The hunt for the origin of AIDS
Jon Cohen
The Atlantic Monthly; Oct 2000; 286, 4; ProQuest Direct Complete
pg. 88

THE HUNT FOR THE ORIGIN OF AIDS

by JON COHEN

The notion that AIDS arose from a polio vaccine made with contaminated chimpanzee cells—the thesis of the best-selling book* The River*—is far from the only theory about how the epidemic started, and it is hotly disputed. The quest for the source of the epidemic is intensifying, as researchers scour the jungle for clues and try to "walk back" the disease genetically with the help of the world's most powerful computers

As Paul Telfer navigated his Land Cruiser through a field of elephant grass at a game reserve in Bakoumba, Gabon, I asked him how many people in the world do what he does. Telfer briefly took a hand off the steering wheel and lifted a single finger.

Telfer is a thirty-seven-year-old field biologist from California. He works with the only team of scientists anywhere engaged in a long-running, systematic effort to track down wild primates in order to clarify the origin of the AIDS epidemic. When I accompanied him to Bakoumba, during a visit to Gabon last March, he was making the ninety-minute trek from the International Center for Medical Research of Franceville, a research station where he works and lives, to an area frequented by mandrill monkeys.

Telfer parked his car on a hill where the savanna abuts the forest. "You have to be patient," he said, leading the way down a footpath into thick, dank jungle. A bridge of vines and planks took us across a river. Telfer stopped suddenly and picked up a leaf that had been rolled into a cone and nibbled at one end. "Gorilla feeding," he said.

At last we came to a clearing. Telfer had tied a hundred ears of corn to the trees ringing it, in hopes that mandrills would begin spending time there and that he would eventually be able to capture them in corn-baited traps. He would anesthetize the animals and draw their blood, and then set them free. If he and his colleagues were lucky, they might isolate from one of the samples a simian immunodeficiency virus—SIV—that could shed some light on the origin of the virus's human cousin, HIV.

But the mandrills hadn't touched the corn, which in the fecund forest had sprouted orchidlike tendrils. We watched the clearing for the rest of the afternoon, leaving only when the jungle began to darken. We heard a few monkey shrieks, but saw no mandrills or any other primates. "Ninety percent of this game is waiting and not seeing much," Telfer said. "But when you do see something, it's pretty spectacular."

Images by Malcolm Linton/Liaison Agency (mandrill courtesy of Paul Telfer).

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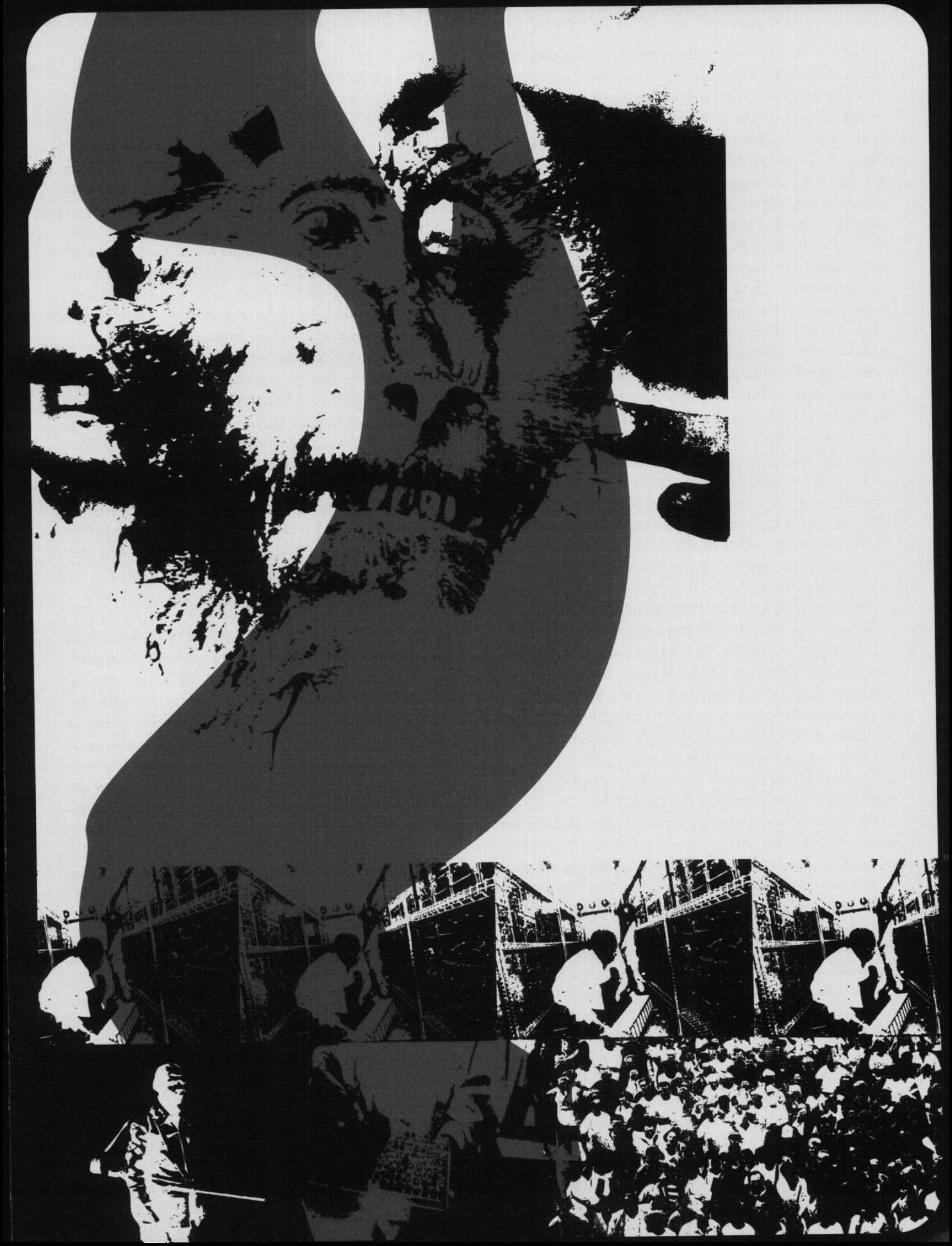

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Those of us who observe the researchers struggling to understand the origin of the AIDS epidemic have likewise done a lot of waiting—and also a lot of listening to arguments. Although scientists generally agree that HIV arose from an SIV in chimpanzees, dubbed SIVcpz (for "simian immunodeficiency virus–chimpanzee"), spirited and sometimes high-pitched battles are waged by proponents of the different theories about how the virus crossed over into human beings and then spread. Most researchers believe that a precursor to HIV first entered people living in African communities where chimpanzees are hunted for food. They posit that urbanization, the introduction of needles, and various other aspects of modernization can explain how and when SIVcpz became adapted to human beings and caused an epidemic that now afflicts some 34 million people.

But a small number of scientists, journalists, and AIDS activists are dissatisfied with this explanation. They argue that the epidemic began because an otherwise largely forgotten experimental polio vaccine that was widely tested in Africa during the late 1950s was contaminated with SIVcpz. This controversial theory has drawn attacks from mainstream researchers, some of whom have brought forth new data that, they say, convincingly refutes it. In turn, the attacks have only fueled the determination of the polio-vaccine adherents to prove their point, and their theory has won increasing attention from both the public and the scientific community.

The consequences of the debate extend far beyond university hallways and letters to the editors of scientific journals. Researchers have found SIVs in nearly two dozen primate species. If, as the mainstream theory suggests, these viruses have repeatedly jumped from nonhuman primates to human beings, in a process known as zoonotic transfer, there are probably new epidemics in waiting that science might be able to derail. On the other hand, if it turns out that the polio vaccine sparked the AIDS epidemic, the implications for even the best-intentioned medical interventions are considerable indeed.

Finding evidence to settle the debate is a formidable undertaking. Although the United States alone spends about $2 billion annually on AIDS research, the bulk of this amount rightly goes toward the search for better ways to prevent and treat HIV infections; perhaps $1 million is spent on investigations into the epidemic's origin. The few people who have committed themselves to the inquiry have done so at great risk, professionally and sometimes physically. Results are hard-won: tests of thousands of old blood samples have revealed fewer than a hundred that contain evidence of HIV infection, and researchers have found SIVcpz in only half a dozen chimps. Critical records from the manufacture and testing of the polio vaccine in question have yet to surface (if indeed they still exist), and libel suits have greeted some journalists who have advanced the vaccine theory. Those who conduct research in Africa must deal with crumbling infrastructure that forces them to move at a maddeningly slow pace, must contend with the ever-present disruption and danger of civil war, and must hope to avoid a long list of infectious diseases, one of which recently took the life of a prominent biologist.

As for the vaccine itself, only a small sample has been found, and portions were only recently released for testing. (The results, as of this writing, were expected to be announced shortly after this magazine went to press.) Although the results will lend weight to one theory or the other, they cannot resolve the debate. If scientists find SIVcpz in the vaccine, that will be the strongest evidence to date that the vaccine *might* have caused the epidemic, and will make many take the idea more seriously; however, several other conditions would have to be satisfied for the theory to be proved. A negative finding would prove only that a very small amount of the vaccine showed no signs of contamination.

Despite the obstacles, researchers are more determined now than ever before to discover the origin of AIDS. During the past year several groups have followed the lead of the Franceville group and begun searching in the wild for HIV-like viruses in chimps and other nonhuman primates. Sophisticated modeling programs, run on the world's fastest computers, have come up with intriguing estimates of the age of the epidemic. And Britain's Royal Society has joined the fray, sponsoring a landmark meeting in London last month that brought most of the principal researchers on the subject together for the first time.

AN EXTRAORDINARY CLAIM

THEORIES about the origin of the AIDS epidemic have abounded ever since doctors first noticed the disease, in five gay men in Los Angeles in 1981. Some were entirely unscientific: most famously, God was punishing homosexuals. Others were grounded to various degrees in science: A contaminated hepatitis B vaccine tested in gay men was to blame. A campaign by the World Health Organization to eradicate smallpox had somehow awakened dormant HIVs that had long infected human beings harmlessly. The CIA had concocted the virus in a lab, or it came from space, or from a distantly related cow virus that had contaminated all sorts of vaccines.

Even the more plausible of these theories failed to attract serious scientific support. Indeed, on the whole the origin-of-AIDS question received relatively little public attention until last fall, when the British writer Edward Hooper published *The River: A Journey to the Source of HIV and AIDS*. A hefty book, containing 851 pages of text and another 174 of footnotes, *The River* makes the case for the polio-vaccine theory in great detail. It has riled many AIDS researchers, but it has also brought a new sense of urgency to solving the riddle; it was the catalyst for the Royal Society meeting last month.

The book's title refers to the Nile. Hooper chose it because of the long confusion concerning the Nile's source, which nineteenth-century explorers erroneously believed was in Uganda. To Hooper, that mistake has been "strangely echoed" by the mistakes AIDS researchers have made in their claims about the epidemic's origins. A former radio reporter who

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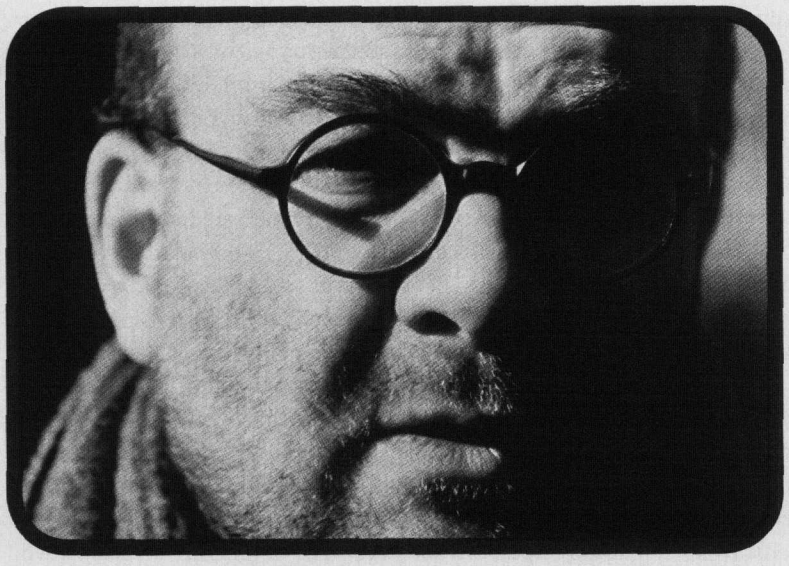
Hooper traces the AIDS epidemic to a polio vaccine tested in Africa in the 1950s. He speculates that the vaccine became contaminated with a chimpanzee virus—but his book contains no proof.



JOHN WOLSTENHOLME

Edward Hooper, the controversial author of The River

covered AIDS in Africa for the BBC, Hooper has devoted the past decade to researching his book; he portrays himself as an indefatigable investigator who will go to enormous lengths in his campaign to confront mainstream researchers with their inconsistencies, illogical conclusions, and outright errors. (*The River* takes me to task as well, for a 1992 *Science* article in which I critically examined a *Rolling Stone* story by Tom Curtis about the polio-vaccine theory.) Hooper's persona in the book is often professorial—"we shall see," "let us," and "one wonders" are among his pet phrases—and even condescending, and many researchers who have spoken with him find him obstinate, overzealous, belligerent, or worse. Still, he is without question an earnest man consumed by a mystery of undeniable import.

Soon after AIDS surfaced in Los Angeles, researchers found cases in other large cities in the United States and Europe, and also in Haiti. In 1984 Robert Gallo, a scientist at the National Cancer Institute, argued that a virus he identified as HTLV-III caused AIDS, and at about the same time, researchers described the first known African cases of the disease.

Gallo, who strongly influenced the thinking about AIDS in the early days of the epidemic, published a paper in *Science* in 1985 in which he traced the epidemic's origins to Africa, suggesting that it might have existed there for some time without being recognized as a distinct disease. His argument had two strands. First, his lab had found antibodies to the AIDS virus in fifty of seventy-five stored samples of blood that had been taken from Ugandan children in 1972 and 1973. Second, he believed that the AIDS virus had close ties to another virus that he and his co-workers had discovered, HTLV-I, which came from central Africa and had striking similarities to viruses found in monkeys there.

Gallo eventually dropped his contention that the AIDS virus belonged to the HTLV family, and the antibody test performed on the Ugandan blood samples was subsequently shown to be highly unreliable. Still, the notion that AIDS began in Africa and came from primates gained wide currency, and other, sturdier data soon backed it. Those data included reports in 1986 of HIV antibodies in a chimpanzee and of HIV itself in a blood sample taken in 1959 from a man living in what was then Léopoldville, the Belgian Congo (now Kinshasa, the Democratic Republic of the Congo).

Of all the immunodeficiency viruses that have been found in primates, SIVcpz is the one that most closely resembles HIV-1, the main type of the virus found in human beings. Indeed, the other SIVs differ dramatically from HIV-1 in their genetic makeup, and scientists concur that none of them could have evolved into the virus that caused the AIDS epidemic.

Hooper, too, thinks that HIV made a zoonotic hop from chimpanzees to people. But when it comes to explaining how and when it spread at an epidemic rate, he parts company with the "natural-transfer" theorists, who believe that the virus entered human beings decades if not centuries before the start of the epidemic, when someone with a cut—perhaps a hunter or someone preparing a meal—was handling an infected chimp. They offer various hypotheses to explain the time lag. Beatrice Hahn, an AIDS researcher at the University of Alabama at Birmingham, subscribes to what has become the most popular view. "These transmissions may have been going on forever and usually didn't do anything—they may have killed the person but they did not go anywhere," she says. "An infected person at some point got out of west central Africa into an urban area, Kinshasa or Brazzaville, and seeded an epidemic."

Hahn specializes in the phylogenetics, or evolutionary genetics, of SIVs and HIVs, studying the SIVcpzs isolated by the research station in Franceville and by primatologists elsewhere. Along with other mainstream theorists, she believes that once the virus reached an urban environment, it spread through sex, improperly sterilized needles, and "who knows what." Infected people may have eventually fanned out, she says, probably traveling up the Congo River and giving HIV a foothold in the eastern Congo, Uganda, Burundi,

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Rwanda, and Tanzania—among the first places in Africa to suffer AIDS epidemics.

The growing epidemic went undetected by the medical establishment, this theory holds, because AIDS is not a single disease with a single telltale symptom; infected people suffer from a variety of ailments. Thus an increase in cases of tuberculosis, wasting disease, and chronic diarrhea—three common AIDS-related diseases in Africa—might have worried doctors, but they would have had no reason to suspect that a new disease had struck, particularly if the increases were modest.

Theorists have some strong support for this hypothesis. In 1976 researchers studying an outbreak of Ebola in Yambuku, Zaire, collected blood samples from 659 people. Five of the samples, or 0.8 percent, later proved to contain HIV antibodies. The researchers returned to Yambuku in 1986. Two of the five people were still healthy, but three had died, having exhibited symptoms such as weight loss, fever, cough, diarrhea, pneumonia, and skin rash. Only one of the five had ever traveled outside the region of her village. A new survey at that time, of 388 people, revealed three HIV infections—exactly 0.8 percent. "These findings illustrate that HIV infection and AIDS could have existed and remained stable in a rural area of Africa for a long period," the researchers concluded in an article published in *The New England Journal of Medicine* in 1988.

Edward Hooper challenges virtually every part of the natural-transfer theory. "Proponents of natural transfer really don't have many facts to support their cause, but rely on speculation," he asserts. Hooper builds on a theory, first publicized in Tom Curtis's *Rolling Stone* article, that traces the AIDS epidemic to an experimental polio vaccine developed in the 1950s by Hilary Koprowski, who became the director of the Wistar Institute, in Philadelphia, in 1957. Although Koprowski developed the world's first oral polio vaccine, or OPV, his vaccine was never marketed in the United States; it was superseded by an OPV made by Albert Sabin (which those who grew up in the 1960s may remember taking on a sugar cube). However, as Hooper documents, from 1957 to 1960 more than 900,000 people in what are now the Congo, Rwanda, and Burundi received an experimental version of Koprowski's vaccine, known as CHAT (an abbreviation for Charlton, the surname of the girl from whom Koprowski took the poliovirus for his vaccine). He speculates that CHAT became contaminated with SIVcpz during the manufacturing process. Although Hooper goes to great lengths to challenge Koprowski's insistence that monkey, not chimpanzee, kidney cells were used to grow weakened poliovirus for his vaccine, *The River* contains no proof to back him up. In the end, as the Cornell University AIDS researcher John Moore wrote in a review of Hooper's book last year in the scientific journal *Nature*, "[as in] the grassy knoll theory, there is no smoking gun."

The undisputed facts outlined in *The River* include rich details about tests of the polio vaccine at Camp Lindi, a former colony of perhaps 400 chimpanzees near what is now Kisangani. Researchers abandoned the camp in 1960, when the Congo won independence from Belgium. Hooper convincingly shows that the researchers "sacrificed" many of the chimpanzees and offers some evidence that they harvested the animals' organs for use elsewhere. He suggests that labs in Philadelphia, Belgium, or the Congo used kidneys from the Lindi chimps to manufacture batches of Koprowski's vaccine.

The cornerstone of Hooper's argument in *The River*, though, consists of geographic links between early HIV/AIDS cases and CHAT vaccinations in human beings. Even his fiercest critics admire his resourcefulness in gathering data to support these links—a process that involved combing through old newspapers from several countries, reviewing obscure scientific articles and digging through archives, interviewing the aging principals from the OPV days, and mastering maps dotted with little-known towns and villages. Hooper wound up focusing on the thirty-eight earliest cases of "plausible" AIDS and on forty-six blood samples, ten of which came from the AIDS group, containing HIV antibodies or pieces of the virus itself. He identified what he called "likely place[s] of infection" for twenty-eight of the people with symptomatic AIDS and for all the people who had given the blood samples. He found that for eighteen of those twenty-eight people with AIDS (64 percent) and thirty-nine of the forty-six people with positive blood samples (85 percent) the likely place of infection was a town where a CHAT trial had been held. Six more of those with AIDS, and all the remaining people with positive blood samples, could be traced to towns within 175 miles of a confirmed or suspected CHAT testing site.

One of Hooper's strongest qualities is his ability to anticipate every argument that might be raised against his theory. "Skeptics would argue that you can propose anything on the basis of epidemiological data," he acknowledges in *The River*. "All those lists and maps and percentages may *look as if* they support the OPV/AIDS hypothesis certainly, but what of the other possible explanations?"

EXTRAORDINARY claims require extraordinary proof. The OPV/AIDS claim is, without question, extraordinary. The proof to date is not. And the arguments that have been mounted against the theory are compelling, especially when viewed in the context of other instances in which scientists have posited links between a medicine-related intervention and a disease.

The River opens with a brief description of one of those instances, involving the British anesthesiologist John Snow's famous conclusion that the pump water on Broad Street in London was responsible for an outbreak of cholera in that city in 1854. At Snow's urging, the authorities removed the pump's handle on September 8 of that year, shutting off the flow of what was indeed cholera-generating dirty water. "One wonders whether a similar date, denoting a 'Eureka moment' for AIDS, will ever be written into the medical textbooks," Hooper writes.

But in the retelling of the Snow story Hooper and many

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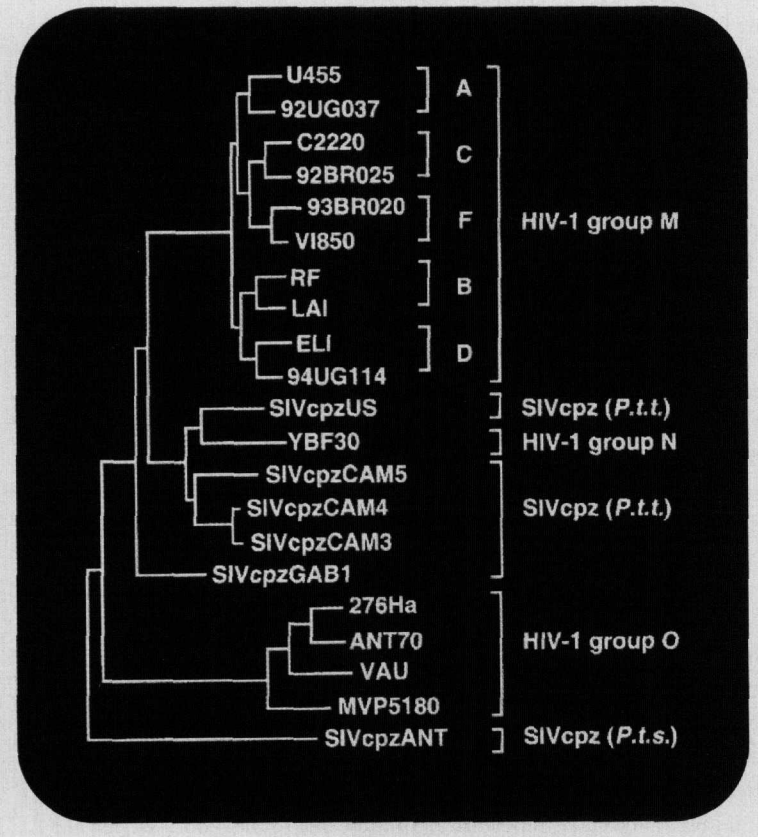
Hahn found that the infected chimps from Gabon had the strains closest to HIV-1 on a viral family tree. She concluded that the epidemic could not have begun in the Congo.



The viral family tree constructed by Beatrice Hahn

others leave out an inconvenient detail: by the time the pump was disabled, the epidemic had already begun to wane. The cause-and-effect relationship, then, is fuzzier than the lore would have it. And in epidemiology, which relies heavily on correlations, fuzziness often prevails.

Consider the following case. From 1955 to 1963 nearly 100 million Americans received polio vaccines that were contaminated with a simian virus known as SV40. The contamination occurred by the same mechanism that Hooper blames for AIDS: the monkey kidney cells used to make the vaccine harbored the as-yet-undiscovered virus. Scientists began looking into the matter in the early 1960s. Those investigators, unlike Hooper in his investigations into OPV and AIDS, did not have to rely on old vaccine samples or on hypothetical infections of particular primates in order to identify the contaminant: the vaccine was still being made, and monkeys infected with SV40 were easy to find.

Still, researchers cannot reach a consensus about whether SV40 harms human beings. An Italian scientist, Michele Carbone, has demonstrated a link between SV40 and a cancer known as mesothelioma, which causes chest and lung tumors; he has even matched viral particles in patients' tumors with particles in old samples of the vaccine. But mesothelioma takes a decade or more to develop, and, as in the case of AIDS, this complicates attempts to understand cause and effect. Some large epidemiological studies have shown no correlation between the virus and the disease, whereas others do show a correlation. And so the debate continues, the issue unresolved. (For an in-depth look at Carbone's theory, see "The Virus and the Vaccine," by Debbie Bookchin and Jim Schumacher, in the February, 2000, *Atlantic*.)

This is not to say that resourceful researchers cannot make persuasive arguments that medical accidents long in the past (of precisely the sort Hooper suggests) have caused epidemics. In 1942 some 50,000 U.S. servicemen developed acute hepatitis, in one of the largest hepatitis B epidemics ever documented. Investigators at the time discovered that the men had been vaccinated against yellow fever three months earlier. Scientists subsequently came to suspect that the vaccine was contaminated with hepatitis B, an unknown agent in 1942. The suspicion was sound, but for many years no one could demonstrate the connection.

Finally, in a study published in *The New England Journal of Medicine* in 1987, a group of researchers made a convincing case for what the connection is likely to have been. Unable to find any stored blood or vaccine samples, they turned to old hospital and payroll records instead. They located 221 servicemen who had had symptoms of hepatitis in 1942, and 171 men who were asymptomatic but whose vaccines had come from one of the lots most strongly linked to the hepatitis outbreak. For a control group they selected 205 men who had joined the Army after a new, safe yellow-fever vaccine went into use. The researchers took blood samples from all the men. They found hepatitis B antibodies in 97.7 percent of those in the first group and in 77 percent of those in the second group—but in only 13 percent of those in the control group. Most scientists now believe that the yellow-fever vaccine caused the hepatitis epidemic.

Last March scientists published a paper in the British journal *The Lancet* that links the staggeringly high prevalence of hepatitis C in Egypt (about 20 percent of the country's population is infected, the highest percentage in the world) to dirty needles used in a public-health campaign. Records show that beginning in the 1920s the Egyptian government gave people infected with schistosomiasis (a parasitic infection acquired primarily by

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swimming in contaminated water) multiple injections of tartar emetic—a highly toxic drug that offered only limited relief.

The researchers describe how clinicians, if they "sterilized" their needles at all before re-use, boiled them only briefly. "The skilful doctor began injecting at 9:20 a.m. and completed 504 injections of men, women and children by 10:10 a.m.," according to one contemporaneous account they cite. "Allowing for a 10-min rest, the time taken for each injection was thus just under 5 [seconds]. . . . This remarkable performance is being repeated at various tempos all over Egypt." Clearly, the needles constituted a likely means of transmission.

Scouring public-health records, the researchers then found that from 1964 to 1982—when an effective drug became available—an average of about 250,000 Egyptians a year received nine injected treatments. They analyzed blood samples from 8,499 Egyptians, breaking the group down according to age and geography (northern Egypt has less schistosomiasis, and so a smaller proportion of the population there received injections). More than half the forty- to fifty-year-olds in southern Egypt had hepatitis C antibodies, whereas only 35 to 40 percent in northern Egypt did; younger Egyptians showed no clear pattern of infection. Although the researchers offer no direct evidence, these figures make a compelling case that dirty needles used in the tartar-emetic campaign caused Egypt's hepatitis C epidemic.

Compared with the theories set forth in the *New England Journal* and *Lancet* papers, the OPV/HIV connection posited in *The River* has a much less plausible mechanism of transmission, a more confusing timeline, and weaker geographic and age correlations. Hooper's documentation of cases is far sketchier, and his theory involves many more speculations. His theory is, of course, still possible—it's just not probable. And science, after all, is the business of sifting the probable from the possible.

THE SECOND STRAIN

SHORTLY after I arrived at the Franceville research station last March, Paul Telfer drove me from his home on the sprawling campus to the facility's primate colony, which houses 151 mandrills, seventy-four chimpanzees, twelve sun-tailed monkeys, eight gorillas, and an assortment of about seventy-five other monkeys. Outside was a loading dock heaped with bananas. Inside I was greeted by a French researcher with a diapered baby chimpanzee in her lap.

A local hunter had brought the baby, Za-Za, to the center after killing her mother. I peered into her sorrowful eyes—the one feature of chimps that looks wholly human—and instinctively began stroking her hand. The researchers told me that after Za-Za arrived, scientists found SIVcpz antibodies in her blood.

Despite the flood of attention that SIVcpz infection has received, the data on this subject have come from remarkably few chimpanzees—which probably reflects only the fact that few chimps have been sampled to date. At the time of Za-Za's arrival at the research station, scientists had isolated evidence of the virus in only seven chimps. Two were in the Franceville station, and three were in Cameroon. One was a chimp named Noah who had been imported to an Antwerp zoo from Zaire. One had died after several years in a primate colony in the United States; she had been captured in the wild in Africa, but no one knew precisely where.

Za-Za, it turns out, isn't really No. 8: researchers found antibodies to the virus but not the virus itself in her blood. By the time I met her, the antibodies had begun to disappear, which typically happens when a baby acquires antibodies during gestation or through breast milk but escapes infection.

Later that evening, after our trip to Bakoumba to look for mandrills, I had a beer with Telfer at his home, a wood-trimmed concrete-block townhouse whose architecture, including a loft bedroom, seemed oddly hip for this remote part of Africa. Telfer told me stories of his fieldwork in Sierra Leone from 1991 until July of 1994, when civil war forced him to flee. With government soldiers riding on the roof of his car and driving armored personnel carriers, he raced in a convoy from his rural lab site to the capital, Freetown, from which he eventually flew out of the country. His boss then and now, the American virologist Preston Marx, soon began collaborating with the scientists at Franceville. Telfer moved to the research station in the fall of 1994 and has lived there off and on ever since.

Telfer booted up his laptop to show me a digital picture taken on a previous trip to Bakoumba. If we were lucky, he said, we might find something similar on the outing planned for the next day. Hunters often cannot eat all their kill, so they display the extra meat in front of their shacks. Driving past one shack, Telfer had noticed a pair of bloody mandrill arms hung up for sale. He pulled over to speak with the woman who lived there and asked what had happened to the mandrill's head. He had photographed the answer.

The gruesome image shows the woman holding the head of a male mandrill. The animal has big, crooked teeth; one eye is open in a death glare, and blood courses across the monkey's face and down its beard. The head partly blocks the message on the woman's T-shirt, so that it reads IS BEAUTIFUL. Close inspection reveals that mandrill blood is dripping onto two of the woman's fingers. "If people asked me how HIV could have entered humans, this is what I would show them," Telfer said.

As Hooper writes in the postscript to the paperback edition of *The River*, he has become "increasingly persuaded" that natural transfer can occur. But he still does not believe that this process was responsible for the AIDS epidemic. Hooper argues that natural transfers of SIVcpz simply "do not result in well-adapted, viable human viruses." Preston Marx, who has appointments at the Tulane Regional Primate Research Center, in Covington, Louisiana, and at the prominent Aaron Diamond AIDS Research Center, in Manhattan, and who has pursued the origin question as persistently as anyone, more or

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less shares that perspective, and also agrees with Hooper that the epidemic arose in the 1950s in the region of the Congo. He differs dramatically from Hooper, however, when it comes to explaining how the epidemic began.

When assessing causality, scientists use a gauge that they call "necessary and sufficient." HIV, for example, is both necessary and sufficient to cause AIDS: you can't get the disease without the virus, and the virus in itself can cause the disease. Hooper thinks that natural transfer is neither necessary nor sufficient to explain the origin of the AIDS epidemic. Marx, who finds the OPV theory implausible, thinks that natural transfer is necessary but not sufficient.

The OPV theory has several flaws, Marx contends. Not even the discovery of SIVcpz in the CHAT samples would prove that the vaccination campaign caused the epidemic, although it would certainly bolster Hooper's case. The amount of virus in the vaccine that was administered may have been infinitesimally small, or it may not have been virulent enough to establish an infection. Without a positive result from the CHAT samples, the theory that some Lindi chimps were infected with SIVcpz cannot be proved: there are no stored blood or tissue samples from the chimps. And chimps apparently do not become ill from the virus, so records of the health of the Lindi chimps (which, oddly, Hooper cites) are meaningless. In any event, Marx questions whether spraying the vaccine into people's mouths—the method by which it was administered—would transmit many viable SIVcpz infections. "Simply dropping virus in the throat is not enough to cause the epidemic," he says. "If pure mucosal exposure to SIV could induce an AIDS epidemic, then we would have seen AIDS a long time ago. Mucosal exposure has been going on for tens of thousands of years in places where they hunt mangabeys and chimps."

Marx brings up mangabeys—a species of large monkey—because they relate to an entirely separate and frequently ignored aspect of the epidemic. When people refer to HIV, they generally mean HIV-1, the most common type of the virus. But a second, weaker, type exists, HIV-2, which is found mainly in West African countries such as Guinea-Bissau, Côte d'Ivoire, the Gambia, and Sierra Leone. "Everyone thinking about this has to deal with the fact that these two diseases emerged within twenty-five years of each other, if not ten years of each other," Marx says. "Some event had to spark that. You can't deal with just one."

As of last January researchers had found at least eighteen distinct SIVs in twenty African primate species. They have known for more than a decade that one of these viruses has strong similarities to HIV-2. It was first isolated in captive sooty mangabeys, and is referred to as SIVsm.

In the early 1990s Telfer and Marx found SIVs in several wild sooty mangabeys in Sierra Leone. They then screened the blood of 9,309 people in the area to see if any were infected with a similar virus. Two people had HIV-2 infections. Although in one case the virus was a common strain, in the other the strain was unique, found in no other people, and it was closely related to an SIVsm isolate. This constitutes "absolute proof," Marx says, that a natural transfer of SIVsm to human beings had occurred.

Marx finds it telling that so few people in their population sample had HIV-2 infections; to him, this fact indicates that SIVsm rarely establishes infections in people. He has found another unique HIV-2 strain, in neighboring Liberia. The existence of unique strains supports the idea that those strains are not easily passed from one person to another. Taken together, these observations suggest that SIVsm and its cousin SIVcpz needed help in order to adapt to human beings and cause the HIV-2 and HIV-1 epidemics. Marx believes that the influx of needles to Africa after World War II, and their improper use there, are to blame.

To test his theory, Marx teamed up with Ernest Drucker, an epidemiologist at the Montefiore Medical Center, in New York. "What we found, looking at the history of injections since World War Two, is that there was tremendous demand for injectable chloroquine in the 1950s, then smallpox vaccine, then antibiotics," Marx explains. "People in Africa learned that injections could often cure a serious illness, and they came to demand them. But at the same time, the medical infrastructure in many parts of Africa was degrading." Marx acknowledges the limitations of this epidemiological argument. "We're dealing in correlations, not proof," he says.

Hooper has attempted to explain the HIV-2 epidemic by introducing another contaminated-polio-vaccine hypothesis. The vaccine he points to here, one developed by Pierre Lépine, of the Pasteur Institute, in Paris, has an even sketchier history than CHAT. Hooper has pieced together much of the history with the help of Simon Wain-Hobson, a leading AIDS researcher who now works at the Pasteur. Hooper posits a number of scenarios in which SIVsm could have contaminated some of Lépine's vaccine and been transmitted to people in West Africa. However, there is no evidence that Lépine used sooty-mangabey kidneys to make the vaccine, or that it was given in the areas that subsequently developed the worst HIV-2 epidemics. "The arguments about how SIVcpz and SIVsm found their way into vaccines are highly contrived," Marx told me. "Anybody can sit here and make up a story."

INSPECTOR JAVERT?

"HOOPER gets on my nerves," Beatrice Hahn, the University of Alabama AIDS researcher, told me recently. Hahn objects not so much to Hooper's research, although she does disagree with his theory, as to his manner and tactics, which she refers to as "annoying bullshit." I heard similar sentiments from several of the researchers I spoke with.

Part of the reason that so much controversy and emotion attend the origin-of-AIDS debate has to do with Hooper himself. He has a brilliant command of facts and the tenacity of a prosecuting attorney, but he is argumentative to a fault and deeply

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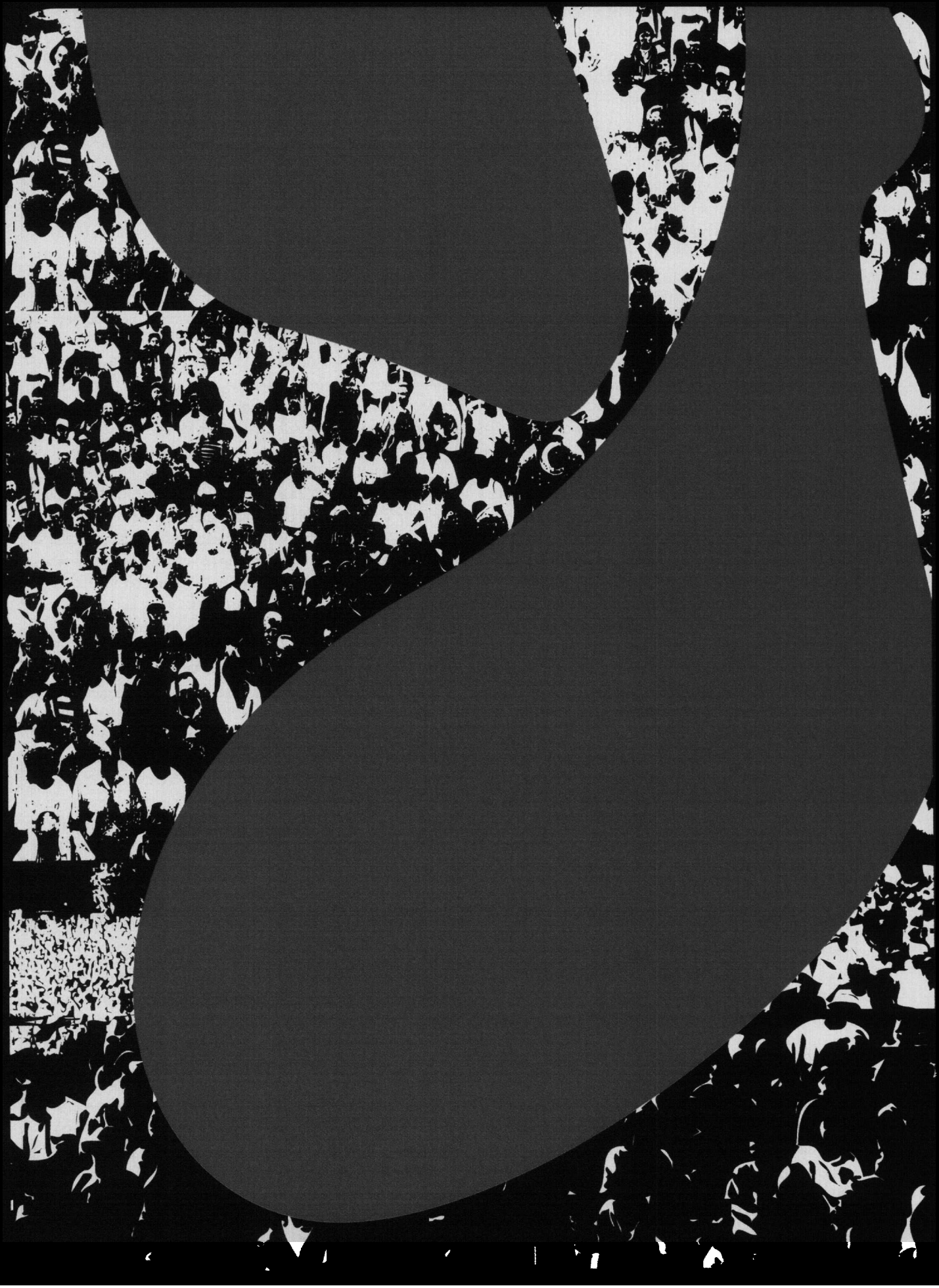

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suspicious of anyone who disagrees with his views. "Try to rise above the defensiveness that surrounds the issue of origin, especially over in the States," he e-mailed me at one point. "We still have much to learn—on that I do agree with you. But *The River* has demonstrated that there is, at the least, a case to answer on the OPV/AIDS theory. Let's address it full on, not ignore it. So be fair. Be honest. Be even-handed. Please." Beatrice Hahn and other natural-transfer advocates, he wrote, "may be unconsciously driven by a desire to arrive at a 'politically correct' explanation for AIDS." *Nature* magazine has "a deep-seated bias against the hypothesis."

The fact that few AIDS researchers put stock in the OPV/AIDS thesis rankles Hooper. "This theory has been dealt with less than fairly by the scientific community," he charged in another e-mail. "People are trying to dismiss this theory by resorting to the worst type of emotional diatribes."

To some extent Hooper is right: scientists and scientific institutions have been vitriolic in their attacks on OPV/AIDS proponents, and they have dragged their feet regarding experiments that could help to resolve the issue. The *Rolling Stone* article that introduced the theory drew a libel suit from Hilary Koprowski, as did a subsequent piece by an Associated Press reporter (both were settled out of court). Koprowski's lawyer also sent Hooper a letter, putting him "on notice . . . that any publication that is scientifically unsound and therefore obviously defamatory in nature will be promptly pursued in the appropriate courts." Several researchers discouraged Hooper from pursuing his hypothesis. Meanwhile, the Wistar Institute failed to follow through on a 1992 recommendation by an outside panel of experts that it test the one relevant vaccine sample still on hand. It finally sent portions of the sample to three independent labs last spring.

And Hooper's analysis of why so many scientists are so agitated about his theory makes a certain amount of sense. "Different groups are threatened by the arguments; that's the heart of it," he says. The idea that CHAT sparked the AIDS epidemic, he contends, scares Beatrice Hahn and other phylogeneticists because it undermines their work. Vaccine makers and advocates fear that the public could lose faith in vaccines, and the governments that supported the CHAT trials are loath to be held responsible for the epidemic. As for scientists who might be tempted to pursue the theory, he says, they worry that their colleagues might ostracize them for stepping out of line and that their funding could suffer.

In what seems an attempt to convey that he is not a fanatical Inspector Javert, Hooper asserts that he does not intend to pursue the OPV/AIDS hypothesis forever. "To be frank, I can hardly wait for the day when I can, in clear conscience, leave the investigation of this business to the scientists, the day when I can withdraw, publicly, from the debate," he told me in an e-mail. "But I won't be doing this until I am certain that Science is really going to investigate the issue properly, fully and honestly. Not much sign of that at present, I fear—bar the [Royal Society] meeting."

In the end, though, Hooper's dire portrait of capital-S science is overdrawn. A group of devoted scientists, albeit a small one, *has* been addressing the issue properly, fully, and honestly. That Hooper finds their work wanting reveals more about him than about the scientists and their efforts.

CALAMITIES IN THE WILD

IN January of last year thousands of researchers from around the world gathered in Chicago for the 1999 Conference on Retroviruses and Opportunistic Infections—the largest annual AIDS meeting held in the United States. Beatrice Hahn stole the show with new data about the origin of HIV and AIDS.

In 1994 a researcher at the National Cancer Institute had cleaned out his freezer, where he had stored the frozen liver, spleen, and brain of a chimpanzee named Marilyn. He called Hahn, because nearly a decade earlier Marilyn had had an odd blood-test result. She had been caught in an unspecified African country and shipped to Holloman Air Force Base, in New Mexico, in 1963; she spent the rest of her life in various primate colonies in the United States. In 1985 researchers looking for HIV antibodies in primates drew blood from Marilyn and ninety-seven other chimps living in a colony in Alamogordo, New Mexico. Marilyn had the only positive test result. She soon gave birth to stillborn twins and then died herself; her body parts ended up in the NCI freezer.

With the technology available at the time, scientists had been unable to isolate SIVcpz from Marilyn's tissues. Hahn extracted pieces of the virus from the samples; the genetic sequence of the strain looked similar to the sequences of the two SIVcpzs that had been found in Gabon at Franceville. On a viral family tree all three of the chimps' viruses are clustered near various strains of HIV-1; this suggested to Hahn that they had all branched off from a common ancestor relatively recently. However, they had distinct differences from the virus in Noah, the chimp in the Antwerp zoo (the infected Cameroonian chimps had not yet been discovered).

At the meeting in Chicago, Hahn proposed a solution to this puzzle, one that would appear later that week in a paper in *Nature*. The combination of the high-profile conference, the publication in a prestigious journal, and Hahn's decision to use her data to assail the African trade in bush meat (generally, meat from chimps and other primates) led to front-page stories in newspapers in the United States and elsewhere. The *New York Times* story opened with the overblown assertion that "the riddle of the origin of the AIDS virus has apparently been solved."

Although Hahn's study did significantly bolster the case that chimps were the "natural reservoir" of HIV-1 (Marilyn, with the fourth SIVcpz isolate, increased the evidence by 33 percent), her real message became lost or garbled in much of the press coverage. Hahn had analyzed the mitochondrial DNA of all four chimps known to be infected. She suggested that

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The virologist Preston Marx questions whether spraying vaccine into people's mouths would transmit many infections: "Mucosal exposure has been going on for tens of thousands of years."

HENRI GOLDSTEIN

Administration of the CHAT vaccine, Léopoldville, 1959

Marilyn and the two Gabonese animals belonged to one of four subspecies, *Pan troglodytes troglodytes*, whereas Noah was a *Pan troglodytes schweinfurthii*. Because chimps do not naturally cross rivers, most scientists at the time believed that each subspecies had a restricted range, with *P.t. troglodytes* found from Cameroon to Gabon and *P.t. schweinfurthii* found in the Congo, including in the area where Camp Lindi had been. Hahn therefore asserted that the HIV-1 epidemic could not have begun in the Congo—a conclusion that makes the OPV theory that much more unlikely. (Hahn's thinking about subspecies would later change, but her conclusion would not.)

Hooper lost no time in mounting a response. In June of last year, hoping to learn more about the Camp Lindi chimps, he traveled to Kisangani. He was accompanied by the pre-eminent Oxford University evolutionary biologist William Hamilton, who wrote the foreword to *The River* and gave Hooper the equivalent of $3,000 toward his research. Once in Kisangani, Hooper and Hamilton split up the tasks: Hooper interviewed former workers from Lindi, while Hamilton collected fecal samples from pet chimps in the area. Hooper hoped that analyses of chimp and viral DNA found in the feces would prove that *schweinfurthii* chimps carry an SIVcpz similar to the most common strains of HIV-1 in human beings: such a finding, he believed, would refute Hahn's theory and bolster the OPV case. And he knew that another species, *Pan paniscus*, also lived in the area and had been used at Lindi; perhaps it, too, could provide clues.

Last January, Hamilton set out for Kisangani again, this time to collect fecal and urine samples from wild chimps. Not only would doing so increase the sheer number of samples, but also, he reasoned, it would increase the proportion of samples likely to contain the virus: pet chimps are typically caught as infants, and it is believed that SIV infections rarely pass from mother to baby—thus infections are more commonly found in adults. Hamilton was accompanied by an Oxford graduate student named Michael Worobey and by one of Worobey's friends; both had been fire fighters and were experienced at climbing trees—a skill that would be helpful in reaching chimpanzees' nests.

Although the group has not revealed the results as of this writing, it did collect several dozen fecal and urine samples—at an extremely high cost. On the first day in the forest Worobey spiked his hand on a palm tree. Four days later, his hand severely swollen, he left the others and walked twelve miles to the nearest village, where he got a bush taxi to Kisangani. By the time he reached medical help, he had developed blood poisoning.

Hamilton returned from the forest two days later. A few days after that he began to feel sick, and he spent most of one day in bed. "The next morning he informed us that he had the sweats," Worobey recalls. Unlike his traveling companions, Hamilton had not taken anti-malarial pills; he had contracted the disease years before, in the Amazon, and believed that his immune system could defeat a new infection. He tried a

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malaria treatment from a pharmacy, but the group decided to head back to London right away. "By the time we got to Heathrow, Bill was as good as we'd seen him," Worobey says. The next day, January 30, Hamilton felt ill again and went to a hospital, where he collapsed and slipped into a coma, his internal organs hemorrhaging. He died five weeks later.

THE CONCLUSIONS OF "NIRVANA"

MEANWHILE, dozens of journalists gathered in San Francisco, for the 2000 retrovirus conference. This year they swarmed around Bette Korber, a scientist at the Los Alamos National Laboratory. Korber had just presented new data that, like Beatrice Hahn's, challenged the OPV theory. The frenzied media reaction created the false impression that she had solved the origin mystery and disproved the OPV theory. It also overshadowed another origin talk presented that day, one that deserved at least equal attention.

The little-noted presentation came from François Simon, the chief researcher at the Franceville lab, who also works in Cameroon. Simon announced the discovery of the three SIV-infected chimps in Cameroon and two new SIVcpzs that had been isolated from them. He and his colleagues had also found strains of HIV-1 in two Cameroonians which closely matched the simian viruses. This was the first hard evidence that an SIVcpz had recently made a leap into human beings and established an HIV-1 infection. It significantly bolstered the natural-transfer argument.

Although the data that Korber had compiled, in collaboration with the biologist Carla Kuiken, Hahn, and others, were more theoretical, they offered a tidier news story. Korber maintains a database that catalogues HIV isolates and viral fragments that have been genetically sequenced. Using one of the world's fastest computers, "Nirvana" (an array of up to 2,048 processors that operate in concert), Korber and her colleagues analyzed the virus's evolutionary history. They focused on the main group of HIV-1, which has eleven strains, or subtypes.

By plugging in known mutation rates of HIV and comparing the genetic makeup of these subtypes, the researchers calculated that an ancestor common to the subtypes dated to 1930, plus or minus twenty years. As a control, the group showed that the program's "molecular clock" could accurately date the 1959 sample from Léopoldville and also the virus's subtype E, which is known to have surfaced in Thailand around 1986.

Korber is a soft-spoken researcher who shies away from dramatic pronouncements and appends caveats to almost everything she says. "Our results don't disprove [the OPV] hypothesis but make it unlikely," she said, pointing out that the CHAT trials did not begin until 1957. Hooper had received advance word of Korber's results and had already challenged them at a press conference about *The River*. He noted, rightly, that no one knows when this common ancestor jumped from chimpanzees to human beings. He then suggested that the various subtypes could have evolved in chimps, and speculated that the OPV manufacturers had pooled kidney cells from ten Lindi chimps infected with distinct SIVcpzs. This, he said, could account for the diverse viruses in human beings. Korber replied with further understatement: "This seems to be quite an unlikely scenario," she said.

The press persuaded Korber to hold an impromptu conference. She grimaced her way through it, explaining at great length and in carefully measured terms precisely why the OPV hypothesis underwhelmed her. "I wouldn't go so far as to say it could not have happened," she said in reply to a question from Lawrence K. Altman, the *New York Times* medical reporter, who last November wrote a favorable column about *The River* that greatly increased the amount of attention paid to the book. Korber went on to say that the OPV thesis simply clashed with the genetic diversity of the main HIV group. If the OPV theory were true, she explained, each of the known HIV-1 subtypes would have had to contaminate the vaccine, enter a human being in a viable form, establish an infection, and then spread exponentially; each "founder" would have had to start a distinct epidemic. "I find the numbers unlikely because it's difficult for zoonosis to take," Korber said. (Hooper and others have also posited that a single chimp had the prototype for every HIV subtype, but Korber says that's even more of a stretch.)

Near the end of the question-and-answer session a reporter remarked that Stanley Plotkin was in the room. Plotkin is currently a consultant to the French vaccine manufacturer Aventis Pasteur; he collaborated closely with Koprowski in the making and testing of CHAT, subsequently developed several vaccines himself, and co-authored the classic textbook on the subject. "I wasn't planning to participate in this conference, which is about Dr. Korber's work," Plotkin said. "I would reiterate, first of all, that no chimpanzee tissues were used in any oral polio vaccine. As far as her work is concerned, clearly it supports the idea that the introduction of HIV from chimpanzees occurred well before the vaccination campaign in the Belgian Congo."

Plotkin had recently helped to find the labs to test the remaining CHAT in Wistar's freezers. After the press conference I asked him what his reaction would be if the vaccine tested positive for chimp DNA—or, even more damning, for SIVcpz. "As a scientist, I have to accept scientific data," Plotkin said. "From what I know, I consider that unlikely." Plotkin told me recently that after the publication of *The River* he got in touch with all the principal scientists and technicians who had worked on CHAT at Wistar and in the labs in Belgium and the Congo. To a person, they said that they had not worked with chimpanzee cells. Plotkin planned to detail their statements, which he had received in writing, at the Royal Society meeting.

Both support for and criticism of Korber's data and her 1930 date (since revised to 1931, with a range of 1915 to 1941)

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have come from unlikely quarters. Jim Moore, a primatologist at the University of California at San Diego, more or less stumbled into the debate over her theory, having published an origin thesis of his own in *AIDS Research and Human Retroviruses* on the eve of the conference. Moore (no relation to the AIDS researcher John Moore) and his co-workers combed the literature on the Belgian Congo and pre–World War II French Equatorial Africa—the region that includes the Republic of the Congo, Gabon, and the Central African Republic. They concluded that the human epidemic probably started between 1890 and 1930.

Moore began by documenting how the colonial powers' use of forced labor to build railroads and other infrastructure led many African villagers to flee to the forest, where they would have depended more on bush meat than they had previously. Labor camps separated families and encouraged promiscuity, and many villagers moved to newly established cities (Kinshasa's population, he notes, grew tenfold from 1905 to 1940). And wars and civil unrest, of course, have been constants in most African countries for much of this time.

In addition to these social forces, which HIV naturally exploits, Moore discovered evidence of shoddy medical practices that could have greatly amplified the spread of the virus. As many as 35,000 people living in French Equatorial Africa from 1893 to 1912 may have been vaccinated against smallpox directly from another person's arm: doctors would withdraw liquid from a pox blister on someone who had recently been vaccinated and inject it into someone else (this method was adopted to save the trouble of transporting large quantities of vaccine to remote locales). A 1917–1919 campaign against sleeping sickness used six syringes for 90,000 people.

I met with Moore earlier this year in his office, whose walls display detailed maps of Tanzania, where he has done fieldwork. He immediately made it clear that he is not hostile to the OPV theory. He greatly respects his late colleague William Hamilton, and is also impressed by Hooper. "Ed has spent ten years of his life pursuing a hypothesis," Moore says, adding that he likes the OPV hypothesis because it is plausible and can to some extent be tested. "I'm betting when it's tested, it will be falsified. But it's not obviously wrong. How are you going to falsify the scratched-hunter hypothesis?" he asks. "It's almost impossible."

However, Moore is skeptical about Hooper's emphasis on geographic links between early cases and CHAT vaccination sites. "I want to see an epidemiologist look at where they were taking samples," he says. "It sounds, as Hooper puts it, like it's remarkably coincident, but until it's looked at carefully, quantitatively, there are grounds for suspicion. I'm just guessing, but it strikes me as plausible that people would be vaccinated at places where there are clinics or where doctors go regularly—and where the clinics are and the doctors go is where you'd have samples."

Donald Burke, formerly the head of the U.S. military's AIDS research program and currently the director of the Center for Immunization Research at Johns Hopkins University, questions the validity of every model that has estimated the epidemic's time of origin, because none has yet allowed for a process called recombination—essentially, the splicing of genes from two sources. A person may become infected with two distinct subtypes of HIV, and they may recombine and form a new strain. Burke believes that HIV may well have relied on recombination to create a strain that could readily spread from person to person. The urbanization of Africa and the imposition by colonialists of a common language, Burke argues, brought together groups—and HIV subtypes—that had previously had little contact with one another, providing opportunities for the development of recombinants and for the spread of viable strains. It is as if someone poured all the various viral strains into one container and then shook it, Burke says. And because recombinant strains form branches of odd lengths in unusual places on a phylogenetic tree, current modeling programs cannot factor in recombination with any accuracy.

Gerald Myers, a scientist at Los Alamos who was once Korber's boss, firmly believes in the usefulness of computer modeling, and has high praise for the process that has allowed Korber to estimate the beginnings of the epidemic; however, he, too, has strong reservations about Korber's conclusions, for reasons that further complicate matters. "The burden is on proponents of natural-transfer theory to tell us what happened between the 1930s and the 1970s," Myers says. Myers's own group approached the question from the opposite direction, working forward from a number of given dates to the present day. "We can model this as a believable process if it started as late as the late 1950s," he says. "We cannot model it, so far, if we start earlier."

Myers is a polymath who speaks slowly and deliberately. He pointed out a pattern that puzzles him: the various HIV subtypes, when placed on the virus's evolutionary tree, are equally distant from one another, indicating that they branched from a common ancestor at roughly the same time. Standard Darwinian evolution displays a more uneven pattern, he explains. "We expect a lot of variance in the HIV tree, and there's very, very little—surprisingly little. So you have to say at first glance at the mathematics that something extraordinary has happened. It could be needles. It could be that somebody blew a whistle and funny things started happening, like in an Anthony Burgess novel."

Myers and his colleagues have analyzed the evolutionary tree formed by subtypes of feline immunodeficiency virus (FIV), a distant relative of HIV that causes an AIDS-like disease in cats. "A lot of things humans did happened to cats," Myers says. "They've suffered urbanization. Cats moved to the cities, they changed their sex habits, and who knows what." And the FIV-subtype tree looks nothing like the one for HIV. "It's a very messy tree by comparison," he says.

Myers clearly recognizes that all modeling is based on assumptions and therefore has limitations; he stresses that at best his work and Korber's will help to guide other scientists

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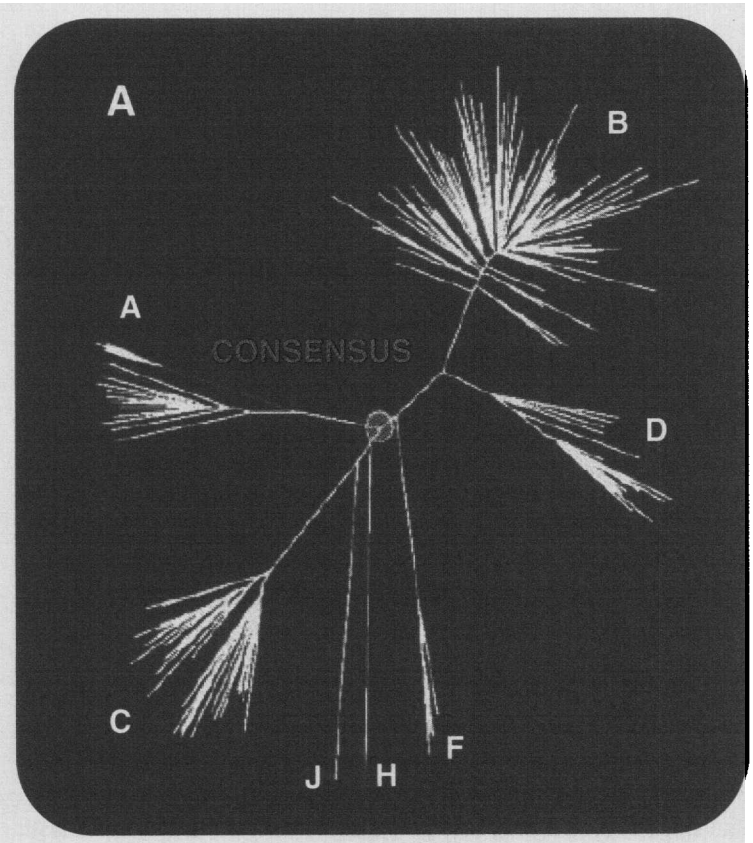
Using computerized models, Korber calculated that an ancestor common to the HIV-1 subtypes dated to about 1930. "Our results don't disprove [Hooper's theory] but make it unlikely," she said.



The HIV-1 family tree created by Bette Korber

in their thinking about which experiments to conduct. "The problem will come back to haunt us if we don't try to get to the bottom of this," he says. "None of us wants the polio-vaccine story to hold up. It's a horrible thought. But I think we need to go ahead and face it squarely."

THE HUNT CONTINUES

FRANÇOIS D'Horpock, a pathologist in Abidjan, Côte d'Ivoire, led me into a dark and dusty, long-ignored room in his laboratory at the University of Treichville. Scattered about were more than 2,000 tissue samples from autopsies dating as far back as 1967; each was numbered and stored in a chunk of paraffin the size of an ice cube. Metal cabinets along the walls held thousands of numbered slides containing blood smears and the like. Giant ledgers contained the case history of each sample.

Before going to Gabon, I met with AIDS researchers in Côte d'Ivoire, Kenya, Uganda, Rwanda, and South Africa. I sought out D'Horpock and other pathologists to see if anyone had old tissue or blood samples that researchers might test for evidence of HIV. Such samples could shore up what is perhaps the single weakest aspect of origin-of-AIDS studies generally: researchers have identified very few cases in Africa prior to 1980, and have even fewer samples of old HIV isolates.

Shortly after the epidemic surfaced, several research groups did screen old medical records and archives of stored blood; this is what led to the discovery of the "plausible" AIDS cases and the positive blood samples that Hooper documents. But, as he details in *The River*, other stored samples exist that no one has checked. My hunch is that Albert Schweitzer's old hospital in Lambaréné, Gabon, which was founded in 1913, might contain samples of particular relevance: the hospital is located in a region where some of the SIVcpz-infected chimpanzees were found.

Although positive evidence of HIV in Abidjan from, say, 1967 would rewrite the history of the epidemic, D'Horpock's samples are not old enough to reveal much about the OPV hypothesis. Furthermore, he says, they were treated with formaldehyde, a process that may have degraded the viral DNA. Still, no one has even approached him to find out whether the samples would be worth testing, though there are large American- and French-funded AIDS-research efforts on the campus. "Research takes time and is expensive," D'Horpock says with a shrug.

Even if a stored sample does provide evidence of an HIV infection from 1956 or earlier, it will have to yield highly detailed information, or Hooper will simply point out that natural transfer sometimes occurs. If the sample contains antibodies but not the virus itself, researchers will not be able to do a phylogenetic analysis. Should someone isolate an archival HIV, it will have to belong to the main group of HIV-1s in order to bear on the OPV theory. And the genetic sequence will have to fit into the evolutionary tree at the right point in time.

Still, there are compelling reasons to try to settle the issue. Kevin De Cock, a leading AIDS epidemiologist at the U.S. Centers for Disease Control and Prevention, who started a large AIDS-research project in Abidjan in 1988 and now works in Kenya, used to question the relevance of origin studies. "Does any of this matter?" De Cock says. "I've changed my mind. You can't have fifty million infected, sixteen million of whom have died, and say it doesn't matter how this came about. Conditions that expose humans to these simian viruses have probably increased. You can't say from a public-health perspective that those are of no importance."

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A better understanding of the origin of AIDS could have an impact on efforts to combat other diseases as well. Omu Anzala, an AIDS-vaccine researcher at the University of Nairobi, says that ripples from *The River* have "caused many problems" in Kenya. "When people read *The River* and they are not very scientific, the arguments are pretty convincing," he says. Claiming that the vaccine contains HIV, some Kenyan clergymen have recently discouraged their countrymen from taking part in the current campaign to eradicate polio (which uses a thoroughly tested, contaminant-free OPV). "In the last six or seven months we've been trying to vaccinate as many people as we can," Anzala says. "But certain segments of society have been saying, 'Who knows whether the vaccine isn't contaminated?'"

PARTWAY down the packed-mud road that leads from Franceville to Okondja, Telfer stopped his Land Cruiser so that we could speak with two hunters. One man had a shotgun slung over his shoulder; the other had a machete and a tall wooden cane. Both appeared to be at least in their fifties. Through an interpreter who works with Telfer, I asked the men their ages. Neither had any idea. The interpreter asked them a question of his own: "Have you ever heard of World War Two?" Again they both lifted their shoulders and shook their heads no.

Telfer was making the four-hour round-trip drive to Okondja to take a blood sample from a pet monkey he had found on an earlier expedition. Farther along the route he spotted a dead monkey for sale, splayed on top of an upside-down empty fuel can. Telfer does not want to pay for animals and thereby indirectly encourage trade in bush meat, and so, with his interpreter's help, he delicately negotiated with a woman living in a nearby shack. She agreed to let him take samples from the monkey, a member of *Cercopithicus cephus*—a species in which no one had yet found an SIV. After putting on latex gloves, he plucked some hair from the animal; he would later do a DNA test to determine where the monkey fits on the cephus family tree. Telfer wrapped a strip of rubber around the monkey and hung it from a hand-held scale: 6.6 pounds. He opened the monkey's mouth and clipped off a bloody piece of tongue. He would have liked to open the belly and take the spleen—a likelier place for SIV to hide—but the village men who by then had clustered around were becoming agitated, and the interpreter discreetly herded us back to the car. A half hour or so later we came upon another recently killed cephus in front of a roadside shack. After similar negotiations with this monkey's owner, Telfer took a tissue sample from the animal's rectum—a location where HIV is frequently found in people.

When we got to Okondja and located the pet, a cephus monkey living in a makeshift cage alongside a house, the owner was not at home. We headed to the marketplace for lunch, where I had a stew made of porcupine (which is not a protected species). The locals took obvious delight in watching us eat there, which pleased Telfer: an important part of his job, he says, is building trust. Over lunch we met another man who has a pet monkey, which Telfer hopes to sample in the future.

We headed back to the caged pet cephus. Its owner had returned, and he agreed to let Telfer take a sample. The first step was to anesthetize the animal with a shot of ketamine. Telfer donned a long leather glove, lifted the tin top off the cage, and tried to grab the monkey. The monkey, of course, wanted no part of this, and madly dodged Telfer's every lunge. Tension rose, amplified by the crowd that had gathered. At last Telfer succeeded in anesthetizing the animal. He placed it on the ground, drew blood from the femoral vein, measured its weight and size, and marked it with a tattoo gun.

As we prepared to leave, a neighbor came up to tell us that she, too, had a pet monkey. We walked a few houses over and saw the animal, a baby cephus, but Telfer decided that it was too small to draw blood from, so we headed back to Franceville. Telfer was pleased with the day's tally: tongue from one fresh kill, rectal tissue from another, blood from a pet, and one adult and one baby pet for future testing.

In June, Preston Marx told me that the pet cephus whose blood we had sampled showed evidence of SIV infection. I sent Telfer an e-mail about it; the subject line on his reply read, "interesting? maybe." As often happens in this kind of work, the preliminary data turned out to be as confusing as they are intriguing: the monkey's blood showed SIV antibodies in one test but not in another. However, researchers extracted strands that appear to be pieces of an SIV, and analysis is proceeding.

FURTHER information about the origin of AIDS will soon emerge from the many research efforts under way. Paul Telfer and his colleagues plan to go to the village where Za-Za came from and take blood samples from human beings there. Telfer is also preparing to collect fecal samples from chimps in the wild. Beatrice Hahn has begun to agree with primatologists who question whether chimp subspecies truly exist. She recently analyzed fecal and urine samples from chimps in Uganda and Côte d'Ivoire and blood from *Pan paniscus* in the Congo. All tested negative for SIVs, which has led her to wonder whether any chimps outside west central Africa are infected. Martine Peeters, a French researcher who has done pioneering work on the chimp isolates from Gabon, has been testing primate meat from a marketplace in Cameroon. Donald Burke has begun working in Cameroon and hopes to start testing primates in the wild there. At the international AIDS conference held last July in Durban, South Africa, Anne-Mieke Vandamme, a Belgian researcher, presented data that support Bette Korber's 1931 date by means of an entirely different methodology. Even more intriguing, Vandamme's work dates the emergence of SIVcpz and HIV-1 from a common ancestor to about 1700. The analysis of the CHAT samples may suggest directions for new investigations. And the Royal Society meeting will undoubtedly fuel new research as well.

But as Telfer so trenchantly observed, standing quietly in the jungle and looking at nothing in particular, 90 percent of the game is waiting and not seeing much—until the day we see something spectacular.

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