS; HIV Prevention Technology;Lifecycle

Introduction

Three decades following the report about a cluster of Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men in Los Angeles and New York, [1] HIV/AIDS remains a global public health challenge. Approximately 36.7 million people were living with HIV/AIDS (PLH) worldwide at the end of 2015. An estimated 2.1 million people became newly infected with HIV and 1.1 million died from AIDS-related illnesses during the same year. The vast majority of people living with HIV are in low and middle income countries. Sub-Saharan Africa is the most affected region, with an estimated 25.6 million people living with HIV in 2015. About 66% of new HIV infections in 2015 occurred in sub-Saharan Africa [2]. Unprecedented efforts of the last thirty years have turned human immunodeficiency virus infections from terrifying lethal diseases to manageable conditions [3]. Combination antiretroviral therapy dramatically reduces the viral load to an undetectable level (<50 RNA copies/mL) resulting in a significant reconstitution of the immune system and prevention of opportunistic infections [4]. Many patients infected with HIV are now living somewhat normal lives.

The impact of the HIV pandemic on women is rising, even in countries where other routes of transmission are more prevalent [5]. Women have few options to protect themselves from acquiring HIV. Efforts to promote abstinence, monogamy and the use of condoms have not been enough to stop the epidemic nor are these approaches practical in many settings [6]. Women face difficulties convincing their male partners, especially husbands and regular partners, to use condoms or to be monogamous or faithful. Female condoms, developed as an alternative to give more control to women to protect themselves, are not widely accepted. Structural issues and high cost have hampered their use. HIV Pre-

Exposure Prophylaxis (PrEP) provides a promising new approach for slowing the spread of HIV in the United States [7].However, Prep is not widely available globally [8], limiting the number of options to women to protect themselves against HIV. The development of products applied inside the vagina or rectum to protect against HIV commonly called microbicides provide great potential for a female-controlled, preventive option, which would not require negotiation, consent or even knowledge of the partners [9]. Microbicides could benefit both men and women. The successful utilization of this preventive method depends on its efficacy and its acceptability.

The discovery of an effective vaccine remains the goal of HIV research. Vaccine technologies have evolved significantly in the last decade. Reports that the prime/boost combination of two vaccines (ALVAC (R) HIV and AIDSVAX(R) B/E) lowered the rate of HIV infection by 31.2 percent in more than 16,000 volunteers in Thailand demonstrated that the development of an effective preventive HIV vaccine is scientifically possible. This discovery has reinvigorated and raised hope among researchers. This review was undertaken to describe promising new initiatives in our continued efforts to fight the HIV epidemic. This update will keep knowledge about HIV/AIDS current among community organizers, health educators and policy makers.

Methods

Search strategy Medline via PubMed and Google search engine were searched for relevant articles published between January 2007 and April 2017. The key search terms applied included: "Lifecycle" or "Antiretroviral therapy" or "New Prevention technologies" or "HIV Vaccines" and "HIV". The formal review process was further informed by searches of published research and technical reports from peer-reviewed journals presented at scientific conferences and reference lists from publications of interest. Some grey literature including conference presentations, project reports, government reports, and released by international organizations such as UNAIDS and the World Health Organization were also considered.

Inclusion Criteria

Original articles published in English and covering any of the above-mentioned keywords regardless of the country were considered for this review. Articles published in any language other than English were excluded. Methods of assessment of documents Citations were examined, titles and abstracts were screened for eligibility. Selected citations were classified as either:

- Primary citations qualifying for inclusion in the synthesis or
- Not relevant citations not included in this study.

Full texts were reviewed in greater detail if deemed relevant, and findings pertinent to this literature review were included in this article.

Results

HIV/AIDS Treatment

Mechanisms of Action of Antiretroviral Drugs

The discovery of the causative agent of AIDS together with the understanding of the virus replication cycle were instrumental in assisting researchers to prosecute drug discovery efforts focused on targeted inhibition with specific pharmacological agents [10]. (Figure 1) summarizes the HIV life cycle. To multiply, the HIV virus infects only cells that carry CD4 receptors on their surface, such as T4-lymphocytes, monocytes and macrophages, glial cells in the brain, chromaffin cells in the intestines and Langerhans' cells in the skin [11]. TheCCR5 or CXCR4 antagonists are antiretroviral drugs that can prevent the viral attachment to the CD4 T-cells.

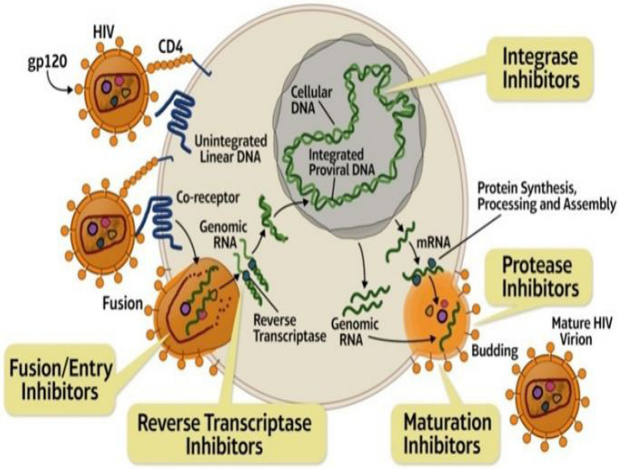

Figure1: HIV Lifecycle.

Once the HIV binds to a CD4+ surface receptor, it activates other proteins on the surface of the human cell known as CCR5 and CXCR4 to allow the HIV envelope and CD4 cell membrane to fuse. A second group of drugs can interfere with the fusion process (Fusion inhibitors). Once inside the cell, the viral capsid that contains the RNA and important enzymes is released into the host cell (Uncoating). A viral enzyme called reverse transcriptase converts its genetic material, HIV RNA into HIV DNA, allowing HIV to enter the CD4 cell nucleus. Reverse transcription can be blocked by NucleosideReverse Transcriptase Inhibitors(NRTIs) and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs). The newly formed viral DNA is then integrated with the DNA of the human host cell using a viral enzyme called integrase (Integration). The Integrase inhibitors can block the integration phase. Once integrated into the CD4 cell, the CD4 machinery produces long chains of HIV proteins (replication). A viral enzyme called protease cuts these long chains of proteins into smaller proteins to form the structure of the new HIV particle, including each of the enzymes and proteins needed to repeat the reproductive process [12].

Once the new viral particles are assembled, they bud off the host cell and can infect other cells. Protease inhibitors can block viral assembly.

Classes of Antiretroviral Drugs

The FDA approved the first antiretroviral drug, zidovudine (AZT), to treat people infected with HIV/AIDS on March 19, 1987 [13]. Since the advent of the first HIV-1 specific antiviral drugs given as monotherapy, significant progress has led to the development of more than 25 FDA-approved antiretroviral drugs. The 6 classes of ARVs include: The Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), Protease Inhibitors (PIs), a Fusion Inhibitor (FI), a CCR5 antagonist, and Integrase Strand Transfer Inhibitors (INSTIs). Other drugs including Ritonavir (RTV) and Cobicistat (COBI) are used to improve the Pharmacokinetic (PK) profiles of some ARV drugs (e.g., PIs and The INSTI Elvitegravir (EVG) [14]. (Table 1) presents the antiretroviral drugs used in the treatment of HIV infection. The description of individual drug is beyond the scope of this paper.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
Brand Name	**Generic Name(s)**	**Approval Date**	**Time to Approval**
Combivir	lamivudine and zidovudine	27-Sep-97	3.9 months
Emtriva	Emtricitabine, FTC	02-Jul-03	10 months
Epivir	lamivudine, 3TC	17-Nov-95	4.4 months
Epzicom	abacavirand lamivudine	02-Aug-04	10 months
Hivid	zalcitabrine, dideoxycytidine, ddC (no longer marketed0	19-Jun-92	7.6 months
Retrovir	zidovudine, azidothymidine, AZT, ZDV	19-Mar-87	3.5 months
Trizivir	abacavir, zidovudine, and lamivudine	14-Nov-00	10.9 months
Travuda	tenofovir disoproxil fumarate and emtricitabine	02-Aug-04	5 months
Videx EC	enteric coated didanosine, ddI EC	31-Oct-00	9 months
Videx	didanosine, dideoxyinosine, ddI	9-Oct-91	6 months
Viread	tenofovir disoproxil fumarate, TDF	26-Oct-01	5.9 months
Zerit	stavudine, d4T	24-Jun-94	5.9 months
Ziagen	abacavir sulfate, ABC	17-Dec-98	5.8 months
Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)			
Brand Name	**Generic Name(s)**	**Approval Date**	**Time to Approval**
Edurant	rilpivirine	20-May-11	10 months
Intelence	etravirine	18-Jan-08	6 months
Rescriptor	delavirdine, DLV	04-Apr-97	8.7 months
Sustiva	efarienz, EFV	17-Sep-98	3.2 months
Viramune	nevirapine, NVP	21-Jun-96	3.9 months
Viramune XR	nevirapine, NVP	20-Mar-11	9.9 months
Protease Inhibitors (PIs)			
Brand Name	**Generic Name(s)**	**Approval Date**	**Time to Approval**
Agenerase	amrenavir, APV (no longer marketed)	15-Apr-99	6 months
Aptivus	tipranavir, TPV	22-Jun-05	6 months
Cixivan	indinavir, IDV	13-Mar-96	1.4 months
Fortovase	saquinavir (no longer marketed)	07-Nov-97	5.9 months

Invirase	saquinavirmesylate, SQV	06-Dec-95	3.2 months
Kaletra	lopinavir and ritonavir, LPR/RTV	15-Sep-00	3.5 months
Lexiva	fosamprenavir Calcium, FOS-APV	20-Oct-03	10 months
Norvir	ritonavir, RTV	01-Mar-96	2.3 months
Prezista	daranavir	23-Jun-06	6 months
Reyataz	atazanavir sulfate, ATV	20-Jun-03	6 months
Viracept	nelfinavir mesylate, NFV	14-Mar-97	2.6 months
Fusion Inhibitors			
Brand Name	**Generic Name(s)**	**Approval Date**	**Time to Approval**
Fuzeon	enfuvirtide, T-20	13-Mar-03	6 months
Entry Inhibitors – CCR5 co-receptor antagonist			
Brand Name	Generic Name(s)	Approval Date	Time to Approval
Seizentry	maraviroc	06-Aug-07	8 months
HIV Integrase strand transfer inhibitors			
Brand Name	**Generic Name(s)**	**Approval Date**	**Time to Approval**
Isentress	raltegravir	12-Oct-07	6 months
Tivicay	dolutegravir	13-Aug-13	6 months
Vitekta	elvitegravir	24-Sept-14	24 months
Multi-class Combination Products			
Brand Name	**Generic Name(s)**	**Approval Date**	**Time to Approval**
Atripla	efavirenz, emtricitabine and tenofovirdisoproxil fumarate	12-Jul-06	2.5 months
Complera	emtricitabine, rilpivirine, and tenofovir disoproxil fumarate	10-Aug-11	6 months
Evotaz	atazanavir sulfate, combicistat	29-Jan-15	9 months
Prezcobix	cobicistat, darunavir ethanavirethanolate	29-Jan-15	10 months
Stribild	elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate	27-Aug-12	6 months

Table 1: FDA-Approved Antiretroviral Drugs. Adapted From: Antiretroviral Drugs Used in the Treatment of HIV Infection, U.S. FDA.

HIV Clinicians and patients may select a regimen based on several considerations including antiviral potency, short- and long-term adverse effects, ease of administration, drug interactions, risk of resistance and cost [15].To address the complexity in HIV management in terms of initiating, switching and discontinuing the Anti-Retroviral Treatment (ART), a panel of experts in HIV research and patient care recommended that all HIV-infected individuals with detectable viremia, regardless of their CD4 cell count, should begin ART as soon as possible after diagnosis to prevent disease progression, improve clinical outcomes and limit transmission [16]. They recommended that the initial regimen should consist of 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) plus an Integrase Strand Transfer Inhibitor (InSTI). They also made recommendations for special populations (e.g. pregnant women, hepatitis B/C virus coinfection) and for context of acute opportunistic infections [15]. Study data supports switching therapy in some patients because of virologic failure, drug resistance or more adverse or toxic effects [17]. For the good management of PLH, the panel of experts in HIV research and patient care recommend that CD4 cell count, plasma HIV RNA, serum chemistries and estimated creatinine clearance be done as close to the time of HIV diagnosis as possible and prior to beginning ART. Strict adherence to antiretroviral therapy is key to sustained HIV suppression, reduced risk of drug resistance, improved overall quality of life, and survival, [18] as well as decreased risk of HIV transmission [19].

HIV/AIDS Prevention

Effective HIV prevention requires a combination of behavioral, biomedical and structural intervention strategies [20]. The early initiation of antiretroviral therapy has been shown to reduce rates of sexual transmission of HIV-1 and clinical events, indicating both personal and public health benefits from such therapy[19].

The evidence to support the use of Antiretroviral Therapy (ART) for prevention of new HIV infection in the form of Pre-exposure Prophylaxis (PrEP) among men who have sex with men, transgender, people who inject drugs, heterosexual men and women and HIV-1 serodiscordant couples, or Treatment as Prevention (TasP) for sero Discordant couples have also grown [21].

Biomedical Intervention

Prevention of Mother-to-Child Transmission

The first success of ART has been in preventing mother-to-child transmission of HIV Prevention of Mother-To-Child Transmission (PMTCT) of HIV in the United States and Europe has been a tremendous success, such that transmission rates of less than 2% have been achieved [22].

Therapy as Prevention

Though long suspected that treatment reduces an individual's viral load resulting in decreased risk of HIV transmission, the HIV Prevention Trials Network 052 (HPTN 052) study was the first to conclusively prove this theory. Early initiation of ART (when cell counts are greater than 350) by HIV-infected individuals reduced the risk of HIV transmission to the uninfected sexual partners by 96 percent compared to initiation when CD4 counts were <250 [23]. However, adherence to ART is critical to achieving effective viral suppression [24].

Pre-Exposure and Post Exposure Prophylaxis

Pre-Exposure Prophylaxis (PrEP), is the concept of HIV-negative individuals taking HIV ART to prevent the acquisition of HIV. The use of an ART for PrEP was approved by the United States Food and Drug Administration (FDA) in July 2012 and has been shown to be safe and effective through the Global iPrEx and Partners Prep studies [25]. There is evidence that Post Exposure Prophylaxis (PEP) can reduce the risk of HIV transmission [26]. PEP is an emergency intervention designed to abort HIV acquisition in the event of occupational (i.e., needle stick or mucous membrane splash) or no occupational (i.e., sexual or injecting drug use) exposure to HIV-infected blood or potentially infectious bodily fluids [27].

HIV Testing and Counseling

Early knowledge of one's positive HIV sero status maximizes opportunities for the person to access care, thereby greatly reducing HIV-related morbidity and mortality, and/or preventing transmission of HIV. Meta-analyses find that PLH who are aware of their sero status are at least half as likely to engage in risky sexual behaviors compared to those unaware PLH [28]. HIV testing is the cornerstone for HIV prevention.

Male and Female Condoms

When used consistently and correctly, male condoms can be highly effective in preventing Sexually Transmitted Diseases (STDs) including HIV [29]. However, they provide less protection against STDs spread through skin-to-skin contact like human papillomavirus (genital warts), genital herpes, and syphilis. Although the female condom has been on the market for more than ten years, adoption by end-users, providers, national governments, and donors has remained low. The high price and certain technical characteristics are often cited as the primary obstacles for end-user adoption [30].

Diaphragmes

There is considerable interest in developing new multipurpose prevention technologies to address women's reproductive health needs. Dapivirine-releasing diaphragm with daily release quantities potentially can prevent HIV transmission [31].

Male Circumcision

Three large Randomized Controlled Clinical Trials (RCTs) conducted in South Africa, Kenya and Uganda showed that medical circumcision significantly reduced male participants' HIV infection risk, ranging from 48% to 61% [32-35]. In addition, circumcision was shown to be associated with a significantly reduced risk of urinary tract infection [35]. Circumcision, however, has not shown a significant protective effect against HIV acquisition among Men Who Have Sex with Men (MSM).

Microbicides

After several disappointing microbicide trials that failed to show protection against HIV infection, [36,37] the results of the Centre for the AIDS Program of Research in South Africa - the CAPRISA 004 trial - demonstrated that a vaginal microbicide gel containing tenofovir reduced the risk of HIV infection for women by 39% (95% CI: 6, 60) [38]. Building on that experience, the NIH-ASPIRE study, also known as MTN-020, showed that a vaginal ring that continuously releases the experimental antiretroviral drug Dapivirine provided a modest level of protection against HIV infection in women with an overall effectiveness of 31 percent [39]. Microbicides may also be preferable to condoms as an HIV prevention option for some women because women would not have to negotiate their use, as they often must do with condoms.

Behavioral Interventions

Given the challenges of further reducing HIV infection rates and developing an effective vaccine, it is critical to focus on behavioral prevention efforts that are based on the best available scientific evidence [40]. Behavioral interventions have been shown to decrease sexual risk behaviors [41] and increase condom use [42]. The compendium of effective HIV prevention interventions exists [43]. Sister-to-Sister is a brief (20-minute), one-on-one, skill-based HIV/STD risk-reduction behavioral intervention for sexually active African American women 18 to 45 years old that is delivered during a routine medical visit. Sister-to-Sister is designed to provide intensive, culturally sensitive health information to empower

and educate women in a clinical setting; help women understand HIV/STD risk behaviors; and enhance women's knowledge, beliefs, motivation, confidence, and skills to help them make behavioral changes that will reduce their risk [44].

Structural Interventions

Macroeconomic and social forces such as poverty, racism, sexism and homophobia, help fuel HIV epidemics, although the pathways between these forces and HIV infection are complex and not always clear [45,46]. Structural interventions seek to address social, economic, political or environmental factors that make individuals or groups vulnerable to HIV infection. For example, laws that criminalize same-sex relationships often hinder men who have sex with men from accessing condoms. A lack of infrastructure, such as transport, prevents many people from accessing health clinics. By successfully addressing these structural barriers, individuals are empowered and able to access HIV prevention services [47].

One example of structural intervention is the Needle and Syringe Programs (NSPs). NSPs are a type of harm reduction initiative that provide clean needles and syringes to people who inject drugs (sometimes referred to as PWID). NSPs are offered at fixed or mobile sites. Fixed sites are typically located where the drugs are bought and sold openly. At fixed sites, additional services such as healthcare services alongside testing and counselling for HIV and other blood-borne viruses [48]. Outreach programs may include mobile units (such as a van or bus), backpacking services on the street or even home deliveries. NSPs substantially and cost effectively reduce the spread of HIV among PWID and do so without evidence of exacerbating injecting drug use at either the individual or societal level [49].

Despite the promise of structural interventions and donor enthusiasm for additional efforts in their implementation and evaluation, less data has been collected on structural interventions than on biomedical and behavioral interventions. Few currently existing programs have been rigorously evaluated against biological outcomes, such as HIV biomarkers [50].

HIV Vaccine

The discovery of an effective vaccine remains the ultimate goal of HIV research. However, several factors have contributed to slowing the international efforts to develop an effective HIV vaccine. The number of circulating viral strains is one of the most intractable obstacles to vaccine development. Extremely rapid and error-prone replication yields a large number of mutant genomes, some of which are able to escape immune control [51]. Another major obstacle is the lack of clear immune correlates of protection in humans. Hard fought advances in basic and clinical research are raising new hope. First, vaccine technology has evolved significantly in the last decade, profoundly changing the future of vaccine development. Reports that the prime/boost combination of two vaccines (ALVAC (R) HIV and AIDSVAX(R) B/E) lowered the rate of HIV infection by 31.2 percent in more than 16,000 volunteers in Thailand demonstrating that the development of an effective preventive HIV vaccine is scientifically possible. Recent advances in isolating broadly neutralizing antibodies and designing new tools and technologies for vaccine delivery have enhanced hope and reinvigorated vaccine discovery efforts [52]. Investigation into additional therapeutic approaches led to the use of gene therapy aimed at a diverse list of disorders including arthritis, HIV infection, dozens of different types of cancers and extremely rare genetic diseases [53].

The Future of HIV/AIDS

Long Lasting Antiretroviral therapy

Although antiretroviral drugs provide durable control of virus replication in many patients, they are not devoid of unwanted secondary effects including long-term side effects, the emergence of multidrug resistance and transmission of drug-resistant HIV strains. Further simplification of treatment and identification of more effective drug combinations are needed to improve patient adherence, the most significant cause of treatment failure. New mechanisms to deliver long-acting ART are being studied and present the potential to improving adherence to treatment and optimizing HIV care [54].

Shock and Kill

Combinatory antiretroviral therapy increases the survival and quality of life of HIV-1-infected patients. However, interruption of therapy almost invariably leads to the re-emergence of detectable viral replication because HIV-1 persists in viral latent reservoirs. Improved understanding of the molecular mechanisms involved in HIV-1 latency has paved the way for innovative strategies that attempt to purge the latent virus[55].One strategy termed "shock and kill" is aimed at decreasing the numbers of latently infected cells after the activation of HIV transcription in order for host cells to produce HIV-1 proteins (shock); this will presumably allow the cells to be cleared by virus-associated cell death or by a host response (kill) [54].A wide variety of compounds are under investigation as candidate Latency-Reversing Agents (LRAs) for the shock step.Latency-Reversing Agent (LRA) combinations exhibit such a potent effect and represent a proof-of-concept for the co-administration of two different types of latency-reversing agents as a potential strategy to reduce the size of the latent HIV-1 reservoirs [56]. The ongoing BCN02 trial adds three doses of Romidepsin between the initial and the final vaccine boosts. This cancer drug can activate hidden HIV reservoirs, making it easier for the immune system to eliminate latent viruses [54].

New Tools and Technologies for Vaccine Delivery

Developing safe, effective and affordable HIV vaccines is the best hope for ending the HIV/AIDS pandemic. Advances in

HIV vaccine development-including the design of new tools and technologies for vaccine delivery-have boosted optimism in the field about the prospects for the development of a safe and effective HIV vaccine. The identification of dozens of broad spectrum antibodies that neutralize a wide spectrum of HIV variants circulating around the world is a major step against the constant ability of the virus to mutate. The cell immunity can be stimulated using a new antigen delivery mechanism. Recombinant vaccines rely on the capacity of one or multiple defined antigens to induce immunity against the pathogen, when administered in the presence of adjuvants or when expressed by plasmids or harmless bacterial/viral vectors [57].

Discussion

This study was undertaken to advances in the management of the HIV infection. This review showed how unprecedented efforts in the fields of biology, pharmacology, and clinical care led to the development of several antiretroviral agents. As a result, the HIV/AIDS causing retrovirus has gone from being an untreatable infectious agent to one eminently susceptible to a range of approved therapies. Approximately thirty antiretroviral agents with different mechanisms of action, formulated either singly or in combination, are available today to treat patients with Human Immunodeficiency Virus (HIV-1).

Despite the impressive results of antiretroviral drugs, HIV-1/AIDS pandemic remains a challenge. While antiretroviral drugs are widely accessible in rich-country, they are not accessible by every PLH, especially those living in developing countries. Current coverage shortfalls, combined with the relentless expansion of the epidemic, underscore the need for effective prevention interventions to control HIV epidemic. Promoting the utilization of condoms, performing male circumcision in poor communities, and making clean needles available to injecting drug users are few interventions known to be effective. They can be easily integrated to curb the spread of HIV in poor countries.

People living with HIV are expected to take antiretroviral therapy for the rest of their lives in order to prevent viral replication and hopefully prevent opportunistic infections. However, long term ARV therapy increases the risk for cardiac and metabolic side-effects, including dyslipidemias, insulin resistance, and abnormal body fat re-distribution (lipodystrophy, which can lead to increased risk for heart disease and type 2 diabetes. Treatment of these chronic health conditions will require additional resources in an already financially challenged health system.

Integrated provirus in memory T cells, dendritic cells, macrophages, and microglia, that persists for long periods, makes true HIV-1 eradication difficult with available technologies. However, Latency-Reversing Agent (LRA) combinations is a promising strategy to reduce the size of the latent HIV-1 reservoirs.

This review found that when the viral load becomes and stays undetectable with successful treatment, the risk for sexual transmission of HIV is negligible. The public health implication of this knowledge underscores the needs for governments in countries hit hard by the HIV epidemic to do every effort to make antiretroviral therapy available to as many HIV-infected people as possible. A concern that low educated people may not adhere to the regimen and give rise to virus resistance has not materialized in sub-Saharan Africa.

Several approaches have been tried to fight HIV epidemic. Gene therapy and viral mediated therapy are few methods that have been used. Regardless of their outcome relative to HIV infection, knowledge gained in the fight against HIV epidemic could have indirect benefit. Lessons learned could be applied to treat other conditions. For example, knowledge in the development gained in the development of an HIV vaccine contributed to the rapid development of the Ebola vaccine. Other techniques are now being used to treat cancer.

This review is by no means a daily account of events that occurred from the discovery of the new disease till today. It highlighted what the authors considered important to provide a broad picture of the important achievement in the fight against HIV/AIDS. The fact that only papers published in English were reviewed, other important events may have been overlooked.

Conclusion

The fight against HIV epidemic has been hard, long and expensive. Yet, progress has been made and the end of the tunnel is perceptible. The HIV prevention toolbox continues to grow steadily, allowing clinicians to safely prevent and treat HIV infection. While waiting for the advent of the magic bullet to cure HIV infection, the combination of behavioral, structural and biomedical interventions can prevent the incidence of new HIV cases, but also prevent the occurrence of opportunistic infections and improve the quality of life for people living with HIV. Efforts are currently being made to address disparities that persist for the attainment of the 90-90-90 targets, which are that 90% of people living with HIV know their HIV status, 90% of people who know their HIV-positive status are accessing treatment and 90% of people on treatment have suppressed viral loads by 2020 [58].

Conflict of Interest

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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