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HIV/AIDS – Past, Present and Future

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HIV/AIDS – Past, Present and Future **(Background Paper)**

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CONTENTS

1	INTRODUCTION.....	1
2	HISTORICAL OVERVIEW	1
3	HIV INFECTION	2
4	PRESENT STATISTICS AND FUTURE ESTIMATES.....	2
5	THE DIRECTION OF AIDS RESEARCH FOR PREVENTION, TREATMENT AND CURE	3
6	CONCLUSION	4
	SELECTED BIBLIOGRAPHY	

HIV/AIDS – PAST, PRESENT AND FUTURE

1 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. For over 25 years, governments have spent billions of dollars and scientists have worked tirelessly to develop treatments, preventative vaccines and a cure for this fatal disease. This paper will briefly describe the origins and present state of HIV/AIDS, as well as recent scientific advances in treatment and disease control.

2 HISTORICAL OVERVIEW

Although AIDS is relatively new in terms of being recognized as a disease, the causative virus has probably been in existence since about 1930, and possibly since the turn of the 20th century. The question of how the disease emerged has been debated for many years. One theory was that a simian (monkey) version contaminated a polio vaccine given to Africans in the Congo between 1957 and 1960, but confirmation that the virus appeared in humans much earlier than this has discredited this theory. Other controversial theories have included a biological warfare experiment that went wrong, the 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 infection with them. The most controversial of these theories was popularized by Peter Duesberg of the University of California, Berkeley, who hypothesized that HIV, on its own, does not cause AIDS but, when combined with drug use, results 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. HIV-1 produces the more severe disease. Evidence suggests a zoonotic (cross-species) transmission of HIV to humans, and implicates a chimpanzee subspecies (*Pan troglodytes troglodytes*) as the source of HIV-1 infection and the sooty mangabey (*Cercocebus atys*, a monkey found in West African rainforests between Senegal and Ghana) 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 (primarily Africa); and, finally, plausible routes of transmission. The origin of HIV-2 was more easily determined than was the case for HIV-1: HIV-2 and SIVsm (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 SIVsm; 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 a plausible route for human infection.

In the case of HIV-1, these specifics have been more difficult to establish for the chimpanzee; however, recent research has essentially confirmed that contact with infected *P.t. troglodytes* chimpanzees through hunting and butchering is the most likely origin. It is widely believed, but not yet proven, that the introduction of the virus into dense populations and increased global mobility provided the circumstances for a full-blown epidemic.

3 HIV INFECTION

When a person becomes infected with HIV there is an initial burst of viral replication, and the individual may 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 imperfectly 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 pathogens such as other viruses, bacteria and fungi.

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

Initially, HIV infection was considered fatal within 10-15 years. However, most industrialized countries, where patients have treatments available to them, have seen a deceleration in the progression to full-blown AIDS and a decline in the death rate over the past decade.

4 PRESENT STATISTICS AND FUTURE ESTIMATES

According to the *UNAIDS Global Report on the AIDS Epidemic, 2010*, approximately 33.4 million people worldwide were living with HIV/AIDS in 2009, of whom 2.6 million had become infected during that year. An estimated 1.8 million people died in 2009 from AIDS-related complications. The HIV/AIDS epidemic has affected sub-Saharan Africa most substantially, although the epidemic appears to be stabilizing. By the end of 2009, 69,844 people in Canada had been diagnosed as HIV positive since testing became available in 1985, 21,681 had been diagnosed with AIDS and 13,499 people had died of AIDS. In 2009 alone, there were 2,368 positive HIV tests and 224 AIDS diagnoses were reported to the Public Health Agency of Canada. Reports of HIV infection fell from 3,000 in 1995 to a low of 2,015 in 2000, but over the past decade,

there have generally been between 2,400 and 2,500 reports per year. An additional 15,000 Canadians are believed to be unaware of their positive HIV status.

In Canada, AIDS diagnoses and AIDS-related deaths have declined markedly over the past decade. AIDS diagnosis was at its highest in 1993 at 1,828 but has been below 500 annually for the past decade. AIDS-related deaths peaked in 1995 at 1,501 but have been below 100 annually since 2004. These encouraging statistics reflect the improvements in treatment regimens over the years. In many countries, the incidence of HIV has declined substantially in the last decade. In particular, in sub-Saharan Africa where the HIV infection rate has been the highest, rates have dropped by 25% during this period. This trend reflects a combination of factors, including the impact of HIV prevention and education efforts, improved access to treatment, and improved anti-retroviral therapies.

5 THE DIRECTION OF AIDS RESEARCH FOR PREVENTION, TREATMENT AND CURE

Prevention strategies have focused primarily on the use of condoms to reduce the sexual transmission of HIV, but researchers are currently pursuing the development of microbicides or creams that women can apply in a manner similar to spermicides. HIV/AIDS advocates feel that such a product is a crucial component of an effective prevention strategy. It is hoped that microbicides will be available within the next five to seven years.

Although prevention strategies such as education campaigns, abstinence, male circumcision, condom use, microbicides and needle programs are important, an HIV vaccine could be the most effective strategy. The search for an AIDS vaccine is as old as the discovery of HIV in 1983. However, development of a vaccine has proven much more difficult than originally expected. The International AIDS Vaccine Initiative (IAVI), founded in 1996, now operates in a number of countries around the world. In Canada, the Canadian HIV Trials Network officially began trials in early 1991. In 1997, former U.S. President Bill Clinton issued a challenge to scientists to develop a vaccine within 10 years, and the HIV Vaccine Trials Network was established.

Clinical trials for candidate vaccines are conducted in three phases. In Phase I trials, the safety of and immunological response to a potential vaccine are tested in 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, after several years of preclinical, basic research. Successful vaccine candidates can then be put through phase II trials, which involve a greater number of individuals representing both low and high risk for HIV infection. This phase helps to refine the dosing of the vaccine and provides additional safety data, and 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, i.e., its effectiveness.

Despite the focussed research on vaccine development following the challenge issued by President Clinton in 1997, few vaccines to date have progressed to phase III trials and none have been shown to be sufficiently safe and effective for approval. Although development of an effective vaccine has been slower than most people anticipated, it should be noted that vaccines against other viral infections such as polio, hepatitis A and B, and measles took two to five decades to develop, and a vaccine for hepatitis C still remains elusive.

The discussion of vaccines so far has focused only on “preventative HIV vaccines” – that is, vaccines that can be given to uninfected individuals to protect them against HIV should they come in contact with it. This is much the same as with other familiar vaccines, such as those for influenza, hepatitis B or chicken pox. The second category of vaccine, which has had little media 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 needs to be administered. Researchers have been even less successful so far in developing therapeutic vaccines than they have been in developing preventative vaccines. However, the vaccine manufacturer Aventis Pasteur has succeeded in getting a number of candidate therapeutic vaccines to the trial stage.

With respect to treatment, the first drug to be approved for use against HIV was AZT (zidovudine) in 1987, and since that time, dozens of other antiviral agents have been added to the HIV arsenal. Combination therapy, altered periodically, is now standard practice as it increases the efficacy of the individual drugs and also reduces drug resistance. Evidence of the effectiveness of antiviral therapy can be seen in Canada’s surveillance data. Despite the persistent infection rate of about 2,500 new reported HIV infections per year since 1997, mortality rates have gone down significantly. The number of people who died from AIDS rose to 1,501 in 1995, but declined steadily thereafter. That number is now considerably lower than 100 deaths per year.

The word “cure” is conspicuous by its absence. As with other viral infections, emphasis is placed on prevention and successful treatment. Many viral infections, such as colds, flu, measles, mumps, rubella and pertussis, “run their course” 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 some viral infections such as hepatitis C may go undetected for decades before causing significant damage. None of these diseases is curable, but medical research has produced treatments for most viral infections, and many of these infections are preventable with vaccines. One day, the development of a preventative vaccine may make the threat of HIV as remote as the threat of polio or smallpox.

6 CONCLUSION

HIV was around long before the emergence of a novel, profound immune deficiency was reported in the United States in 1981. However, societal changes and increased global mobility helped to create the conditions for a worldwide epidemic that has

claimed an unimaginable number of lives. Efforts to contain the epidemic have had limited success, and there is some evidence, given the rise in the number of positive HIV tests in Canada since 2000, that prevention strategies, although initially encouraging, are losing their impact. Research into fighting this virus shows promise in a number of areas, but scientists are hopeful that work on vaccine development will ultimately prove 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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