



REVIEW PAPER

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The history of the Human Immunodeficiency Virus research

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ABSTRACT

The authors summarize the current knowledge of the beginnings of the human immunodeficiency virus (HIV) infections. Most of the studies have so far supported the theory that HIV infections had in their initial years been a typical zoonosis which had been present among African tribes for over 300 years. Most likely, infection was transferred from monkeys, particularly from chimpanzees, on multiple occasions. The most recent publications allow us to describe the transfer of the virus into humans, and new epidemiological data allow us to carry out analysis of the global spread of the virus. Studies of histopathological samples taken from patients in the 1960s have cast new light on the issue of virus presence in the US population, and the previous theories tracking the beginning of infections to the 1980s have had to be modified. Greater awareness of pandemic mechanisms should allow for more effective future counteraction of the spread of new pathogens.

Key words: AIDS, HIV, SIV, zoonosis.

Virus isolation

In 2013 30 years has passed since the identification of the HIV virus as a cause of immune deficiency. The rapid increase in the incidence of diseases associated with immune deficiency in the early 1980s prompted molecular biologists and virologists to carry out coordinated research on a previously unknown scale [1].

In 1983 Luc Montagnier, head of the virology laboratory at the Pasteur Institute, with his research team, including Françoise Barre-Sinoussi, isolated a virus from the blood of infected subjects and called it lymphadenopathy associated virus (LAV). The virus, isolated from the lymph nodes of subjects at an early stage of lymphadenopathy, was found to have reverse transcriptase activity, and was classified as a retrovirus. *In vitro* studies demonstrated that LAV had the potential to infect lymphocytes of healthy individuals, and reacted with antibodies isolated from patients with advanced immune deficiency syndromes, which finally confirmed its pathogenicity [1].

One year later, an independent study by Robert Gallo and his team carried out in the USA led to the isolation of

a virus named human T lymphotropic virus type III (HTL-III) [2]. Another year later, in 1985, researchers found that both identified viruses were the same, and in 1986 they were given the name of the human immunodeficiency virus (HIV-1) [3, 4]. The world of science recognized the discovery of the HIV virus by awarding the French researchers the Nobel Prize in medicine in 2008 [5]. Despite the scientific consensus, there were some separate voices, that argue correlation between trends in drug abuse and AIDS cases [6]. Prof. Peter H. Duesberg states the theory that HIV is a harmless bystander of AIDS [6]. That theory has been rejected by the scientific community.

Further development of large-scale studies resulted from the spreading epidemics of various diseases which had previously been diagnosed only in people with immune deficiency, mainly during immunosuppressive treatment. The first historical records on atypical infections are found in the epidemiological reports from the Centers of Disease Control (CDC) concerning pneumonia of a rare aetiology (*Pneumocystis jirovecii*) diagnosed in five homosexual men in Los Angeles, and

in patients with haemophilia A who had received clotting concentrations and who developed pneumonia of mycotic aetiology, not previously recorded [7, 8].

In 1987, genome of the virus responsible for the acquired human immunodeficiency syndrome was isolated from the West African population and sequenced [9]. Despite the similarity between the clinical manifestation of AIDS in the African population and that among American homosexuals, the weak cross reaction of antibodies only pointed out the distant relationship between the two strains [9]. According to the established nomenclature the microorganism was given the name of human immunodeficiency virus type 2 (HIV-2) [9].

HIV infection as a zoonosis

The search for an animal model of AIDS led to studies on the virus previously known as simian T-cell lymphotropic virus type III (STLV-III) [10]. Researchers found a close genetic relationship between STLV-III and HIV-2, and named it, according to the existing nomenclature, the simian immunodeficiency virus (SIV) [10]. As standard, a suffix denoting the species from which the virus was isolated is added to the virus' name, e.g. SIV_{md} for mandrill, SIV_{sm} for sooty mangabey, and SIV_{mn} for mona monkey. The vast majority of SIV infections in monkeys were asymptomatic. A significant discovery was the identification of the SIV_{cpz} virus originating from the chimpanzee [11]. Unlike the initially isolated SIV, the SIV_{cpz} strain demonstrated an antigenic similarity with HIV-1 [11]. The phylogenetic analysis demonstrated that strains originating from chimpanzees and macaque monkeys are closely related to HIV-1 and HIV-2 viruses, respectively [11, 12]. The role of these viruses in transmitting infection to humans was confirmed by *in vitro* studies which supported their potential for infecting humans [13]. Research supported the theory that HIV-1 and HIV-2 infections had in their initial years been zoonoses which had occurred for thousands of years among West African tribes hunting for primates [14].

Spread of the epidemic

Endemic infection with HIV-1 and HIV-2, previously limited to the population of central and western Africa, spread to the entire sub-Saharan region due to colonial expansion by European countries and resulting population changes [15]. Also, the accelerated spread of epidemics occurred after the introduction of parenteral antibiotics and vaccines delivered in unsterile injections [16]. In the early 21st century a popular theory coined by

Hilary Koprowski attributed the epidemics of the HIV-2 infection to the widespread use of the polio vaccine. Concerns were raised with respect to the cultures of cells derived from kidneys allegedly originating from infected chimpanzees. However, the theory was strongly rejected after the complete analysis of the vaccine's manufacturing process [17]. The epidemic's first outburst occurred in Léopoldville (now Kinshasa) in Congo, and David Carr, an English printer working in Africa in the 1950s, who died in 1959, was the first patient diagnosed with AIDS based on tissue samples [18]. Sharp et al. analysed the risk of the spread of HIV outside the African continent, and pointed out the fact that the spread must have occurred before 1940 [15]. Haiti was the first place in the Western hemisphere with a confirmed incidence of AIDS. The analysis of pathomorphological specimens originating from deceased patients allowed for estimation of the arrival of HIV in Haiti as about 1966 [19]. Through intensive commercial contacts with the Republic of Congo the population of infected people in Haiti increased gradually, while economic migration to the USA caused the spread of the virus among the American population three years later [19]. In the USA, Robert Rayford, a 16-year-old Afro-American from St. Louis, Missouri, was the first confirmed fatal case of HIV-1/AIDS [20]. Rayford died in 1969 due to opportunistic infections, and also suffered from Kaposi's sarcoma. Doctors treating Rayford during his hospitalization found that he was homosexual, probably a male prostitute, and had engaged in repeated receptive anal intercourse [20]. The risk of infection due to blood transfusion was excluded, thus suggesting that the HIV-1 virus has been present in the homosexual environment since the early 1960s [20]. In the same year in Europe, a man whose true identity is officially unknown died, and tests carried out 20 years later confirmed that he was infected with the HIV virus [21]. It is known that the man was a Norwegian sailor who had visited Africa on many occasions, and had been treated earlier for gonorrhoea. Tests carried out later confirmed infection with HIV-1 in his daughter and wife [21]. It was established that after ending his career as a sailor the patient worked as a lorry driver throughout Europe, and was sexually active with prostitutes, mainly in Germany and Denmark [21]. Gaëtan Dugas, a Canadian airline steward, was referred to as 'Patient Zero' in the first epidemiological AIDS study [22]. Auerbach et al., who analysed the spread of HIV epidemics, concluded that the virus must have been transmitted by a person engaged in numerous homosexual contacts throughout America [22]. The analysis drew attention to the fact that Gaëtan Dugas had homosexual partners in California, New York, and several other states

in America. Dugas died in Quebec in 1984 as a result of kidney failure caused by AIDS infections [22]. The initial theory implying that Dugas was the first person to bring HIV to the American population was not confirmed. Also, his role in bringing HIV to Los Angeles and New York is currently being questioned due to the short time between sexual contact and the onset of symptoms in his partners (10.2 months), because later studies estimated the period to be on average 10 years long [22]. Dugas claimed to have had at least 2,500 partners across North America in the 12 years of his sexual activity, which shows the scale of sexual partner exchange in homosexual environments in the 1970s [22].

Summary

The history of research on HIV epidemics shows how the globalisation of lifestyle in the 20th century influenced the spread of endemic infections. Studies carried out to date demonstrated that for at least 8,000 years SIVcpz and SIVsm viruses, occupying the same ecological niche, have been transferred from species to species and have infected *Homo sapiens*. In addition, high genetic variability allowed viruses to develop the potential for vertical and horizontal infections, which for a long time were restricted to tribes endemic in today's Cameroon and the Republic of Congo. Colonial movement in the 20th century led to the establishment of large urban centres connected via marine routes with countries in Europe and America. Kinshasa, being a port city, was the first confirmed location from which epidemics spread [15]. The efficient work of the Centers for Disease Control (CDC) led to the identification of the disease and within a week they released a report on atypical cases of pneumonia among homosexuals and persons receiving blood substitutes, prompting the scientific environment to search for pathogens [7, 8].

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