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# Lessons from HIV

Boriana Marintcheva

**U**ndoubtedly, everyone has heard about HIV (*Human Immunodeficiency Virus*), and many are questioning why, decades after HIV emergence, we still do not have a cure or a vaccine. The great news is that the path to HIV eradication is clear and within reach.

**To start, it is critical to recognize that while HIV is still a deadly virus, HIV infections are no longer a death sentence.** UNAIDS, a UN program focused on HIV eradication, estimated that in 2022 new infections were down by 60% after peaking in 1995, and HIV-related deaths were down by 70% after peaking in 2004. Presently, the HIV prevalence in adults is 0.7% worldwide with half of all HIV-infected individuals (20.8 million) living in southeastern Africa. In the USA, the largest number of HIV-positive individuals live in the South, whereas the Northeast has the highest infection rate, with disproportionately high levels among transgender individuals (10.3%), men having sex with men (7.7%), and injectable drug users (5%).

When HIV infections are treated, one is posed to have a long and productive life. For example, if a 20-year-old individual was infected with HIV before the availability of anti-HIV drugs, they were expected to live only until the age of 30. After anti-HIV drugs became widely available (2002), the life expectancy gradually increased and in 2010 an infected 20-year-old was expected to live until the age of 75, only 5 years less than an uninfected counterpart.

**Today we have tools to combat HIV because we understand how it works.** HIV is a fast-propagating retrovirus with complex biology. If left untreated, it gradually destroys the immune system leaving individuals

immunocompromised and dying from diseases that a healthy immune system would have easily neutralized. In the early days of HIV, society saw clusters of unexplained deaths in homosexual communities, blood transfusion recipients, and sex workers. Through the power of research, today we recognize that the initial HIV infection results in mild flu-like symptoms that are frequently disregarded. The body recovers swiftly and years may go by without any symptoms while HIV quietly deteriorates the immune system, leading to AIDS (*Acquired ImmunoDeficiency Syndrome*). If the HIV infection is detected, a completely different scenario could unfold. Individuals start treatment, HIV propagation is controlled, the immune system works, and life could bring great things as it did for Magic Johnson, a renowned NBA player who announced his HIV diagnosis in 1991 and is still thriving.

Once HIV was recognized as the causative agent of AIDS (1984), research aimed to understand its biology and transmission routes to inform development of reliable testing, prevention, and treatment. One can think about HIV testing as the switch between the two alternative scenarios sketched above because it provides us with powerful information to keep ourselves healthy. HIV testing can be done at home with a pharmacy-purchased self-test or in clinical settings using saliva or blood samples. It is recommended for all adults to test at least once per lifetime

or as frequently as necessitated depending on risk. Any contact with blood, semen, vaginal fluid, anal mucus, or breast milk presents an opportunity for HIV exposure and should trigger consideration for testing. Testing is highly recommended for pregnant women and routine for infants born to HIV-positive mothers. Testing and treatment together led to 1% risk for mother to child transmission, down from 35%. Tests are covered by insurance, Google is helpful for locating testing facilities by ZIP code, and HIV/AIDS advocacy websites offer plenty of advice on how to approach personal issues frequently associated with HIV testing and HIV status. Simply stated, one can contribute to stopping HIV by getting tested and encouraging people to do so. Over the years, testing has been refined tremendously, allowing for fast, reliable, and convenient processes. Most importantly, testing leads to HIV status awareness, which allows access to treatment.



Figure 1: Pitt County AIDS Service Organization, Greenville, NC ([picaso.org/testing-program.html](https://picaso.org/testing-program.html)).

HIV treatment is known as *Highly Active Antiretroviral Therapy*, or *HAART*. HAART entails a cocktail of three anti-HIV medications, each targeting a key step in viral propagation. HAART therapy works because it is based on understanding how HIV works. As a retrovirus, HIV inserts copies of its genetic material in the host DNA and thus becomes an inseparable part of the infected individual. The longer HIV infection goes unchecked, the more HIV copies accumulate and the greater is the damage of the immune system. A

typical sterilizing cure for HIV is currently not possible because we cannot cut HIV out of our DNA. HAART is delivering a functional “cure,” effectively stopping HIV propagation by supplying a continuous stream of anti-HIV drugs for the duration of one’s life. In that sense, we have effective treatment but no cure for HIV.

The first drug against HIV (1987) was AZT, a repurposed anti-cancer medicine. Unfortunately, AZT extended the life of HIV-positive individuals by only two years due to mutations conferring drug resistance. The development of new anti-HIV drugs paralleled the increasing understanding of HIV biology and the realization that fast HIV mutation rates are a huge obstacle. HAART was introduced in 1996 with the rationale that three drugs taken together will shut off HIV propagation with minimal risk of resistance. Initially, following HAART protocol required taking multiple pills several times per day to mitigate harmful side effects. Medicine refinement and introduction of slow-release formulations allowed doses to be lowered, thus lowering side effects, simplifying treatment protocols, and increasing treatment adherence. Declining infections and increased life expectancy followed. Meanwhile, science delivered new milestones. In 2019, ART (Anti-Retroviral Therapy) protocol, employing two instead of three drugs, was introduced and 2021 brought to market a monthly injectable treatment for virally suppressed patients. Viral suppression refers to a state where virus propagation is halted and HIV is no longer detectable. If HIV is undetectable, it is untransmittable, thus the popular slogan “undetectable=untransmittable.” Keep in mind that HIV remains present in the patient’s DNA. If therapy is discontinued, propagation picks up and immune system damage progresses. In summary, once HIV-positive status is identified, treatment must start

immediately, aiming to achieve viral suppression as quickly as possible. Viral suppression is a ticket for good personal health and curtails HIV spread.

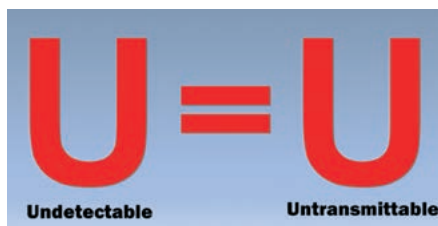


Figure 2: National Institutes of Health (directorsblog.nih.gov/tag/undetectableuntransmittable/).

Anti-HIV drugs are prescribed for three purposes: therapy, PrEP (Pre-Exposure Prophylactics) and PEP (Post-Exposure Prophylactics). PrEP is recommended for HIV-negative individuals with ongoing high risk for HIV infection and entails taking a daily pill or a monthly injection along with regular testing. PrEP on demand refers to a four-day schedule where medicine doses are spread before and after a high-risk event. PEP is a tool to manage potential HIV exposures in emergencies (accidental needle stabbing, broken condom, sexual assault) and must be started within 72 hours. PrEP and PEP are relatively new and currently a subject of active awareness and education efforts.

Even though there is still no cure for HIV infections, the available knowledge has taken us to the point where

society has a meaningful plan for HIV eradication within reach. Frequently the plan is described as 90/90/90, referring to three targets: detecting 90% of HIV cases, 90% of the HIV-infected individuals starting treatment, and 90% of the people in therapy becoming virally suppressed. The initial goal was to reach 90/90/90 targets by 2020, aiming to achieve 95/95/95 levels in 2030. However, the COVID pandemic complicated things. According to UNAIDS, in 2022 the world stood at 86/89/93 globally with broad variability margins. The USA standing by region is shown in Figure 3.

Despite the tremendous efforts and funding dedicated toward HIV vaccine development, the prospects of having one soon are not promising due to the complex nature of the virus and its profound impact on the immune system.

**Understanding where HIV comes from matters.** Since 1999, science knows that HIV originated from Simian Immunodeficiency Virus (SIV), which likely jumped from chimpanzees to humans when the animals were hunted for food and individuals were exposed to infected blood. Currently, it is believed that HIV arose in Central Africa and over decades “rode” the wave of industrialization and human migration unrecognized. HIV arrived in the USA sometime in

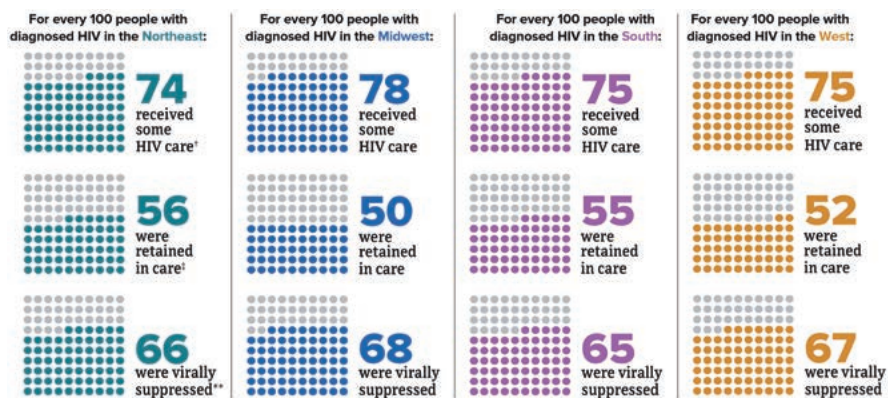


Figure 3: USA progress toward HIV eradication by region as of 2021. Center for Disease Control. Estimated HIV incidence and prevalence in the United States 2017–2021. HIV Surveillance Supplemental Report 2023; 28(3) (www.cdc.gov/hiv/statistics/overview/in-us/status-knowledge.html).

the mid-1970s, years before its first documented appearance in Los Angeles in 1981. Of course, in those early years the question of where HIV comes from was asked in a very practical way to understand the modes of transmission. Although the answers and prevention recommendations came quickly, it took a while for reason to replace fear.

The story of Ryan White, the poster child of HIV/AIDS in the USA from the mid-1980s, illustrates a broad range of issues. Ryan White got infected with HIV through a blood transfusion while receiving treatment for a blood clotting disease. After his diagnosis became public, his family found themselves in the middle of a legal action to keep him in school. Despite the recommendations of his doctors and the clear rationale why he did not present a risk for the school, there was a strong pushback from the local community. The case sparked national conversation and political action. The family won the legal battle and Ryan White was allowed to return to school, however community reactions escalated, and the family moved. White's legacy continues to live through the *Ryan White CARE (Comprehensive AIDS Resources Emergency) Act* which dedicates resources to help HIV infected individuals manage their condition. For example, because of the CARE Act, health insurance is required to cover HAART and PrEP for qualified individuals.

Understanding that HIV is transmitted through blood allowed HIV testing to be developed. Screening of donated blood for HIV became a standard practice. Fast-forward to today the number of infectious agents donor blood is tested for has tripled. It is important to realize that when HIV screening of donated blood began, the practice already existed for Syphilis and Hepatitis B, i.e. learning from the past provided a fast solution for

HIV in 1980s and other infectious agents afterwards.

The history of HIV denialism offers an example of how detrimental the disconnect between science and personal beliefs can be when the burning question is "Where is AIDS coming from?" Between 1999 and 2008, the government of South Africa shaped national public health policies based on the notion that the roots of AIDS are socio-economic, while denying HIV as the infectious agent causing AIDS. The introduction of anti-HIV medicines in health care was discouraged and resulted in unthinkable loss of life. After changing policy and accepting the science, the country changed course and by 2022, it was experiencing positive changes in HIV/AIDS management at record rates.

One can only hope that truly embracing the knowledge of origins and modes of transmission of HIV will soon erase its label as a "homosexual issue," and when the next virus emerges from the wild, there will be less room for conspiracy theories and labels, which quickly grow into social injustices that take forever to eradicate.

**Societal attitudes and support infrastructure are essential for science and medicine to deliver to their fullest potential.** Social issues can become life or death for people struggling with HIV because they are directly connected to people's access to HIV testing and life-saving medications. Homophobia, stigma, and inequalities are often recognized as the biggest obstacles of our time to combating HIV and AIDS. They rob people of access to resources, limit choices to exercise HIV prevention, propagate misconceptions, and stop individuals from seeking treatment. In many communities around the world, homosexual activities and drug use are illegal, thus criminalized, and penalized. HIV infected individuals are

less likely to seek testing and treatment when fearing that they will be questioned and penalized. Similarly, gender-based violence increases the risk of HIV infection and diminishes access to care. Misinformation and fear create and increase stigma toward HIV-infected individuals, further exacerbating the complexity of combatting HIV. On the other hand, economic stability, supportive social networks, access to specialized health care, and a holistic approach to managing life with HIV have been shown to improve adherence to treatment and long-term outcomes.

Educating the public about HIV is a must to ensure prevention of new infections, to empower HIV positive individuals to have productive lives, and to reduce stigma. There is no shortage of knowledge and tools for HIV education. The good news is that their focus is somewhat changing in recognition of the needs of different risk groups, inclusivity, and social connectivity. HIV infections are complex and multidimensional and are best contained when addressed with human-centered, complex, and multidimensional measures. Regardless of how many and how powerful tools and strategies are available in the clinic, there is no replacement for HIV awareness, equitable access to care, and humanity.



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