

HIV/AIDS – PAST, PRESENT AND FUTURE

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INTRODUCTION

The first case of AIDS (Acquired Immune Deficiency Syndrome) in Canada was reported in February 1982, and the virus responsible, the human immunodeficiency virus (HIV), was discovered in 1983. Over the past 20 years, governments have spent billions of dollars and scientists have worked exhaustively in order to develop treatments, preventative vaccines and a cure for the fatal disease. This paper will briefly describe the origins of the epidemic, the present state of the epidemic and the recent scientific advances in the fight to contain and treat the infection.

HISTORICAL OVERVIEW

Although AIDS is relatively new in terms of being recognized as a disease, the human immunodeficiency virus has been in existence quite possibly since 1930, with a confidence interval of 1910-1950. The question of how it came about has been a topic for debate for many years. One theory that has been discredited was that a simian (monkey) version contaminated a polio vaccine given to Africans in the Congo between 1957 and 1960; it is now confirmed that the virus appeared in humans much earlier than this, so the theory has now been all but abandoned. Other controversial theories have included a biological warfare experiment that went wrong, reuse of unsterilized needles in vaccination programs, and the injection of malaria-infected blood into “volunteer” prisoners who then left the prison environment and carried the infections with them. The most controversial of the theories was popularized by Peter Duesberg of Berkeley, who hypothesized that the human immunodeficiency virus is a harmless passenger virus that does not cause AIDS but that drug use, combined with HIV infection, would result in AIDS. Substantial epidemiological, virological and immunological evidence has disproven this hypothesis.

There are two genetically and evolutionally distinct types of the human AIDS viruses, HIV-1 and HIV-2. Evidence suggests a zoonotic (cross-species) transmission of HIV to humans, and implicates the chimpanzee (*Pan troglodytes troglodytes*, a subspecies of the common chimpanzee) as the source of HIV-1 infection and the sooty mangabey as the source of HIV-2 infection in human populations. The strain responsible for the majority of infections worldwide, HIV-1 group M, appears to have arisen from a single cross-species transmission event.

Several lines of evidence have been used to substantiate these conclusions. These include the genetic similarities between the animal and human virus; the prevalence of infection in the natural host; geographic coincidence of the natural host and areas where HIV is endemic; and finally, plausible routes of transmission. The origin of HIV-2 was more easily determined than HIV-1. HIV-2 and SIV_{sm} (the simian equivalent to HIV-2 in the sooty mangabey) were found to be genetically very similar, as many as 22% of sooty mangabeys are infected in the wild with SIV_{sm}, and their populations coincide with endemic areas of HIV-2 infection in West Africa. Finally, sooty mangabeys are hunted for food and the orphans are frequently kept as pets, which identifies the plausible route for human infection.

In the case of HIV-1, these criteria have been more difficult to establish for the chimpanzee; but recent evidence confirmed significant infection of chimpanzee subspecies *P. t. troglodytes* in the wild and established that the geographic coincidence was Cameroon. The proposed likely route of transmission is hunting. It is widely believed, but not yet proven, that social, economic and behavioural changes occurring in the early and mid-twentieth century then provided the circumstances whereby these viruses could expand and reach epidemic proportions.

HIV INFECTION

When a person becomes infected with HIV there is an initial burst of viral replication and the individual may, or may not, experience flu-like symptoms for a few weeks. Antibodies to the virus are detectable from between 6 and 18 weeks after the initial infection; there is also a slow and steady decline in the level of CD4+ cells. The CD4+ cells are one component of a very complex and poorly understood human immune response. These cells secrete chemicals that help to stimulate the immune response; therefore, a reduction in CD4+ cells translates into a reduced immune response to foreign invasions such as other viruses, bacteria, fungi, etc.

The onset of HIV antibody production is followed by a long but variable incubation period of about 10 years, between infection and the onset of AIDS. This latency period is followed by an early symptomatic stage in which there is a renewed decline in CD4+ cells and an increase in infections, but these are generally not life-threatening. A late-symptomatic stage of HIV disease follows, characterized by more serious infections and a continuing decline in CD4+ cells. The final stage of the illness is often referred to as full-blown AIDS and is the end stage of a progressive and continuous process of profound immune deficiency and infections. At this stage, CD4+ cell counts are very low, and opportunistic disease and infection are the greatest threat to the patient's survival.

HIV infection generally proves fatal within 10-15 years. However, most industrialized countries, where patients have treatments available to them, have seen a decline in the death rate over the past decade.

PRESENT STATISTICS AND FUTURE ESTIMATES

Approximately 40 million people worldwide were living with HIV/AIDS in 2004 and an estimated 3.1 million people died in that year alone due to complications from HIV infection. The HIV/AIDS epidemic has affected sub-Saharan Africa most substantially, where it appears to be stabilizing, but most experts feel that the world has yet to see the pinnacle of this global epidemic. In Canada, over 57,000 people have been diagnosed as HIV+ since the test became available in 1985, while 13,111 people had died of AIDS by the end of 2004. There has been a 20% rise in the number of positive HIV test reports in the past five years, rising from 2,111 in 2000 to 2,528 in 2004. An additional 15,000 individuals are believed to be living with HIV/AIDS in Canada but are unaware of their status.

It is estimated that in the next 20 years, about 70 million people will die from AIDS, 55 million of these in sub-Saharan Africa. These large numbers will cause a dramatic decline in the average life expectancies, eradicating decades of progress that led to increases in life expectancies. Difficulties that have been cited as obstacles to containing the epidemic include: the large proportion of individuals believed to be infected but unaware of their status; the success of treatments in maintaining relatively good health in infected individuals and reducing mortality, thereby increasing the window of their infectivity; and complacency due to living with the viral threat for such a long time. As Canada's infection rate has not yet shown sustained decline, it is likely that we have not yet seen the worst of this disease's impact.

THE DIRECTION OF AIDS RESEARCH FOR PREVENTION, TREATMENT AND CURE

The first drug to be approved for use that was active against HIV was AZT (zidovudine) in 1987.⁽¹⁾ Although work continues into new antiviral drugs to circumvent the resistance that HIV seems very capable of acquiring, the prospect of an HIV vaccine is more attractive. A vaccine would eliminate the difficulty of supplying vast amounts of expensive, and often toxic, drug therapy medications to the impoverished, developing countries most affected by this disease.

The search for an AIDS vaccine is as old as the discovery of the HI virus in 1983. However, development of a vaccine has proven much more difficult than originally expected. The International AIDS Vaccine Initiative (IAVI) was incorporated in 1996, although the Canadian HIV Trials Network (CTN) officially began its first trials in early 1991. In 1997, President Clinton issued a challenge to scientists to discover a vaccine within 10 years, and the HIV Vaccine Trials Network was established.

Clinical trials for candidate vaccines are divided into three distinct phases. In Phase I trials, the safety of and immunological response to a potential vaccine are measured on a small number of healthy individuals who are not considered to be at risk of contracting HIV. The first phase generally takes about one year to complete. Successful vaccine candidates can then be put through Phase II trials, which comprise a greater number of individuals representing both low and high risk to HIV infection. This phase helps to refine dosing of the vaccine and provides additional safety data; it can usually be carried out over two years. Finally, Phase III trials, which take a minimum of three years to conduct thoroughly, are performed with thousands of volunteers who are at high risk of contracting HIV. The final phase of vaccine trials provides information on how well the vaccine protects an immunized individual from contracting HIV in a high-risk environment.

To date, only a few vaccines have progressed to the third phase of trials. Two of these, produced by Merck and Aventis Pasteur, failed. A third candidate vaccine is undergoing Phase III trials in Thailand. Currently, there is considerable optimism with respect to another vaccine by Merck currently in Phase II trials. Canada is one of the countries participating, along

(1) For a detailed description of the drug therapies available against HIV infection, please see Sonya Norris, Alan Nixon and William Murray, *AIDS: Medical and Scientific Aspects*, Background Paper PRB 93-5E, Parliamentary Research Branch, Library of Parliament, Ottawa, 18 December 2001.

with the United States, the Netherlands and Thailand. Although development of an effective vaccine has been slower than most people anticipated, vaccines against other viral infections such as polio, Hepatitis A and B and measles also took two to five decades to develop.

The discussion of vaccines so far has focussed only on “preventative HIV vaccines” – that is, vaccines that can be given to uninfected individuals to protect them against the HI virus should they come in contact with it. This is much the same as with other, familiar, vaccines such as those for flu, Hepatitis B or chicken pox. The second category of vaccine, which has had little coverage and little scientific success thus far, is that of “therapeutic HIV vaccines.” Such a vaccine would, in fact, be a therapy given in conjunction with drugs, with the aim of reducing the length of time and dosage of the drugs that need to be administered. As such, a therapeutic vaccine is one that would be given to an infected individual, along with the prescribed drug regimen, to allow a reduction in future drug therapy. Researchers have been even less successful so far in achieving therapeutic vaccines than they have been in achieving preventative vaccines. However, the company Aventis Pasteur has succeeded in getting a number of candidate vaccines to the trial stage.

The word “cure” is conspicuous by its absence. As with other viral infections, emphasis is placed on prevention and successful treatment. Many viral infections “run their course” like colds, flu, measles, mumps, rubella and pertussis, and are generally not considered life-threatening, although all have claimed some lives. Other viral diseases can leave victims disfigured, as with smallpox, or maimed as with polio, while viruses like Hepatitis C may go undetected for decades before causing significant damage. None of these diseases is curable, but all (with the exception of Hepatitis C) are treatable and – perhaps more significant – are preventable with vaccines. One day, the threat of HIV may seem as remote as the threat of polio or smallpox, should a preventative vaccine be discovered.

CONCLUSION

The HI virus was around long before “patient zero” in the United States in 1979. Changes, however, in social structure and global mobility provided the climate for the worldwide epidemic that has claimed an unimaginable number of lives. Containing the epidemic has had only limited success, and there is some evidence that prevention strategies, although initially encouraging, are losing their impact. Research into fighting this virus shows promise in a

number of areas, but scientists hope that work on vaccine development will soon be successful. Vaccines to prevent HIV transmission would be the most effective means of containing the epidemic, while a therapeutic vaccine would be much more realistic as a means of treatment in impoverished, developing countries.

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