HIV: The Decades-Long Crisis

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Abstract
HIV remains a devastating global health challenge, affecting millions of lives and perpetuating societal concerns. This article provides an in-depth exploration of the origin, impact, and treatment strategies for HIV/AIDS, aiming to enhance our collective understanding and contribute to effective preventive measures. As of 2022, there are almost 39 million people worldwide who are living with HIV, underscoring the urgency to find ways to curb its spread. While there is a tendency to use HIV and AIDS interchangeably, it is crucial to understand the difference between them. HIV (Human Immunodeficiency Virus) is a viral infection that attacks the immune system, while AIDS (Acquired Immunodeficiency Syndrome) is the most advanced stage of the disease. This article traces the historical emergence of HIV, notably its transmission from chimpanzees to humans in the early 1900s, marking the beginning of a devastating global epidemic. The societal response, especially in the early 1980s, is examined, shedding light on the stigmatization associated with AIDS and the delayed governmental acknowledgment of the crisis. Detailed insights into the molecular mechanisms of HIV infection are provided, elucidating how the virus utilizes host cells to replicate and spread. The evolution of HIV testing methods is also explored, from the early ELISA tests to contemporary rapid testing and at-home self-testing kits. Presently, antiretroviral therapy (ART) stands as the primary treatment for HIV, involving a combination of drugs categorized by their resistance profiles.

Introduction
HIV is a heart-breaking disease that impacts people every day and continues to leave its devastating mark on the world. HIV/AIDS has hurt and affected countless people around the world and continues to do till this day. Understanding the origin, impact, and treatment techniques helps us take steps as a society toward preventing the spread of this disease. As of 2022, according to HIV.gov, approximately 39 million people currently have HIV. However, what is the difference between HIV and AIDS? HIV stands for human immunodeficiency virus and is a viral infection that attacks the body's immune system and impacts the body's natural

resistance to diseases. HIV goes through various stages, and its most advanced stage is called Acquired Immuno-Deficiency Syndrome (AIDS). When the body's immune system gets badly damaged by the virus, AIDS eliminates CD4 cells, which play a crucial role in fighting infections. CD4 T lymphocytes are essential for coordinating an immune response by activating other immune cells.[i] Since HIV targets these cells, the loss of these increases an individual's susceptibility to acquiring additional infections, regardless of their severity. Typically, the Virus is transmitted through contact with the bodily fluids of an individual infected with HIV and can spread through unprotected sexual activity or the sharing of injection drug equipment.

Additionally, an HIV-positive mother can also transmit the virus to her child during pregnancy and delivery. However, belying common misconceptions, people cannot be infected by HIV positive individuals through ordinary day-to-day contact such as hugging, kissing, shaking hands, or sharing personal objects such as food or water.[ii] If an HIV infection is left untreated, it can result in severe AIDS, a very late-stage HIV infection. The development of AIDS is due to a severely damaged immune system invoked by an untreated HIV infection. Thankfully, according to HIV.gov, as of recently, most people in the US with HIV do not develop AIDS.[iii]

Origin and Evolution of HIV

Scientists have been aware of HIV for a very long time. In fact, according to the Center for Disease Control and Prevention (CDC), studies have shown that HIV has jumped from chimpanzees to humans since the early 1900s. In the past, chimpanzees were known to carry the Simian Immunodeficiency Virus (SIV). HIV and SIV are a part of the Lentivirus genus and the Retroviridae family. Lentiviruses are a group of single-stranded RNA viruses that cause fatal diseases in humans and other mammalian species. Like all viruses, SIV needs a host cell to infect an organism. While SIV was originally only found in African monkeys, it was transmitted to humans, resulting in the outbreak of HIV and AIDS. HIV has two variants – HIV-1, which is similar to the SIV strain found in chimpanzees, while HIV-2 originated from a disease found in sooty mangabey monkeys.[iv] HIV-1 is a more dominant strain and is often found in humans. The stress of HIV-1 is believed to have come from the consumption of monkey meat contaminated with the SIV infection. The first known human case of HIV-1 infection was first found in a man in the Belgian Congo in 1959. Since then, the virus has spread across Africa and swiftly spread worldwide, infecting and killing many unsuspecting people. While AIDS and HIV were spreading for a couple of decades, the epidemic was officially recognized as a severe illness in June of 1981. During this period, diseases such as Pneumonia and Kaposi’s Sarcoma spread rapidly among gay men in New York and California. Upon careful analysis, scientists deduced that it was neither a disease nor that a new

disease was on the rise. In 1983, researchers at the Pasteur Institute in France discovered a virus associated with AIDS and later declared it a Lymphadenopathy-Associated Virus (LAV).[v] However, scientists in the US working at the National Cancer Institute found a similar virus, which they re-named HTLV-III. After further research, they concluded that LAV and HTLV-III were the same virus, and hence, the new name HIV was born. Since initially, the prime demographic impacted by AIDS was gay men, fear spread quickly among the community as the "gay plague" theoretically threatened to "out" members of the LGBTQ+ community if they were diagnosed with AIDS. Unfortunately, with the stigma associated with the name at the time, government regulation was minimal. The epidemic has led to the loss of people who hold important cultural knowledge and skills. This puts the continuation and preservation of cultural traditions at risk. As a result, the effects of HIV/AIDS are felt in many parts of society, highlighting the need for thorough strategies to deal with its widespread consequences. For example, without government intervention, San Francisco took the initiative to shut down their bathhouses and private sex clubs and instead opened community-based research projects and provided prevention education. On September 17th, 1985, 4 years after the rise of the epidemic and after countless lives had been lost, President Ronald Regan finally admitted to the urgent crisis. However, it was only at the end of 1987 that the country formally took the initiative to raise awareness for AIDS. As the problem became more pressing, scientists made research available to the general public, hoping to spread awareness and prevent infection.[vi]

HIV Infection Mechanisms

How does HIV infect human cells? Any virus that infects a human needs a host cell to bind to. Retroviruses, the category of viruses that HIV falls under, work in the same fashion yet are slightly different from a regular virus. However, retroviruses contain two complete copies of single-stranded RNA. Then, the virus uses the host cell's genetic processes to convert the viral RNA into DNA to replicate itself. The single strands of RNA inside the virus come together near their starting points without forming strong chemical bonds, creating a double-stranded structure called a dimer linkage. Typically, DNA tells the cell and RNA how to create specific parts of the body.[vii] Retroviruses are named after an enzyme known as reverse transcriptase, indicating a reversal of the usual direction of cellular transcription. HIV infection occurs when the virus binds to the cellular membrane, delivering the viral pathogens directly to the cytoplasm.[viii] However, instead of DNA instructing the cell to create RNA, RNA instructs the cell to make DNA in retroviruses. Then, the DNA tells the cell to develop replicates of itself to reproduce. This process makes it possible for the genetic material from a retrovirus to permanently incorporate the infected retroviral DNA into another cell, which can produce.[ix]

Advances in Testing and Diagnosis

Thankfully, we can combat this. Since the 1980s, HIV testing has become advanced and very accessible. At the time, HIV tests were not used to diagnose AIDS or HIV but rather to screen blood in patients to determine if an infection was present. According to Time Magazine, the first test that used blood was known as an "enzyme-linked immunosorbent assay" or the ELISA test.[x] These first tests were primarily used to ensure that donated blood did not have the virus crucial to society's overall well-being, as there was great uncertainty about whether the blood a patient received was infected. According to the Natural Museum of American History, a tiny percentage of cases (2% of the approximately 8000 cases) reported between 1981 and 1985 were linked to contaminated blood transfusions. There are three main types of HIV testing: Antibody tests for blood or oral fluid, Antigen tests to detect HIV antibodies, and NATs to look for HIV in the blood.[xi] These tests do not detect HIV by themselves but instead notice the immune response to the virus. The most widely used way of detecting HIV-1 and HIV-2 is through the use of ELISA testing.[xii] The test includes a vial containing resin beads coated with viral proteins of HTLV-III. Following the addition of a blood sample, antibodies to the virus can be determined by their binding to the antigen-coated beads. Two chemicals are added to determine the positivity of the test: 1, to see if the antibodies bind or get washed away; and 2, which would turn the sample yellowish if the test was positive. However, the test was often falsely positive, which indicated that while the person had the virus in their blood, there was no surety they would develop AIDS.[xiii] While the tests denoted an essential step in the fight against AIDS, many worried that their results would be made public, "outing" their gay identity and thus ostracizing them socially.

Antiretroviral Therapy (ART)

Today, HIV is treated with a series of antiretroviral medicines. The way these drugs work is by reducing the amount of HIV in the body by preventing the multiplication of the infected cells. During this process, the drugs stop the spread of HIV and give the immune system time to repair itself for the damage done. Typically, an individual with HIV does not only take one medicine but a relatively select few. This combination helps prevent the spread of HIV as the virus can become quickly resistant to any medication. With recent technology, we have innovative ways to combat this resistance. The treatment for HIV is called antiretroviral therapy (ART). This procedure entails adhering to a treatment plan that involves a daily dosage of a combination of HIV medications. These drugs are split into six different categories based on their resistance profiles. According to the National Centre for Biotechnology Information, these six categories are as follows: nucleoside analogue reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), integrase inhibitors, protease inhibitors (PIs), fusion inhibitors, and

coreceptor antagonists.[xiv] The initial two classifications, NRTIs and NRTIs, attach to a targeted pocket on the enzyme. This group of medications collectively constitutes almost fifty percent of the antiretroviral drugs approved. Nevertheless, the distinction between these two lies in the location of their interaction with the enzyme. Category 3, integrase inhibitors, are the most recent HIV-1 enzyme to be successful in drug development. This enzyme is commonly referred to as integrase strand transfer inhibitors or INSTIs. According to the NCBI, INSTIs are comprised of two essential components: a metal-binding pharmacophore, which isolates the active site magnesium, and a hydrophobic group, which interacts with the viral DNA as well as the enzyme. The fourth type is the protease inhibitors or PIs. Since it is tiny, it was hypothesized that the resistance to the protease inhibitors would be rare. All protease inhibitors (PIs) exhibit a comparable chemical composition and resistance potency. Typically, primary mutations causing resistance are observed near the enzyme's active site, near the location of the inhibitor binding site. For fusion inhibitors, which is the 5th category, proteins must interact with each other to promote fusion. Finally, for HIV to infect a cell, it needs to bind to a chemokine coreceptor. The last category, coreceptor antagonists, blocks the virus from binding to the coreceptor.[xv] While ART cannot cure an HIV infection, it can help patients live longer and reduce the risk of HIV transmission.

While that may be true today, self-testing kits were first approved in 1996. In the original kit, a blood specimen would be collected and sent to a laboratory for further testing. Then, users would be told their results over the phone. Since then, HIV rapid testing has evolved. For example, in 2002, the FDA approved a Rapid HIV-1 Antibody Test to detect HIV-1. While there were many variations till then, in 2012, the OraQuick InHome HIV Test was recognized as the first at-home HIV rapid test available over the counter. According to WHO, As of 2022, 98 countries have a policy for HIV self testing, yet as many as 52 countries do not implement those policies. Most of these 52 are lower-income countries, and WHO estimates that donors would acquire 10 million self-test kits for these countries. While this progress on rapid testing is steady in developed countries, positive change will occur if research and manufacturing happen locally in developing countries. It would cut costs, considerably making them accessible to many more.[xvi]

Unfortunately, because of its high prices, HIV treatment is not accessible to everyone. According to WebMD, one study estimated the cost of treatment in the range of $1,800 to $4,500 each month, depending on the severity and type of treatment plan. However, part of this cost is that some name brand medications cost more than others. The frequently prescribed medication, Truvada, costs around $1,700 for a monthly provision of tablets. In comparison, the drug Epivir costs about $400 for the same purpose. While consuming the generic version of prescribed drugs seems like a wise financial decision, there are substantial health

risks involved. For example, one of the prime reasons for multiple medications is due to how quickly HIV can adapt to them. Higher quality drugs tend to have more robust resistance prevention, proving effective but also increasing costs. If HIV becomes resistant to most of the common drugs, doctors will have less control of the infection, resulting in the prescription of an injection-based treatment. This treatment is known as long-acting antiretroviral therapy, and compared to tablets, it can cost up to $9,000 every month.[xvii] Sadly, those with HIV tend to have hepatitis C as well, increasing their medications and the overall cost of treatment. On top of these costs, lab tests increase it even further. To track progress, doctors often send blood samples in for testing. However, recent studies show that for people with HIV, testing is unnecessary.

In the past, however, many countries, due to issues like social strains, poor funding, and infrastructure, considered the provision of ART. For example, in 1995, Brazil introduced research for local production of ART and subsidized free antiretroviral drugs for those who need them. In late 1997, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the Drug Access Initiative. As a follow-up to this initial effort, the World Health Organization's Accelerating Access Initiative, implemented in the year 2000, played a crucial role in lowering the cost of Antiretroviral Therapy (ART) for individuals in more than 30 countries globally. Following that, in 2002, The Global Fund to Fight AIDS, Tuberculosis, and Malaria was established, leading to President George W. Bush's $15 billion Emergency Plan for AIDS Relief in 2003. In 2006 and after that, companies dealing with antiretrovirals entered into voluntary licensing agreements, allowing generic companies to distribute these medications at significantly reduced rates for developing nations. Due to this progress, access to ART increased worldwide as the safety of medicine consumption increased. The impact of HIV/AIDS spans various dimensions, significantly affecting productivity, healthcare systems, households, and key industries. Loss of productivity is a notable consequence, as the illness can lead to reduced workforce participation, and premature death, impeding economic growth. On a more household level, families grappling with HIV/AIDS may encounter heightened financial strains stemming from medical costs or increased caregiving responsibilities leading to a perpetuating cycle of poverty and vulnerability.

These constraints also impact the healthcare sector. As the severity of HIV/AIDS became worse globally, shortages of healthcare providers, medications, and infrastructure have become increasingly prevalent, exacerbating the challenges faced in delivering comprehensive care. Because of this, there has been a necessary reorientation of healthcare priorities, with a pronounced emphasis on prevention, testing, and treatment initiatives tailored to combat HIV/AIDS. Unfortunately, due to this focus on HIV/AIDS, other pressing illnesses have been neglected. Nonetheless, thankfully, the advancements in care have skyrocketed due to

fostering the expansion of community-based care, the implementation of mobile clinics, and the adoption of telemedicine solutions. Moreover, in 2014, UNAIDS formulated the 90-90-90 plan with the aim of "ending AIDS." This initiative aimed to achieve the following goals by 2020: ensuring that 90 percent of people living with HIV are aware of their HIV status, 90 percent of those diagnosed receive treatment, and 90 percent of those individuals attain suppression.[xviii] However, while they made significant progress, the outbreak of the COVID-19 pandemic made it challenging to achieve this goal. Research labs redirected their focus to developing a vaccine for COVID-19, and governments stopped subsiding HIV prevention efforts. Through all this, the prices of treatment escalated, and it became the individual's responsibility to fund it.

Given the widespread impact and highly virulent spread of COVID-19, governments, health organizations, and research labs worked tirelessly to develop and provide a vaccine for people. Contrastingly, it has been nearly four decades, and the only treatment available for HIV is an oral or injectable medicine. While this does not seem like progress, the reason for this difference is that COVID-19 is a milder virus than HIV. Vaccines work by inserting a weaker virus component, which triggers an immune response in the body. In normal circumstances, the body will create antibodies to the virus, creating an immune response to the antigen.[xix] Unfortunately, during the research stages of a potential HIV vaccine, the participants enrolled in the study with respiratory issues were more likely to contract HIV. As the virus binds to a host cell's DNA, it limits the region of the vaccine's permitted area. The risk of an HIV vaccine is the infection binding to the DNA of a host cell and causing it to spread rapidly. In more recent times, healthcare professionals are experimenting with cure research. This entails the “shock and kill" strategy.” This method holds the potential for effectively targeting and eradicating persistent viral reservoirs within the body. Another such treatment is stem cell transplantation, particularly for individuals possessing a genetic mutation known as the CCR5-delta32 mutation, which confers resistance to HIV.

A misconception occurs with the use of vaccines. Some think that by taking a vaccine, they are immune to a virus or infection, when in reality, the body is familiar with the infection, making it easier for the body to fight the infection. In some cases, studies have observed a natural immunity to HIV in some individuals around the world. For example, Stephen Crohn was the first known person to be HIV-resistant despite having partners infected with the virus due to the absence of a receptor that prevents HIV from inhabiting a cell. Due to a mutation known as delta 32 mutation, these people can never contract the virus.[xx] These studies looked into immunogenetic associations with resistance to HIV and tried to create a vaccine from this. While ART slowed the progression of the infection, gene therapy created a resistance to HIV. One study discussed how the replacement of HIV genes with hematopoietic stem cells and

engineered particles would prevent the infection from ever entering the body.[xxi] These anomalies created hope for many people who have HIV, but unfortunately, to this date, there is no official vaccine nor permanent cure for HIV.

Prevention Strategies

Luckily, there are ways to prevent contracting HIV. Since HIV spreads through either blood or bodily secretions, it is essential to understand the risks. According to the CDC, prevention of HIV comes from being careful. Many ways to prevent HIV include having safe sex, having conversations with your partner about HIV testing, or practicing abstinence. Another effective way to prevent the spread of HIV is through PrEP (pre-exposure prophylaxis). Preexposure prophylaxis (PrEP) is designed for individuals at risk of HIV. While this medication reduces the risk of acquiring HIV through sexual activity, its effectiveness is diminished if not prescribed.[xxii] Another yet significant prevention method is to limit the sharing of needles. Through injectable drug intake, an infected syringe can significantly increase your risk of contracting HIV or viral hepatitis. Disinfecting needles and keeping yourself safe can go a long way into preventing the spread of this awful disease.

Conclusions

This article provides a thorough examination of the persistent global health challenge presented by HIV/AIDS, emphasizing the pressing need for ongoing efforts to mitigate its impact. The historical journey of the virus, from its transmission to humans in the early 1900s to the societal responses of the 1980s, highlights the gravity of the epidemic. Despite significant strides in understanding the molecular mechanisms of HIV infection and advancements in testing methods, the article underscores the continued importance of antiretroviral therapy (ART) as the primary treatment. Challenges in accessibility to HIV treatment are acknowledged, particularly in the context of high costs. The article concludes by reiterating the significance of prevention strategies, such as safe practices, HIV testing conversations, and the utilization of Pre-exposure Prophylaxis (PrEP) in at-risk populations. Ultimately, a collective and sustained global effort is crucial in addressing the multifaceted aspects of HIV/AIDS and working towards a future where the impact of this deadly disease is significantly reduced.

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