

Introduction

June 1981 is the official birth date of the AIDS epidemic. In a short article published in the Centers for Disease Control's *Morbidity and Mortality Weekly Report* (MMWR), American clinicians described a cluster of five cases of *Pneumocystis carinii* pneumonia, an infection of the lungs hitherto seen only in patients with severe impairment of their immune system. These five initial cases had been diagnosed in 1980–1 among gay men, all living in Los Angeles, who had been previously healthy and were not receiving drugs that suppressed the body's immune response. At the time, the standard treatment for *Pneumocystis* pneumonia was an old drug called pentamidine, developed during WWII for the treatment of sleeping sickness, which happened to be highly active against *Pneumocystis*. Pentamidine was not commercially available and had to be distributed centrally from the CDC in Atlanta. An astute CDC technician found it strange to have received several requests for pentamidine within a short period of time from hospitals in California and, a bit later, from New York as well. This became the first step in the identification of the new syndrome by this federal agency.^{1–2}

Nobody could have imagined that, within three decades, more than twenty-nine million individuals would have died of AIDS, leaving in the process sixteen million orphans. By 2009, another thirty-three million were living with its HIV aetiological agent, making it by far the most dramatic epidemic since the Black Plague devastated Europe 500 years ago. Since that fateful day in 1981, more than 300,000 scientific articles and thousands of books have been published on HIV/AIDS. Most are biomedical but others analyse the psychosocial, historical, economic, geographic and even photographic features of AIDS. Thus the history of HIV/AIDS from 1981 to 2011 has been described in great detail. Randy Shilts' *And the band played on* and Laurie Garrett's *The coming plague* contain captivating descriptions of the early years of the pandemic in the US and Europe. Some books have chronicled the AIDS epidemic in

Africa after the initial description of the disease, its devastating impact on the lives of so many, a few success stories and unfortunately many more failures in the response to HIV/AIDS, most tragically in South Africa. For a summary of the dissemination of the virus between 1981 and 2006, I recommend John Illiffe's *The African AIDS epidemic. A history*.^{2–10}

However, what happened before 1981 – how did the human race reach that point? – has, to my knowledge, only been addressed in Edward Hooper's *The river. A journey back to the source of HIV and AIDS*. This book was written in support of the hypothesis that the emergence of HIV/AIDS was triggered by the contamination of an oral polio vaccine with a simian immunodeficiency virus through the use of chimpanzee cells during vaccine production. There is now overwhelming evidence that this did not happen, as we will see later.¹¹

This book will summarise and assemble various pieces of the puzzle that have gradually been delineated over the last decade by a small group of investigators, to which I have added historical research of my own. Some elements are irrefutable, such as the notion that the *Pan troglodytes troglodytes* chimpanzee is the source of HIV-1. Other elements are less clear, for example the exact moment of the cross-species transmission (sometime in the first three decades of the twentieth century). My own contribution focused around the idea that medical interventions requiring the massive use of reusable syringes and needles jumpstarted the epidemic by rapidly expanding the number of infected individuals from a handful to a few hundred or a few thousand. This set the stage for the sexual transmission of the virus, starting in core groups of sex workers and their male clients and later spreading to the rest of the adult population. Some parts of the story rely on circumstantial evidence, such as the links between the Congo and Haiti and the potential contribution of the blood trade in triggering the epidemic in Port-au-Prince, from where it moved into the US. Potentially sceptical readers should look at the whole story before making a judgement. I believe it is coherent, and that the weaker parts are supported by a strong body of evidence immediately before or after these uncertain areas.

My own background is that of an infectious diseases physician and epidemiologist. I started my career in the early 1980s as a medical officer in a bush hospital in Zaire, where I spent the four most challenging years of my life. The type of medicine that I practised there was not

much different from that of my colonial-era predecessors: approximate diagnoses, empirical treatments, lack of human and material resources, systematic re-use of syringes, needles and other medical supplies. I developed a fascination with sleeping sickness, a disease which happened to be epidemic in my district and around which I conducted research for the next twenty years. After completing my training in infectious diseases in Canada, I went back to Africa, this time as a clinical researcher at the Medical Research Council Laboratories in The Gambia, working on the epidemiology of HIV-2 infection and its interaction with sexually transmitted diseases (STDs). I returned to Canada in 1990 as an academic infectious diseases physician, but I also coordinated AIDS control projects in central and West Africa, which provided preventive and curative care to a large number of sex workers. During a sabbatical, I studied for a master's degree in epidemiology. Epidemiology is a science which connects exposures (for instance, to some infectious agent) and outcomes (developing AIDS or cancer, death, etc.). I will not use much epidemiology in this book though I confess to an inborn love of numbers which, Mark Twain notwithstanding, can often prove or disprove an argument.

Eventually, these various professional interests coalesced, when I belatedly understood that there was probably a link between HIV-2 infection in Guinea-Bissau, its epicentre, and programmes to control sleeping sickness during the colonial era, when that country was known as Portuguese Guinea. An epidemiological study among elderly individuals in Bissau confirmed that subjects who had been treated for sleeping sickness or tuberculosis decades before were more likely than others to be HIV-2-infected (in contrast with HIV-1, HIV-2 infection is compatible with prolonged survival, which enabled us to document such associations).¹²

I realised that during my time in Zaire patients under my care were probably infected with HIV-1 during health care. In the rather primitive 110-bed Nioki hospital, in the Mai-Ndombe region about 500 kilometres north-east of Kinshasa, we used glass syringes and reusable needles. Normally, these would go through the hospital's autoclave after each use, which should have killed all pathogens, including viruses. However, I did not pay too much attention to how long they were boiled for by the nurses in between patients when the hospital ran out of electricity so that the autoclave could not be used. Power outages could last up to two months at a time, when the whole country was short of the diesel fuel needed for generators.

For sleeping sickness patients (up to 400 per year), we mostly relied on 6–12 intravenous (IV) injections of an old arsenical drug called melarsoprol. Melarsoprol was in short supply, so that even 0.1 ml remaining in the vial after administering the dose for a first patient would be used for the next. I also remember the unfortunate tuberculosis patients, who were given intramuscular (IM) injections of streptomycin every day for sixty days (or even longer for those who did not tolerate one of the oral antituberculous drugs), with fairly dramatic adverse effects (the drug was toxic to the inner ear, and many patients had a hard time walking, some of them permanently). At the time, ‘international health’ resources were an order of magnitude lower than they are today, and the much more effective and less toxic treatment for tuberculosis, comprising only oral meds, was deemed far too expensive at \$50 per patient, compared to \$10 for the streptomycin-based regimen. Potentially even worse, in the twenty or so rural health centres which I supervised, several of which could only be reached by dugout canoe, formol tablets were put into a metal box along with the syringes and needles as a sterilisation measure. Abscesses following injections were rare, so this process killed the bacteria, but what about the viruses?

I do not believe that transmission via medical interventions plays an important role in HIV dynamics today and I agree with the experts who maintain that it contributes to less than 5% of recent HIV infections, although even a single case is unacceptable. However, I became convinced that transmission during health care contributed to the simultaneous emergence of HIV-1 and HIV-2 in different parts of the African continent fifty to seventy-five years ago.¹³

These were sobering thoughts, and I started trying to connect the dots in the history of HIV. This book is the result of these efforts over the last five years. It would not have been possible without the support of my wife Lucie, a Congolese nurse, who kept my interest for Africa very much alive. Several friends and relatives died of an AIDS-like illness before and after the disease was identified in Africa.

Some may say that understanding the past is irrelevant, what really matters is the future. I disagree. There are at least two good reasons for attempting to elucidate the factors behind the emergence of the HIV pandemic. First, we have a moral obligation to the millions of human beings who have died, or will die, from this infection. Second, this tragedy was facilitated (or even caused) by human interventions:

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colonisation, urbanisation and probably well-intentioned public health campaigns. Hopefully, we can gain collective wisdom and humility that might help avoid provoking another such disaster in the coming decades.

1 | *Out of Africa*

Ex Africa semper aliquid novi

Out of Africa, there is always something new, wrote historian Pliny the Elder more than 2,000 years ago. He was quite right. As early as 1984, just three years after the first description of the new disease, it was suspected that HIV, its recently discovered aetiological agent (then known as human T-cell lymphotropic virus (HTLV)-III in the US, LAV (lymphadenopathy-associated virus) in Europe), originated in central Africa. This was mainly because the first studies in Africa, conducted in Zaire and Rwanda, showed that AIDS was common in Kinshasa and Kigali, where nearly 90% of sex workers were infected. These field studies were prompted by the observation that of the first few hundred cases of AIDS diagnosed in Europe, about half occurred among patients coming from central Africa, mostly from Zaire. Over the following years, the epidemiology of HIV-1 infection in Kinshasa would be described in great detail by a group of American, Belgian and Congolese researchers known as *Projet Sida*, based at Hôpital Mama Yemo (Mama Yemo was dictator Mobutu's mother, a former sex worker, and she suffered the same fate as the Belgian colonists after her son was overthrown: this institution is now called Hôpital Général de Kinshasa). *Projet Sida* came to an abrupt end in 1991, when the whole of Kinshasa was looted by the city's poor people. During the same period and until the 1994 genocide, similar epidemiological work was conducted in Kigali, 1,500 kilometres east of Kinshasa.¹⁻³

In retrospect, this early vision of central Africa as the source of HIV-1 was rather naive. Researchers assumed that since this was at the time the region with the highest prevalence (i.e. the proportion of the population that is infected) among groups representative of the general adult population, the virus must have originated there. There were at least two problems with this assumption.

First, there was an obvious bias, as little information on HIV prevalence was available from other parts of the continent, especially East and

southern Africa. Belgian researchers, the most prominent being Peter Piot, from the Institute of Tropical Medicine in Antwerp (who would later become the founding executive director of UNAIDS, the UN programme specifically dedicated to the control of HIV/AIDS), had naturally initiated HIV research in the former Belgian colonies where their institutions had maintained networks and contacts over the preceding decades. Much to their credit, Zaire and Rwanda were open to AIDS research from the start, but this was not the case in other countries such as Burundi and some English-speaking countries of East Africa, where there was a strong temptation to keep AIDS under wraps: if we ignore it, perhaps it will go away.

Second, the relationship between HIV prevalence and duration of the epidemic is not straightforward: it all depends on the annual incidence (the proportion of previously uninfected individuals who acquire HIV each year). We now know that in Kinshasa the HIV incidence among the general adult population was probably never higher than 1% per year. However, in some countries of southern Africa, annual incidence reached the extraordinary level of 5% in the 1990s (one seronegative adult out of twenty got newly infected with HIV each year). A prevalence of 10% could reflect an annual incidence of 1% continuing for more than ten years, or an incidence of 5% over just a couple of years. However, even if these assumptions about a central African origin of HIV/AIDS were naive, eventually they proved to be correct, showing that in the scientific domain intuition can sometimes be trusted!

Archival samples

Additional support for a central African origin of HIV-1 came from the testing of archival samples of blood. In the mid- and late 1980s, to understand the dynamics of HIV in the recent past, researchers tried to locate collections of sera obtained earlier for other purposes and kept frozen. Scientists tend to clean out their freezers once in a while to make room for new samples, or their samples are destroyed when they retire or move on to other positions. However, sometimes samples are forgotten for a long time or deliberately conserved. In Kinshasa, among mothers attending a well-baby clinic in the Lemba district, HIV-1 prevalence was 0.25% in 1970 ($n=805$) and 3.0% in 1980 ($n=498$). In the remote Catholic mission of Yambuku and surrounding communities of the Equateur province of Zaire, 0.8% of 659 samples collected in 1976

during an investigation of an epidemic of Ebola fever were found to be HIV-1 seropositive when tested ten years later. This proved that the virus had existed in this part of the world for some time, but not necessarily that it originated there; testing of archived samples of serum from American gay men who participated in epidemiological studies of hepatitis B also retrospectively documented cases of HIV-1 in the late 1970s, and even earlier for drug addicts.⁴⁻⁸

The Yambuku epidemic of Ebola fever which had prompted the collection of these samples had largely been 'iatrogenic' (healthcare related). In this small rural hospital, syringes and needles were scarce and constantly re-used, fuelling transmission of the blood-borne Ebola virus between patients attending the hospital for other reasons (malaria, gonorrhoea, etc.). The nuns issued only five syringes to the nurses each morning, which were then used and re-used on the 300 patients attending each day. Three-fourths of the first 100 cases of Ebola in Yambuku were infected through injections received at the hospital. The epidemic came to an end after the hospital was closed following the death of several nurses and nuns, infected by their patients. Clearly, noble intentions for providing health care to the underprivileged could have disastrous consequences when the risk of transmission of blood-borne viruses was not appreciated. This unfortunate situation was not new or specific to the Yambuku hospital, and had already had infinitely more dramatic consequences, although this was not known at the time, than these few hundred deaths from Ebola fever. It was decided to call this new disease after a nearby river rather than after the Yambuku mission, to avoid further stigmatisation after all it had gone through. The contrast between the two diseases is an excellent illustration of the genius of HIV. People infected with the Ebola virus quickly fall ill and die. This causes a spectacular epidemic, which triggers a massive (and always successful) reaction to control it. People infected with HIV, on the other hand, can live and quietly pass on the virus for ten years or more, and it will take even longer before physicians can recognise the emergence of this new disease, because symptomatic cases are not clustered within a short period of time.^{9,10}

Elsewhere in Africa, no trace of HIV was found before the 1980s, which increasingly pointed to a central African origin of this 'new' virus. In West Africa, out of more than 6,000 samples obtained in Nigeria, Liberia, Ivory Coast, Togo, Senegal, Sierra Leone, Mali, Niger and Ghana in the 1960s and 1970s, not a single case of HIV-1 infection

was found. A few cases of HIV-2 infection were documented, however. Among 789 samples obtained in Senegal in 1981, one was positive but it is unclear whether this corresponded to HIV-2 or HIV-1.^{11–16}

Meanwhile in East and southern Africa, in samples obtained from low-risk groups between 1959 and 1981, HIV was not found in Mozambique, Zimbabwe, Zambia, Uganda, Tanzania and northern Kenya, nor in mine workers in South Africa (who originated from Mozambique, Malawi, Lesotho, Botswana, Angola, Swaziland and South Africa itself). The earliest evidence of HIV in East Africa comes from Nairobi in 1980–1 where 1% of patients with STDs and 5% of sex workers were HIV-1-infected. Just three years later, 82% of Nairobi sex workers were HIV-1-infected. This exponential transmission among prostitutes is central to the story and will be examined later.^{14,17–19}

Documentation of early cases of full-blown AIDS was also achieved retrospectively. First, let me say that no conclusions can be drawn from isolated cases of apparently immunocompetent patients found to have had, many years ago, a diagnosis of a condition now frequently associated with AIDS such as *Pneumocystis* pneumonia, if this is not substantiated by a specimen positive for HIV in the patient or his/her spouse. This is because there are rare non-infectious diseases of the immune system which lead to very low counts of CD4 lymphocytes (the cells which are the main target for destruction by HIV), and subsequently to any of a long list of opportunistic infections. Short of an archived specimen positive for HIV, the clustering of cases, geographically or temporally, or within a couple, is more suggestive of AIDS but never conclusive.^{20–21}

Valuable journalistic information about some documented early cases can be found in *The river* as well as in *And the band played on*. The most interesting is that of a Norwegian family (father, mother and nine-year-old daughter), who all tragically died in 1976 from AIDS caused by HIV-1 group O, and whose sera were found to be HIV-positive when tested twelve years later. The child was born in 1967, which implies that the mother was already HIV-infected by then. The father had been a sailor, visiting a number of ports in Africa in the early 1960s, where he developed STDs, presumably after contacts with prostitutes. He probably acquired HIV-1 group O in Nigeria or Cameroon, where his boat stopped for a few days in 1961–2. A Danish surgeon died of AIDS in 1977, after working at the Abumonbazi rural hospital in Zaire in 1972–5 and in Kinshasa in 1975–7, following an earlier stint in

the same country around 1964. An eight-year-old Zairean child, infected perinatally in 1974–5, died in Sweden in 1982, and AIDS was serologically proven later on. A very unfortunate Canadian pilot involved in a plane crash in 1976 in northern Zaire, where he had surgery and received a blood transfusion, died of AIDS in 1980; his serum was later found to be HIV-1-positive (transfusion-acquired HIV infection progresses rapidly to AIDS, because of the huge quantity of viruses present in the blood bag). Former physicians at the university hospital in Kinshasa reported seven cases of AIDS diagnosed retrospectively, five of them confirmed serologically, which had been acquired sexually in the DRC (or Burundi in one case) in the late 1960s or the 1970s, mostly among Belgian nationals. Then in 1979, cases of AIDS started trickling down among the small proportion of Zaireans rich enough to seek health care in Belgium.^{22–30}

We do not know whether other researchers tested ancient samples from other parts of Africa without reporting their findings. Studies with negative results tend not to be published in scientific journals, a phenomenon known as ‘publication bias’. Thus although sketchy, testing of archival samples suggested that HIV-1 was present in the 1960s and 1970s, albeit at a low prevalence, in several locations in central Africa but not in West or East Africa.

The next step came from the documentation of the earliest case of HIV-1 infection in a sample obtained in the Belgian Congo around 1959, during the course of a study on genetic diseases of red blood cells. Of 672 samples, collected in Léopoldville and other locations, and miraculously kept (probably forgotten) in a freezer, one was found twenty-six years later to contain antibodies against HIV-1. Apparently, the HIV-1-positive specimen came from a male adult recruited in Léopoldville. HIV genetic material was amplified from this sample, and analyses confirmed that this was indeed the oldest HIV-1 isolate ever documented. It was named ZR59.^{31–33}

It took more than twenty years for another ancient specimen containing HIV-1 to be located. Finding old tissue blocks collected between 1958 and 1960 and kept at the pathology department of the University of Kinshasa, scientists discovered HIV-1 sequences in a lymph node biopsy obtained in 1960 from an adult woman. It was given the name DRC60. Twenty-six other specimens (lymph nodes, livers and placentas) did not contain HIV. DRC60 and ZR59 differed by about 12%. It was calculated that DRC60 and ZR59 shared a common ancestor