1 THE HISTORIES OF HIVS

The Multiple Viruses That Caused the AIDS Epidemic

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The AIDS pandemic is one of the deadliest medical disasters in the past century. Since it was first recognized forty years ago, the disease has killed over thirty-five million people, and an equal number are living with AIDS. Almost two million people are newly infected annually, and over 750,000 die each year from AIDS (WHO 2019). Only the 1918 influenza pandemic was comparable (CDC estimate of fifty million deaths worldwide), but it subsided almost as quickly as it appeared. Moreover, AIDS was identified near the height of the "miracle" medical discoveries following the Second World War that established overwhelming confidence in modern medicine, including, among other things, advances in vaccines that resulted in an unprecedented reduction in infectious diseases (Brandt and Gardner 2000; Le Fanu 1999; Burnham 1982). In fact, the first cases of what was eventually called AIDS were identified in 1981, only a few years after the eradication of smallpox and all that it promised. As a result, the AIDS epidemic shook the health field to its core.

Once the disease was recognized in 1981, its cause was found a few years later to be human immunodeficiency virus, or HIV, which is spread by exposure to bodily fluids during blood transfusions and through contaminated needles, sexual intercourse, and breastfeeding. Once entering the body, the virus is initially suppressed, but eventually (in as long as ten years) it weakens the immune system, allowing death from otherwise suppressed diseases such as rare cancers and pneumonia. Tests for diagnosis of HIV were developed in 1985, and a treatment to suppress the virus was developed by the mid-1990s. Because of the long delay between infection and appearance of symptoms, plus limited access to diagnosis and treatment in large parts of the world, the virus spread to become a major cause of death by the end of the 1990s.

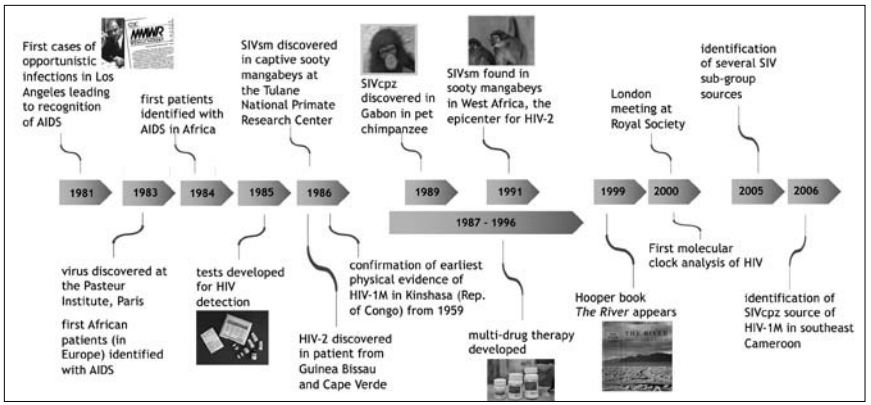

FIGURE 1.1. Timeline of HIV and SIV discoveries.

After the viral cause of the AIDS pandemic was discovered, attention turned to its origin. But these efforts took a back seat to the more immediate search for detection, prevention, and treatment. These priorities continued even after the animal origins were discovered, although there was greater monitoring of emerging viruses. The importance of such monitoring is all too obvious from the example of Coronavirus Infectious Disease-2019 (COVID-19), a human disease also arising from an animal virus that is transmitted as a new human virus, spreading in a matter of months from a single event in Wuhan, China, to over a hundred million people with over three million fatal infections as of this writing (WHO, n.d.). Although COVID-19 likely emerged by a different mechanism than HIV, the explanation of this difference and other animal-virus differences is our fundamental thesis: that benign animal viruses can transition to become epidemic or pandemic human viruses with lethal outcomes.

This volume examines the origin of the AIDS pandemic by presenting a broader historical and cultural study of the emergence and initial spread of the viruses that caused it. Until now, most studies of origins have focused on the HIV-1M strain, but this was only the most dangerous of several HIVs that emerged. In addition to the limited scope, the explanations have usually been based on limited historical and cultural perspectives and sources. With only a few exceptions, the result has been simplistic scenarios and general references to when, how, and why HIV emerged and became pandemic.

In contrast, this study accepts the fact that the pandemic was the result of multiple human immunodeficiency viruses that emerged independently in multiple locations in different regions of Africa during

the last century, and that more than one of these HIVs became epidemic or pandemic. As a result, any explanation of the origin of AIDS must explain the emergence of all the new HIV viruses, which could not have simply been the product of a one-time random event. The emergence of the viruses and their epidemic spread depended upon new but similar circumstances at different places and times. The AIDS pandemic was therefore not a chance, natural occurrence; it is much better understood as a human-made disaster. To understand this, it is useful first to describe in more detail the basic features of AIDS.

Scientific Facts of the Disease: Cause and Course, Means of Transmission

AIDS the disease was first recognized in Los Angeles in 1981 (Gottlieb et al. 1981), and the HIV that causes it was identified in 1983 by a group at the Pasteur Institute in Paris (Barré-Sinoussi et al. 1983). This was followed by the discovery of a second HIV in West Africa (Clavel et al. 1986). Thus, there are two types of genetically distinct HIVs (HIV-1 and HIV-2). As table 1.1 shows, in the years of research that followed, thirteen strains of HIVs were found: four HIV-1s and nine HIV-2s, with more strains likely to be found.

TABLE 1.1. Known HIV groups, geographical origins, dates, and number of cases

Virus	*Infections*	*Year discovered*	*Reference*	*Origin of earliest detected sample*	*Est. date of emergence*
HIV-1					
Group M	70 million	1982	Barré-Sinoussi et al. 1983	Dem. Rep. of Congo	1909–33
Group N	15	1995	Simon et al. 1998	Cameroon	1948–67
Group O	25,000–100,000	1987	De Leys et al. 1990	Cameroon	1903–48
Group P	2	2004	Plantier et al. 2009	Cameroon	
HIV-2					
Group A	750,000	1986	Clavel et al. 1986	Guinea-Bissau	1928–47
Group B	750,000	1986	Dietrich et al. 1989	Ghana	1931–59
Group C	1	1989	Gao et al. 1992	Liberia	
Group D	1	1989	Gao et al. 1992	Liberia	
Group E	1	1990	Gao et al. 1994	Sierra Leone	
Group F	2	1993	Chen et al. 1997	Sierra Leone	
Group G	1	1992–94	Brennan et al. 1997	Ivory Coast	
Group H	1	1996	Damond et al. 2004	Liberia, Ivory Coast	
Group I	1	2007	Ayouba et al. 2013	Ivory Coast	

The HIV-1 strains (or groups) have a common genetic origin: the simian immunodeficiency virus (SIV) of a chimpanzee species found in Central Africa. This is one of forty-six SIVs found to date across sub-Saharan Africa, each named for the species they naturally infect. For example, SIVcpz is found in chimpanzees of Central Africa, including southeastern Cameroon, SIVgor is found in the gorillas in southern Cameroon, and SIVsm in the sooty mangabey monkeys in West Africa. There are different groups of HIV-1 because they were the result of a separate jump or crossover to humans from the SIVcpz in four different animals. In the case of HIV-1, they were named M, N, O, and P, with the designation of M (for "main") given to the first virus discovered, while the second HIV-1 strain was named O (for "outlier"). The other two HIV-1 strains were labelled N and P to follow the letter sequence (Simon et al. 1998; Plantier et al. 2009).

The multiple strains of HIV-2 were likewise the result of crossovers that occurred nine times from a different simian species with a different SIV, sooty mangabey monkeys that live two thousand miles away in West Africa. These strains were named groups A through I, more or less following the chronological order they were discovered (Ayouba et al. 2013; Damond et al. 2004).

It is important to stress that each of the thirteen HIV strains are distinct because their simian sources were separate individual monkeys or apes. In other words, they did not branch from one HIV ancestor. It is equally important that only four viruses among the thirteen known HIVs, two each within the HIV-1 and HIV-2 groups, have been found capable of both causing AIDS and sustaining epidemic or pandemic outbreaks. The remaining nine have been found in twenty or fewer persons, with six HIV strains known to have infected only one person each (see table 1.1 and chapter 2).

These HIVs are passed by bodily fluids, a method of transmission which is relatively less efficient than airborne passage of pathogens or those which have vector intermediaries (e.g., animals or insects). Once contracted, the virus attacks the immune system of the human body, with varying success and resulting viral load. The greater the viral load at different stages, the greater the likelihood of passage of the virus to others. For a brief period following the initial infection (a few weeks) there is rapid increase in the virus load in the body and the person is more contagious than later in the HIV infection. Shortly thereafter the viral load declines

dramatically as the body responds to suppress it. This remains so for an extended period, up to ten years, during which time the infected person is without AIDS symptoms but remains contagious, although at a lower level than in the early phase. Eventually, after this long period of asymptomatic infection, the HIV overcomes the body's immune system and the viral load spikes again. The increasingly enfeebled immune system then cannot prevent opportunistic infections (e.g., pneumonias, otherwise rare cancers, and tuberculosis), which are among the more prominent late-course opportunistic diseases of full-blown AIDS.

The epidemiological nature of the virus is an important reason why medical services in Africa did not recognize the unusual AIDS symptoms earlier. This includes its initial slow spread because of a relatively inefficient means of HIV transmission, compared to the flu, for example, and the long period after infection before symptoms appear. Moreover, there was no obvious and easily recognized symptom of the disease. Rather, there were symptoms of multiple other diseases that appeared after the HIV had compromised the immune system. This was unlike more familiar epidemic diseases with much more distinct symptoms such as smallpox, bubonic plague, or, more recently, Ebola. These rare opportunistic infections were quickly recognized in Los Angeles because of the availability of much better medical infrastructure compared to the African locations where HIV infections undoubtedly occurred much earlier, but victims had very little access to doctors or facilities that could diagnose them.

Methods and Techniques Used to Discover, Diagnose, Prevent, and Treat HIV/AIDS

Diagnosis of HIV was a problem from the start because of the way the virus works. Symptoms after initial contraction of the virus are not very distinct (fever and aches, like other viruses), and because more symptoms do not appear for a long period of time, it is only after HIV compromises the body's immune system that the symptoms of opportunistic diseases are apparent. The methods and techniques used to identify, diagnose, prevent, and treat the new outbreak are, therefore, a testimony to the remarkable abilities of modern biomedicine, but these unprecedented resources ironically made researchers initially overconfident that infectious diseases were waning. Doctors, scientists, and other health authorities ultimately used a variety of tools and laboratories,

sophisticated knowledge, and monitoring agencies to recognize and confront the disturbing and mysterious new disease outbreak.

According to the well-documented story, Michael Gottlieb, a young assistant professor of immunology at UCLA, published a brief report in June 1981 about five patients he found with rare diseases in the *Morbidity and Mortality Weekly Report* (*MMWR*) of the Centers for Disease Control, the central epidemiology monitoring agency of the US government (Fee and Brown 2006). Soon after that article appeared, a doctor notified the CDC about even more cases he had found of a rare cancer in homosexual men in New York and California, and within a month the CDC published the finding of twenty-six similar cases in the *MMWR* (CDC 1981).

The CDC quickly created a task force on these opportunistic infections, but even as more reports appeared in journals and newspapers, it still took months to conclude that these infections were connected to a possible infectious agent (HIV.gov 2019). The common factor of victims being homosexual was a competing explanation that led researchers as well as the press to use terms such as "gay cancer" and GRID (gay-related immune deficiency) to describe the syndrome. Only in September 1982 was the term AIDS first used by the CDC to describe the acquired immune deficiency syndrome, and even though in May 1983 researchers at the Pasteur Institute reported the identification of a retrovirus that could cause AIDS, a competing claim was made the following year by researchers at NIH (using the name of HTLV-III). It was not until May 1986 that the International Committee on Taxonomy of Viruses announced that HIV (human immunodeficiency virus) would officially be designated as the term for the viral cause of AIDS.

The recognition and especially naming of the disease and virus is a striking case of what medical sociologists call the "social construction" of disease, a view proposed in the 1970s that disease is not simply a physiological state but rather a condition that requires time for researchers and practitioners as well as the public to understand and reach agreement about. As Charles Rosenberg interpreted this in the late 1980s, with the case of AIDS in mind, "Disease does not exist until we agree that it does, by perceiving, naming and responding to it" (Rosenberg 1986; Rosenberg and Golden 1992). HIV and AIDS were particularly difficult because the workings of the virus are complex, and the first cases involved homosexuality, which was quite controversial.

Only after reports appeared beginning in July 1982 of rare pneumonias in three hemophilia patients who received frequent transfusions of a blood-clotting factor did researchers go beyond the homosexual connection and adopt the term AIDS (CDC 1982). The first cases of women with symptoms were reported in January of 1983 (CDC 1983), and as doctors and epidemiologists continued to track new cases, they reached the conclusion that the virus was passed though bodily fluids in blood transfusions and unsterile needles, as well as hetero- and homosexual intercourse. Another mode of infection was identified after cases were reported by pediatricians who found HIV-positive expectant mothers who transmitted the virus to the fetus in utero (reports as early as Ammann et al. 1983) as well as viral passage to newborns from breastfeeding, which was first discovered in 1985 (Oxtoby 1988).

The report of the discovery of the virus in May 1983 made it possible to begin work on a test, but it took two years before virologists and microbiologists developed two different blood tests for antibodies produced by immune reactions to the virus. This was a crucial tool for the early diagnosis of HIV infection, but its use depended largely on the ability and willingness to obtain and use the tests. Among the first and most interested were blood banks, which were eager to test blood supplies and screen donors. In fact, in January 1983, months after the detection of infections in hemophilia patients, the CDC called a meeting to warn of the dangers to the nation's blood supply (HIV.gov 2019).

Contaminated blood and blood products are by far the most efficient way to transmit HIV, and one of the most dramatic cases reported was that of Ryan White. He was an Indiana schoolboy with hemophilia who contracted AIDS from blood treatments before a test was available for screening donors. His exclusion from school when it was revealed he had HIV drew national and international attention plus support and assistance from such celebrities as Michael Jackson and Elton John. The Ryan White Act passed shortly after his death in 1990 remains one of the most important resources for combatting AIDS in the United States. Even before the White case became public, blood centers in the United States moved quickly to implement testing and declared by July 1985 that the blood supply was free of HIV. It took somewhat longer to do this in the poorest countries of the world, but blood-donation screening was one of the earliest and most effective first steps to prevent spread of HIV there, thanks to help from WHO, the US PEPFAR project, and private

foundations (Schneider 2013). Individual testing took much longer to be adopted for reasons of cost, fear, and false security mentioned above.

Testing quickly became an essential tool for public health prevention, and so, too, were the use of condoms and other safe sex practices. To prevent transmission by unsterile injections, needle exchange programs were developed for drug users and much stricter protocols were adopted for the use of sterile and disposable needles in medical care and vaccination programs. Like safe blood procedures, the stricter needle-use practices were adopted more quickly than safe sex education efforts. Not all efforts of scientists were successful, most notably the failure to develop a vaccine for AIDS. In 1987, however, a drug initially used for cancer, AZT, was approved to treat AIDS, and within ten years its use in combination with other new antiretroviral drugs (for example, protease inhibitors) became a multidrug therapy that effectively suppressed HIV replication, thus preventing death and also blocking transmission of the infection causing AIDS. Even more than in the case of testing, the cost of therapy and need for continual treatment proved to be a significant barrier to widespread adoption, especially in resource-poor countries where AIDS had the most victims.

As a result, these technical successes were of little solace to researchers and public health officials who saw the number of AIDS cases and deaths grow into the millions by the beginning of the new century, with the peak of the pandemic in 2004 when there were an estimated 1.7 million AIDS-related deaths (WHO 2019). Figure 1.2 shows that the subsequent decline has been slow. As mentioned at the beginning of this chapter, in 2018 the United Nations AIDS organization (UNAIDS) estimated 770,000 deaths (61 percent in sub-Saharan Africa) and 1.7 million new cases (two-thirds in sub-Saharan Africa).

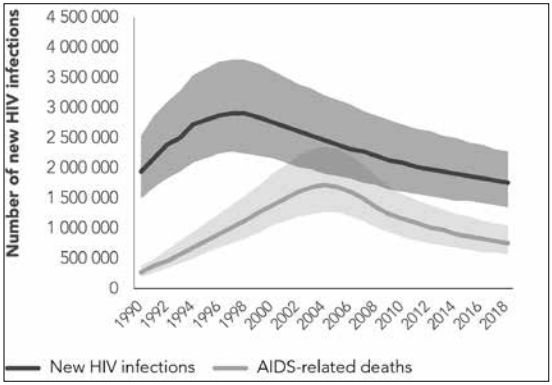

FIGURE 1.2. Number of new HIV infections and AIDS-related deaths, global, 1990–2018. *Source:* UNAIDS 2019.

Given the statistics about victims of AIDS, it is understandable why most attention continues to be focused on slowing or stopping the spread of the virus and treating the victims. The question of origins of the virus, despite being a lower priority, is nonetheless of long-term crucial importance because of the continuing problem of emerging viruses such as Ebola and those producing SARS. As a result, there has been a good deal of research on this question, taking full advantage of the same biomedical science used to discover the cause and diagnosis of AIDS and to develop the means of prevention and treatment. The findings include the following key questions about HIVs: the animal sources of the viruses, the number of times plus when and where different strains emerged, the mechanism of the jump from animal to human, and when and how four of the viruses became widely spread.

Naturally, some of these are better understood and agreed upon by researchers than others. Moreover, laudable as the success of this biomedical research has been, the question of origin is fundamentally a historical one, yet historians have rarely been part of the research. If there was no obvious new development that caused it, merely describing a technical adaptation—how an animal virus became a human one—that only occurred once can effectively avoid the question of why it happened by simply attributing it to chance. The fact that new HIVs emerged multiple times, however, means they cannot be seen as random or chance events. Rather, they were almost certainly produced by changes in circumstances that allowed or favored the viruses' emergence. This means they are much better understood as a human-made disaster. Scientists have suggested some past social changes that likely explain this, including population movement and urbanization, changes in sexual relations, new medical procedures, and war, but very few have examined these developments in depth. The purpose of this volume is to apply historical and social science scholarship to help find better answers to some of the questions about why multiple HIVs emerged.

Like any epidemic, the first appearance of AIDS raised the question of origin as well as cause, and among the numerous popular responses were talk of government conspiracy and God's vengeance on homosexuality. There were more serious responses by scientists and public health officials using the tools of modern biomedicine, but a common thread

among these professionals was the assumption that the new affliction was a one-time occurrence—that is, that the disease was the result of chance, if not an act of God or a secret government project. This was satisfying enough while more pressing questions of cause and prevention were pursued, while also being reassuring in that it minimized, rightly or wrongly, the immediate danger of more epidemics.

Nevertheless, very soon (beginning in 1986) a number of virologists recognized the phylogenetic proximity of HIV to simian viruses found in Central and West Africa (Clavel et al. 1986; Hirsch et al. 1989; Peeters et al. 1989; Marx et al. 1991), and they arrived at some surprising findings. The first was that there were two very different simian sources of these new human viruses. One was the great apes in Central Africa (initially chimpanzees but soon also neighboring gorillas with a related SIV) who carry the precursor SIVcpz from which researchers found the related HIV-1 viruses to have emerged. The other source was discovered a few years later in West Africa: the sooty mangabey monkey, whose different simian immunodeficiency virus (SIVsm) was found to have adapted to humans as HIV-2, and which produced a separate parallel epidemic. Of note, the habitats of the two simian sources are very distant from each other (at least two thousand miles apart). So, unlike most epidemics in the past which have been attributed to random mutations or singular events like wars or new contacts between previously isolated peoples, these HIVs developed more than once in different places and very close in time. As mentioned earlier, to date, four HIV-1 strains have been discovered and nine HIV-2s, all of which originated from separate SIV sources. In other words, there have been thirteen different crossovers so far.

Although there is general agreement about the number of HIVs, the answer to the question of where the different viral strains emerged largely depends on the habitat of the simian species with the HIV precursors, and the best estimate of where the earliest human identified with the virus might have encountered the simians. There is agreement among simian virologists about the two regions where HIV-1 and HIV-2 emerged, based on the habitat of the chimpanzees and sooty mangabey monkeys with the corresponding SIVs. But these are quite large regions, and only in a few cases have researchers been able to narrow the search for where a specific HIV strain emerged.

The most extensive search has naturally been to find the simian source of the HIV-1M strain responsible for the pandemic. Through

testing of DNA in 599 feces samples of chimpanzee species in southeastern Cameroon, researchers have found the likely SIV strain from which HIV-1M emerged (Keele et al. 2006). Another location has been suggested in southern Cameroon for the simian source of subgroup N, but no findings were made for HIV-1 group O or P. Of course, a question may be raised whether the location now of the chimps with the SIV subgroup for HIV-1M is the same as when the crossover is estimated to have occurred (as long as a hundred years ago). As to the crossover of HIV-1M, the earliest physical evidence of the human virus has been found in Kinshasa, the capital of the Democratic Republic of Congo (former Belgian Congo). This has led to a number of suggestions about where the crossover may have taken place in the approximately five hundred miles that separate southeastern Cameroon and Kinshasa. This question will be explored in more depth in succeeding chapters.

Research on the multiple HIV-2 strains and their SIV precursors in sooty mangabey monkeys in West Africa has mostly linked their emergence to the countries of origin of the earliest individuals detected with HIV. Most of these have been cases of only one or two people: HIV-2 groups C, G, and H cases from the Ivory Coast, group D from Liberia, and groups E and F from Sierra Leone (Sharp and Hahn 2011; Faria et al. 2012; Chen et al. 1997). There is little known about the earliest people with the more widespread HIV-2A or B strains, except for some stored physical samples and early reports of testing, as will be seen below.

Given the variation in the number of cases and the lack of early physical evidence, the location of the SIVs linked to the HIV-2 strains is still a very open question. The most frequently cited study, published by Santiago et al. in 2005, examined fecal samples from 35 sooty mangabeys in a troupe of 120 in the Taï Forest of southwestern Ivory Coast. Researchers found "close phylogenetic relationships" of SIVs in the samples that "suggest geographic links between five of the eight HIV-2 groups and SIVsmm strains from Côte d'Ivoire." Specifically, links of group A with Guinea-Bissau, groups B, G, and H with the Ivory Coast, and group C with Liberia. Despite the close relationship, researchers concluded that "the phylogeography of SIVsmm is not entirely straightforward." Among other things missing is "the molecular epidemiology of SIVsmm in Liberia, a country which lies between Côte d'Ivoire and Sierra Leone," but no such information exists.

Crossover and Timing

In addition to location, there is limited knowledge and lack of consensus about other features of emergence such as the mechanism of crossover, difference in epidemic spread, and the timing of both. These topics are the core of the chapters that follow, but they merit some background description here. At first, there was little attention paid to the explanation of crossover. This is probably because of an implicit assumption that the jump was the result of the simple and common encounters between simians and humans, one of which produced a chance HIV mutation. For example, Hirsch et al. (1989), who discovered the SIV source for HIV-2 in a sample from a sooty mangabey at the Tulane National Primate Research Center, indicated that the "limited information regarding origins" created "an enigma" as to just how SIV from a West African monkey "successfully infected a human and evolved as HIV-2."

Gao et al. (1999), who established the origin of HIV-1 in the SIVcpz of the chimpanzee species (*Pan troglodytes*), offered a simple explanation of the mechanism of crossover, based on suggestions about the HIV-2 crossover: "close contact between sooty mangabeys and humans is common because these monkeys are hunted for food and kept as pets." The authors extended the suggestion in their conclusion about crossover of SIVcpz to produce the HIV-1 strains, because "chimpanzees are commonly hunted for food, especially in west equatorial Africa, and as a consequence represent a ready source for zoonotic transmission of SIVcpz to man."

Edward Hooper was the first to dramatically bring this question into the spotlight in 1999 when he published his book *The River,* which proposed a radically different and focused hypothesis about crossover. After first providing extensive evidence that HIV was of recent origin, he then claimed that the cause was the use of chimps for polio vaccine production in the Belgian Congo in the 1950s. This elicited a dramatic response by researchers, mostly negative, quickly culminating in an international conference at the Royal Society in London in 2000 (Cohen 2001, 2016; Martin 2001). The majority of papers criticized Hooper and discredited the polio vaccine theory, but there were only two alternative explanations of crossover offered by researchers that have persisted.

One was a repeat of what was soon labeled the "cut hunter" hypothesis, which stated that HIV was little more than the result of a

chimp-human encounter that transmitted an SIV zoonotically to a human. As stated by Hahn et al. (2000) following the London conference, the crossover was not the result of the polio vaccine production that Hooper maintained. Rather, they state that "in humans, direct exposure to animal blood and secretions as a result of hunting, butchering, or other activities (such as consumption of uncooked contaminated meat) provides a plausible explanation for the transmission of lentiviruses from primates to humans." There was little effort to explain how this SIV transmission produced an HIV infection in humans, or to answer why it had not happened much earlier when in fact hunters likely often had their open cuts exposed to chimp blood. Nor was there much explanation why HIV crossover happened multiple times in the early and mid-twentieth century other than the observation that "the hunting and consumption of wild animals as a food source, traditionally a subsistence activity, has been transformed into a commercial enterprise termed the 'bushmeat' trade."

The only paper at the Royal Society conference that examined in depth the mechanism of jump was by Marx and Drucker (later published as Marx et al. 2001), which proposed the serial passage theory. This began with the fact that human exposure to SIV did not immediately produce HIV, but, rather, potential unadapted viruses. These could be passed in turn to other humans because of the introduction of and increase in unsterile needle injections in Africa in the twentieth century. Through the passage of these infections between humans at an increased rate, the viruses of SIV origin could better adapt to their human hosts and in some cases survive in the evolutionary niche that permitted HIV. There will be much more about this theory in the next chapter, but to summarize its impact on subsequent research, Marx and colleagues continued to expand and find evidence to support the theory, although most other researchers ignored it. Instead, the majority of research on emergence concentrated only on HIV-1M, simply assuming the "cut hunter" explanation of jump, while focusing mostly on the question of timing.

One reason for the great attention to timing was the increased use of the technique of molecular clock or phylogenetic analysis. The use of molecular clocks dates back to the 1960s and is based on the idea that molecular evolution occurs at an approximately uniform rate.

Beginning in 2000, researchers applied this technique to HIV, taking advantage of the fact that there are errors when the viruses replicate, resulting in the evolution of subtypes of the different strains. With advancements in DNA sequencing, it became possible to map genomes of samples of new subtypes from recent years to determine the rate of change and extrapolate back to estimate the date range of the most recent common ancestor (MRCA). Using HIV samples beginning from the 1980s, researchers attempted to determine the crossover event establishing HIV (Kumar 2005). These molecular clock analyses pushed back the estimated emergence dates of the HIVs to as many as thirty to forty years before the earliest date of tested samples (Korber et al. 2000; Lemey, Rambaut, and Pybus 2006; Faria et al. 2012, 2014).

There are technical problems with this method because of genetic recombination and the potential for variation from recent rates of change, which will be examined in more detail in the next chapter. Recent research points out that estimates have changed since Korber's early work, finding that "variability in these TMRCA estimates among datasets indicates that an optimal dataset that fully captures HIV-1 group M's natural evolutionary history over the past century has yet to be retrieved" (Gryseels et al. 2020; see also Aiewsakun and Katzourakis 2016).

There is also an additional problem of biomedical researchers using molecular clock methodology to estimate crossover dates without paying sufficient attention to the prevailing social and ecological conditions which were likely to facilitate cross-species transmission. In a typical article, only after the authors arrive at an estimate of the MRCA do they cite events or circumstances at that time that could have facilitated the adaptation. In other words, they start with the molecular clock date, then, in order to lend credence to their estimated date, they select broad historical developments such as the imposition of colonial rule and changes that followed. One example comes from a frequently cited evolutionary biologist working on the MRCA of HIV-1M (Worobey et al. 2008). At the close of one article devoted primarily to a reworking of the previous phylogenetic analyses, he suggested that the establishment of Leopoldville (now Kinshasa) as the Belgian Congo's capital and, more generally, "the rise of cities" and "the founding and growth of colonial administrative and trading centres such as Kinshasa may have enabled the region to become the epicentre of the HIV/AIDS pandemic" (Worobey et al. 2008). As will be seen in a subsequent chapter, the establishment

and growth of Kinshasa and other colonial centers have very specific histories, requiring careful analysis of historical records in order to determine their likely influence on crossover and epidemic spread.

Two key features of research followed from this attention to timing. One was the focus on HIV-1M and efforts to explain the early estimate for crossover, presumed to be in southeastern Cameroon, including the extended time gap between the molecular clock estimate for the crossover of HIV-1M (circa 1920) and the much later recognition of the spread of HIV (i.e., the early 1980s). In contrast, the second feature of this research on timing is the relatively few studies of these questions in regard to the HIV-2 strains.

Research to Date and the Value of Social Science

A main purpose of this book is to use social science research to fill these gaps in understanding the emergence of HIVs. The few accounts that have examined historical records are to be commended, but their analysis is flawed or incomplete in several ways that this book proposes to remedy. First, previous writers who have looked at historical records typically do not evaluate the colonial sources critically or consistently; neither do they assess sufficiently the political and professional influences that too often shaped colonial claims. Thus, these scientific researchers use archival records as if they offer indisputable proof of past reality. In contrast, historians recognize the blind spots, biases, predilections, and broader contexts of such primary sources, which require interpretation.

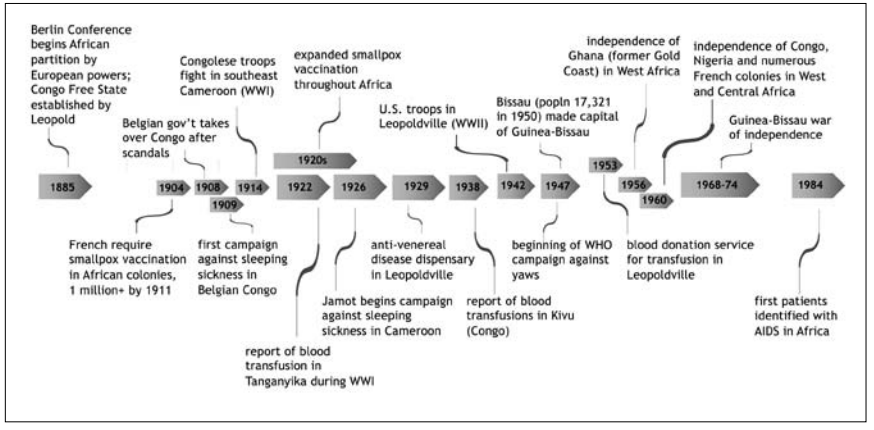

FIGURE 1.3. Timeline of HIV in context of African history.

For example, among the biomedical researchers who have attempted archival research are Joao de Sousa and colleagues. They consulted secondary literature and archival holdings in Europe and argue that an "unprecedented" epidemic of genital ulcer disease (GUD) among prostitutes and their African clientele in 1920s Leopoldville effectively facilitated HIV transmission (Sousa et al. 2010, 2016). But linking HIV emergence to expanding sex work in Africa between 1890 and 1920 projects a view of prostitution that developed in Europe—occasional or regular transactional sexual services that individuals provide to multiple partners in exchange for money and/or goods—that was largely absent in the Belgian Congo until after World War II. This is shown in several sources and is explained in detail in a subsequent chapter (Delafosse 1930; Gondola 1997). Until World War II, the prohibition of single women from legally residing in the city of Leopoldville meant that cohabitation arrangements that were called "prostitution" by authorities offered the sole possibility for their survival. Thus, the nature of these arrangements demands closer attention than Sousa and other biomedical researchers have given it. As Gondola and Lauro point out in chapter 5, folding these practices under the term "prostitution" employs a misnomer that reflects the colonial authorities' ignorance of African urban life as well as their metropolitan obsession with a "venereal peril" that had little to do with the colony itself (Lauro 2005).

A more extensive, book-length account by physician Jacques Pépin, *The Origins of AIDS* (2011), draws on an impressive amount of colonial archival sources for the first part of the work. A major focus is to add evidence to the "cut hunter" explanation of the origin of HIV-1 group M, based on the changes unleashed by colonial rule in the cities of Brazzaville and Kinshasa, such as the forced labor project to build the Congo-Océan Railway. In addition, he mentions population expansion, human mobility, urban gender imbalances, sexual and domestic activities of *femmes libres,* sexually transmitted diseases, and colonial medical practices. There are important shortcomings in Pépin's account, such as the failure to address directly the question of cross-species adaptation. He mentions iatrogenic transmission and briefly references earlier research by Marx, Alcabes, and Drucker that highlights the role of mass disease campaigns against sleeping sickness, yaws, and syphilis that likely used unsterile injection practices (Marx et al. 2001; Gisselquist

2002; Pépin and Labbé 2008). But Marx and colleagues proposed a "serial passage theory," explained in greater detail in the next chapter, which in a more complex way explains how contaminated syringes may have increased the chances of the simian virus adapting to its human host. Pépin, however, sees contaminated needles as just another mechanism that spread the virus to other humans. He describes injection campaigns in two chapters of his book, but primarily as a key mode of transmission of an already fully adapted human virus that enabled the spread of HIV.

An even bigger gap is Pépin's treatment of "the other immunodeficiency viruses," in a single chapter with that title, later in the book. These viruses are considered only of secondary importance to the extent that they offer "insight into the events that led to the emergence of pandemic HIV-1 group M" (Pépin 2011). Thus, Pépin misses the larger and more important questions raised about when and why multiple HIVs emerged at the same historical moment in widely separated parts of sub-Saharan Africa, and why some became epidemic at the same time.

A related methodological shortcoming of Pépin and other studies explaining the beginnings of HIVs is the failure to use important sources that have gone entirely unexplored. While biomedical researchers have largely based their analyses on secondary literature and a few on colonial medical documents, historians and anthropologists investigate a much wider array of sources—oral history testimonies, material culture, the popular press, photography, and other technologies—that offer important new insights into changing relations and practices that could have facilitated HIVs' emergence. These histories require close analysis of how African social and professional groups depict changing hunting and butchering technologies and practices, mobility, gender relations, and domestic, sexual, and livelihood practices in urban centers, as well as medical practices in hospitals and clinics. Such histories are further enriched by attention to social, political, economic, and cultural conditions that produced varied sources.

Topics of Following Chapters

This review of the discoveries and work to date on the emergence of HIVs and their early epidemic spread permits some initial conclusions and identification of questions to be answered in the chapters

that follow. The most obvious conclusion is that there were multiple HIVs that emerged from simian viruses at different times in different locations in Central and West Africa. This is still not widely appreciated but is of great significance because it contradicts the common assumption that epidemics are one-time, chance events. This also leads to two related questions that will be addressed in the next chapter by Preston Marx: Why did multiple HIVs emerge, and are there other HIVs that have not yet been discovered? The answer to the first question is complex. There are probably other HIVs, although not likely many more. If so, they are almost certainly nonepidemic HIVs, like the majority of those discovered to date, because there is no evidence of other widespread viruses.

Marx's chapter reviews the adaptation of the simian viruses from chimpanzees, gorillas, and monkeys to humans and some of the circumstances that enabled these changes. As mentioned above, this story has been told in articles and parts of books. Much of the attention, however, has been on determining the time of the viral adaptation, with usually only brief suggestions to explain why and how they occurred. This second chapter focuses on the virology of the adaptation process that enabled several ancient simian viruses to successfully establish themselves in their new human host. The vital question is, "Why, after thousands of years of human-simian contact, did several crossovers happen in two separate regions of Africa in the twentieth century?"

The third chapter, by Ernest Drucker, examines the epidemiology of these HIVs, which is crucial to understanding how and why four of them became widespread. These features include their relatively difficult initial transmission, plus the unusually long period (as much as ten years or more) between infection and compromise of the immune system allowing the opportunistic infections of AIDS. The chapter concludes with an examination of the surprising findings of the new tests in the 1980s that showed when and how widespread the viruses had become. Together, the Marx and Drucker chapters provide the scientific framework for the remaining chapters, which examine the circumstances whereby some of the HIVs adapted and became fully epidemic and produced the global pandemic we see today.

Chapters 4 and 5 look at the example of the HIV that is thought to have been the first fully adapted human virus and is recognized

as being most responsible for the AIDS pandemic: HIV-1 group M. This particular HIV has been studied the most, for obvious reasons, but these chapters look much more closely and systematically at two key developments. Chapter 4 by Tamara Giles-Vernick and Stephanie Rupp is the first anthropological and historical examination of the prevailing conditions in southeastern Cameroon, the part of Africa that researchers have identified as the location of the simian reservoir from which the SIV crossed over. They also explore the possible routes by which the human virus came to the Belgian Congo, where it first became epidemic. Sources include archival holdings and extensive field work in southeastern Cameroon.

Chapter 5 by Didier Gondola and Amandine Lauro is based on archival research about the former Belgian Congo. It reconsiders the question of Kinshasa being the "epicenter" of the AIDS epidemic. The chapter offers the first in-depth look at the role in the beginning of HIV spread that was played by women and extramarital sex in the colonial capital as well as changes in the demography and population movement in the colony. Gondola and Lauro conclude with an assessment of the role of new biomedical practices in the virus becoming epidemic.

Guillaume Lachenal's chapter examines the other HIV-1 virus that became epidemic but remained in Cameroon: HIV-1 group O. This is an important reminder that more than one epidemic human virus developed from chimpanzees in Central Africa. Chapter 6 also shows that the central region of Cameroon was the site of intensive medical campaigns against sleeping sickness, which have been linked to an epidemic of hepatitis C (HCV). The latter offers evidence of the likely influence of unsterilized injections in the emergence of HIVs.

Chapter 7 by Jorge Varanda examines the other important HIVs that emerged in the 1940s and 1950s, but in an entirely different region: the HIV-2 viruses in West Africa. The original host for the simian virus precursor was the sooty mangabey monkey, from which HIV adaptations have been found to have crossed over to humans nine times, with two becoming fully epidemic in an estimated 1.5 million cases to date. These have been less studied, but they are very important in confirming one of the main conclusions of this book: that recent changes in human activity produced new viruses independently in two different parts of Africa. Most of the chapter is a close examination of the

epidemic development of one of these HIV-2 viruses in Guinea-Bissau, a small former Portuguese colony that endured a war of independence in the 1960s and 1970s and where the highest prevalence of HIV-2 virus was discovered when testing first began. A concluding chapter draws together the findings and shows their importance not only for understanding the history of these two HIVs and their successful evolution into a disastrous human epidemic but also the lessons for the future to be learned from the past emergence of new viruses and epidemics.

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