

GENESIS OF AIDS: Mother Nature, or the Hand of Man?

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From 1981, when the condition was first recognized in American gays, to the present, the origin of the epidemic, the pandemic, has always intrigued people. From molecular biologist to taxi driver, everyone has an opinion. By the Millennium, 50 million people around the world had been infected with HIV, of whom 15 million had developed AIDS. Most of the latter had already died. AIDS is now the world's biggest killer infectious disease.

But one thing which, even back in the early 1980s, was overwhelmingly clear both to the gay communities of New York and Los Angeles, and to the villagers of southern Uganda who witnessed the first epidemic outbreak in the general population, was that this syndrome, this collection of diseases, was something entirely new.

Many, including many of those dedicated and overworked AIDS physicians, would ask whom the question of origin benefits: what purpose does it serve to try to answer the unanswerable? The battle is raging already, they would argue; we need to treat the wounded, not apportion blame.

A fair point, on one level; but doctors, of all people, should know that very often diseases can be cured, or treated, only after we have a proper understanding of their aetiology. (The classic example is the cholera outbreak of 1854, which killed 500 Londoners before an epidemiologist, John Snow, deduced the crucial role of the water supply, and stopped the epidemic by removing the handle of the Broad Street pump.) Furthermore, if the genesis of AIDS has involved avoidable events or human error, then perhaps we can learn useful lessons, and thus avoid similar disasters in the future.

So this is not just an academic question. It is one to which, as a species, we need answers.

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■ QUESTION OF TIMING

My own quest into the origin of AIDS began in the summer of 1990 in Covent Garden, at one of those wobbly tables out on the cobblestones, where waitresses bring *cafetieres* and expensive sugary pastries. By that stage I had been working on AIDS for 4 years, and my first book, *Slim*, about the epidemic in East Africa, had just been published (Hooper, 1990). During the round of interviews and discussions that followed, I was once again struck by the sheer volume and range of explanations for the advent of the syndrome, which ranged from the carefully reasoned, via the paranoid, to the seriously wacky.

Thinking that a book on the subject might take a couple of years to research and write, I decided to investigate further, and my first step was to interview a haematologist called Alan Fleming, who had written a series of articles (mostly for a fairly obscure German journal) in which he documented the earliest traces of HIV infection in Africa, stretching back as far as 1959. By this stage, the proposition that AIDS had emerged from Africa was still viewed as controversial, although the scrupulous epidemiological evidence assembled by Professor Fleming left little doubt.

As I scribbled notes among the pastry-plates, Fleming made three very powerful points. The first was that the immediate ancestors of the HIVs, the simian immunodeficiency viruses or SIVs, were found naturally only in African primates. (In these animals, the SIVs caused no disease, which—together with the large number of African primate species which had already been identified as SIV carriers—suggested that these were ancient infections.) At that juncture, two variants of HIV (HIV-1 and HIV-2) had been identified. However (and this was his second point), in that huge—albeit unintended—biological experiment called the Slave Trade, over 10 million people from central and west Africa had been transported to Brazil, the Caribbean and the south-eastern United States. Other viruses, including two other human retroviruses, had been transported with them, but the two HIVs had not, even though central and west Africa are nowadays widely considered as the ‘hearths’, or original homes, of HIV-1 and HIV-2. It therefore seemed likely that both the HIVs had emerged in man after the 1860s. Fleming’s third point was that when transferred to other primates, such as Asian monkeys and humans, the SIVs caused immunodeficiency and death. This was yet

another indicator of the recency of the HIVs, in that they appeared to be SIVs which had not yet had time to adapt to a state of benign co-existence with their new (human) hosts.

Professor Fleming summed up his position about origin by posing a simple question: why now?

He suggested that if I seriously wanted to follow up on these issues, I should start off in a decent medical library. I packed up tape recorder and notebook (to this day, the relevant pages have a tendency to stick together), and that same afternoon began what turned out to be many months of burrowing through the stacks. First, I tried to unearth ancient AIDS cases hidden in the medical literature, cases which involved unexplained immunodeficiency in otherwise healthy adults, but which had been diagnosed at the time as diseases like *Pneumocystis carinii* pneumonia (PCP) or cryptococcal meningitis, which are two of the most characteristic opportunistic infections of AIDS.

During the next couple of years, I followed up eight of the most clinically plausible cases on the ground. The patients in question had died between 1945 and 1969 in Britain, America, Canada and Sweden. I interviewed pathologists, hospital consultants, GPs, friends, family and colleagues, and—with permission from the next-of-kin—examined the medical records. In each instance, there eventually turned out to be a far more plausible explanation than HIV disease. The charts of some patients revealed that they had received extensive radiotherapy or heavy treatment with steroids during their hospital stays. Some had been exposed to toxic substances or radiation in the course of their work, or as a result of where they lived. Others seemed likely to have been infected by a quite different retrovirus, HTLV-1. All these were factors which, in themselves, could have compromised the immune responses. So even if my search was, in the end, unproductive, it provided a useful perspective on the true nature of AIDS.

I also investigated some 20 different theories of origin, trying to find supporting or repudiating evidence for each. Some were fairly easy to disprove—such as those involving intergalactic debris brought in on the tail of a comet, bestiality with farmyard animals, or ill-advised germ warfare experiments. Others took a little more investigation—such as the hypotheses that AIDS began during malaria experiments conducted in the first half of this century, or

when monkey blood was injected as an aphrodisiac by the Idjwi people, based on an island in Lake Kivu. For various reasons, however, it soon became apparent that most of these theories were insubstantial.

However, in the late 1980s, a vital clue had emerged from the field of genetics. The development and gradual adoption of the polymerase chain reaction (PCR) as a laboratory tool meant that it had become possible to identify, and sequence, the individual nucleotides making up simple organisms such as viruses, thus allowing the immediate source of HIV to be revealed. HIV-1, the virus responsible for over 99% of all AIDS fatalities, was found to be genetically closely related to the SIV of the common chimpanzee found in sub-Saharan Africa; and the second human virus, HIV-2, was revealed as being almost identical to the SIV of the sooty mangabey, a north-west African monkey. What remained a mystery was how the simian to human transfers had been effected.

■ 'NATURAL TRANSFER', OR 'CUT HUNTER', HYPOTHESIS

At this stage, there seemed to be only one plausible hypothesis still standing, a hypothesis which soon became widely adopted as almost an official explanation for how AIDS had come into being. The SIVs had jumped the species barrier, it was argued, when chimps and sooty mangabeys had been killed by hunters, and then butchered. On occasions, the skinning and cutting up would have been carried out by hunters who were already bleeding after grappling with their prey, or by others who had cuts on their hands, as is common among those who work in the African bush, and thus monkey viruses had been transferred to human bloodstreams. This hypothesis was sometimes called the 'natural transfer theory', in that it proposed that these viruses had crossed to humans 'naturally', during the process of obtaining food—in this case, monkey meat.

There were inherent problems with the theory, however. The major problem pertained to the timing. My own research into cases which medical doctors had proposed as possible instances of early AIDS had provided no support for the hypothesis that there had been sporadic outbreaks of the syndrome decades before the recognized epidemic. The earliest confirmed case of AIDS caused by HIV-1 involved a young Norwegian merchant seaman who had

travelled to Africa, who showed his first symptoms in 1966, and who (together with his wife and youngest daughter) had died in 1976. For HIV-2, the first recognized AIDS patient was a Portuguese restaurant owner who had lived in Guinea-Bissau, who fell sick in 1974, and died in 1978. Yet Africans had always hunted monkeys and apes and butchered them for the pot, so why had there apparently been no outbreaks of AIDS until the 1960s?

The natural transfer people had a number of different responses to the 'why now?' question, none entirely convincing. The HIVs had always been present in Africa, they said, but before now had never broken free from isolated tribes living in the bush or the rain forest, to infect persons such as European visitors, whose diseases were recorded and tissues stored for subsequent analysis. Probably, they surmised, it was the period of rapid urbanization and new sexual interminglings which coincided with the gaining of independence in the late 1950s and early 1960s, which allowed previously sequestered HIVs to break free from their hearths.

For several reasons, this subsidiary hypothesis seemed implausible. Even after the Slave Trade officially ended in the 1860s, there had been other mass movements of populations within Africa—prompted by internal slavery, by colonial recruiters for plantations and mines, and by French and British generals needful of extra cannon-fodder for the two world wars. And yet, despite these huge movements of peoples within Africa and without, the first retrospective evidence of any of the HIVs was still the blood sample cited by Fleming, which had been obtained in 1959 from an unidentified African man in Leopoldville, now Kinshasa in the Democratic Republic of Congo (DRC). That sample had first been tested, and found to contain HIV antibodies, in 1985, but in the years since then, nobody had managed to come up with a sample of HIV from *before* 1959.

In 1990, when I began my research, there were just two known types of HIV, but nowadays scientists recognize four variants, including three different versions of HIV-1—the main group, Group M (which causes the vast majority of all AIDS cases), and two minor groups, N and O. So if the four HIV variants are indeed *ancient* viruses (as the 25 or so recognized African SIVs would appear to be), this leaves the proponents of natural transfer still seeking to explain why—until the last forty years—the SIVs have apparently only infected members of *isolated* tribes.

Other proponents of natural transfer suggested that it had taken modern medical interventions, such as mass inoculations against yellow fever and smallpox, for the HIVs to spread from body to body on unsterilized needles, to become fully human-adapted (and perhaps pathogenic), and thus to enter their epidemic phase. Again, this seemed possible, but not very persuasive. Extensive smallpox and yellow fever campaigns and 'bum-punching' against yaws (the endemic form of syphilis) had been staged in the British and French colonies of Africa in the 1930s. Many millions of arms and bums had been inoculated, often without proper sterilization procedures between jabs—and yet the first convincing cases of AIDS had not emerged until 30 or 40 years later.

Others again suggested that it could have been the advent in Africa of blood transfusions, or the arrival of disposable needles (which were then recycled rather than discarded), which transferred the occasional SIV from hunter to non-hunter, and thus triggered the various explosions of AIDS. These latter explanations were superficially more credible, in that they related to the period after the second world war. It was unlikely, however, that they could ever be proved—or disproved.

■ VACCINATION HYPOTHESIS

Then, in the spring of 1992, the goal-posts shifted perceptibly. A new theory of origin was announced, and from an unexpected quarter. A Texan journalist, Tom Curtis (1992), had written an article for the venerable rock magazine, *Rolling Stone*, in which he proposed that an experimental oral polio vaccine (OPV) administered in central Africa in the second half of the 1950s might have been linked to the emergence of the major HIV-1-related AIDS pandemic.

I came across a review of the article, but it was several days before I managed to get hold of the piece itself. I read it through once, and was amazed. By this time, I had spent many months following up on the emergence of HIV and AIDS both in the West and in Africa, and I knew that the correlations embraced by the story, especially those between vaccination sites and the subsequent first appearances of AIDS, were even more dramatic than Curtis seemed to have realized. I went out for a long walk on the South Downs, and when I

came back I read the piece again. Then I wrote some letters—both to Curtis and to another researcher, Blaine Elwood, whom he credited as being the author of the theory.

They, in turn, told me about others around the world who had arrived at similar conclusions. Among them were two professors from South Africa, Jenny Alexander and Mike Lecatsas, who had written a controversial letter to their national medical journal back in 1989 about the potential risk of SIV contamination of live polio vaccines.

They also put me in touch with the extraordinary Louis Pascal, a New York-based armchair philosopher who had been proposing almost exactly the same theory since the summer of 1987. Pascal turned out to be a recluse, who communicated only by letter. Whether or not this had militated against him was unclear, but his refreshingly clear and well-argued articles had been turned down by many of the major medical journals. The more rejection he suffered, the more stubborn and determined he became. His latest piece, a 19,000-word treatise trenchantly entitled *What Happens When Science Goes Bad. The Corruption of Science and the Origin of AIDS: A Study in Spontaneous Generation*, had eventually been published at the end of 1991 as a working paper by an Australian university. By the time that I first came across Pascal's extended article, only a couple of hundred people had actually read it, though he encouraged readers to promulgate it *samizdat*-style. These were the days just before the takeover of the worldwide web.

I wrote to Pascal too, and before long received the first of several fat packets in return, containing his responses to my questions and ideas, copies of his correspondence with various scientists and scientific journals, and of a variety of articles and pieces of evidence relevant to his thesis.

Over the months and years that followed, I investigated the OPV/AIDS hypothesis with an ever-growing sense of wonder. For, unlike with other hypotheses (including that of natural transfer), the more information I discovered, the more compelling the hypothesis became. It was, to borrow one of Pascal's own metaphors, like sifting through the broken stones beneath a rock-face. Before too long, one could be fairly sure that the shards dated from a specific era, and represented what remained of a single event, such as the tumbling to earth of a single huge piece of rock. Later, one found that each new

fragment provided a slightly clearer impression of the size and shape of the original boulder. Even if many of the pieces had still not been found, those which had been retrieved fitted together precisely, and allowed one to gain an ever more accurate impression of the missing portion. Furthermore, there were no significant shards which went against the single boulder hypothesis, suggesting, for instance, that the debris had emanated from several different geological eras, or had been dropped off recently by a dumper truck.

This would seem to be a good point at which to summarize the OPV/AIDS hypothesis, and to detail some of the fossil evidence which my field-trips of the last 7 years have uncovered. This particular explanation for the emergence of AIDS goes considerably further than the foregoing theories (of natural transfer plus blood transfusions, or reusable needles), which postulate that Western doctors unknowingly amplified certain simian viruses which were already sporadically present among human groups such as hunters, for the OPV/AIDS hypothesis proposes that it was the hand of man (in fact, once again, the hand of the physician) which was the unwitting agent of the original *transfers* of viruses from non-human primate to man.

Many scientists in the AIDS field have come across the polio vaccine hypothesis, but seem to believe that it has been discredited, disproved. In fact, nothing could be further from the truth. As it happens, it is one of the few hypotheses of origin that is capable of proof, provided, that is, that certain doctors and organizations choose to cooperate.

The hypothesis centres around an experimental polio vaccine known as CHAT, which was developed in the 1950s by Dr Hilary Koprowski, a Polish research biologist who had emigrated to America during the second world war. In May 1957, Koprowski arrived in Philadelphia to take over as director of the Wistar Institute, a small, moribund research establishment that had previously been dubbed 'The Morgue' by local students. Within months, the Wistar prospered, attracting bright young scientists and research grants, and it became a leading player in the race to produce the polio vaccine of choice for America and the rest of the world.

Koprowski's previous position had been assistant director of viral and rickettsial research at Lederle Laboratories in upstate New York, where he had fallen out with his director, Herald Cox, partly over the question of which was the most suitable material in which to

manufacture polio vaccine. Cox, who was always wary of the danger of contaminating simian viruses, had favoured using chick embryos, whereas Koprowski (in common with other leading polio vaccine-makers, such as Jonas Salk and Albert Sabin) favoured a tissue culture made from monkey kidneys. From a practical viewpoint, the latter group was right, for when removed from the influence of the body's immune system and put into glass bottles, these primate kidney cells proved to be the ideal substrate for growing polioviruses.

But the key question from our perspective is the species of monkey that was used. Sabin, whose OPVs have since been fed to hundreds of millions around the world, favoured the cynomolgus macaque from Asia. Salk, whose inactivated polio vaccine (IPV) has been injected into tens of millions of arms, used another Asian monkey, the rhesus macaque. But in his dozens of polio articles of the 1950s Koprowski, rather surprisingly, never revealed which species he used as his vaccine substrate. And although Koprowski's vaccines were fed to some nine million people around the world, they were effectively *experimental* vaccines, in that they were never formally licensed.

■ LIVE ORAL POLIO VACCINE

Because Koprowski's (like Sabin's) was a live polio vaccine, there was no way of guaranteeing that it was free from other viruses, in addition to the weakened poliovirus that was the basis of the vaccine. (The addition of an antiviral agent would have destroyed the vaccine itself.) In fact, by the end of the 1950s some 39 simian viruses had been discovered as contaminants in the various monkey kidney tissue cultures that were used to make polio vaccines. Fortunately, most of these seemed to have no adverse effect on humans, although in 1960 the fortieth virus, SV40, caused a scare when it was found to cause tumors when injected into hamsters.

In short, the scientists of the 1950s were unable to ensure the safety of their live polio vaccines. What they did do was filter them (to weed out harmful bacteria), administer them to various test animals, like rabbits, rats, guinea-pigs and monkeys—and then, if there were no bad effects, they fed them to humans, in gradually increasing numbers.

Koprowski was no exception—save, perhaps for the fact that he

seemed rather more ready than most to proceed to human experimentation. In February 1950, he was the first man in the world to feed a live polio vaccine to a non-immune human—a 6-year-old boy so severely disabled that he had to be fed through a stomach tube. For the next 6 years he continued using disabled children for testing his vaccines, although by 1955 he also began trying them out at Clinton State Farms, a women's prison in New Jersey, where they were fed to more than half of all the babies born to inmates over the next 5 years.

Koprowski's CHAT vaccine has a rather unusual history. He developed it in late 1956 by passing SM, a vaccine he had already produced for Lederle, four times through the human gut. (SM vaccine was fed to a child, and the excreted live virus was extracted from the stools, cleaned, fed to another vaccinee, and so on.) The original CHAT preparation was then fed to two infants at Clinton, without apparent ill effects.

Two months after the first of these feedings, in January 1957, Koprowski and a valued Lederle assistant, Tom Norton, set off for Africa, where they tried to sell their vaccines in Kenya, before moving to the Belgian Congo, where Koprowski had previously helped to establish a large chimpanzee colony at Lindi camp, just outside Stanleyville. Their idea, apparently, was to inject the new vaccine into the spinal columns of five chimpanzees, as an additional safety test. If the chimps failed to develop lesions or paralysis (which was the case), then this would help to prove that CHAT was sufficiently attenuated to be fed to humans. They also proposed to vaccinate the chimps and then challenge them with wild poliovirus—although by then this was known to be a rather imprecise test of vaccine efficacy in humans.

Whilst out in Africa, Koprowski and Norton did not identify their new vaccine by name, and did not, it seems, present themselves formally as Lederle employees. The reason why became clearer in May 1957, when the two men decamped to the Wistar, and the new vaccine—now named CHAT—arrived with them. What this suggests is that in late 1956 and early 1957, Koprowski had not been developing the vaccine for his then-employers, Lederle, but for himself.

At around this time, the vaccine was apparently also fed to the African 'caretakers' at Lindi camp (to protect them from the wild

poliovirus being used there), and to a few persons in Stanleyville itself. Thereafter, the number of African vaccinees increased exponentially. In May 1957 (by which time CHAT had been fed experimentally to just eight of the Clinton infants), the new vaccine was given to nearly 2000 African (and a handful of white) school-children at Aketi, a small town some 250 miles from Stanleyville. It seems that the only monitoring of vaccinees that took place was passive; in other words, none was recorded as having developed serious illness after vaccination. Within the next 8 months there were outbreaks of polio in four small towns in this same north-eastern region, and the Belgian doctors promptly fed CHAT to virtually the entire populations of the towns, some 25,000 people in all.

Then, between February and April 1958, Koprowski's American and Belgian collaborators fed CHAT to a much larger number—215,000—in the Ruzizi Valley that lies between present-day Burundi and the Congo. The main justification for this huge field-trial was apparently to see whether mass-vaccination by mouth was viable as a public health measure. Again, there was only passive monitoring of vaccinees' health (Courtois, 1958).

Over the next 2 years, CHAT vaccine was fed in many different parts of the Belgian Congo and Ruanda-Urundi, the Belgian protectorate that has since become the independent countries of Rwanda and Burundi. In the Congolese capital, Leopoldville, nearly every child aged up to 5 years was fed the vaccine. Altogether, some 320,000 African CHAT vaccinees are recorded in the medical literature of the era.

However, by interviewing doctors, vets, government officials and missionaries who once worked in the Congo, and by searching through Belgian foreign ministry archives and articles in colonial newspapers, I have discovered that between 1957 and 1960 over one million Africans were vaccinated in at least 28 separate campaigns in these three countries.

CHAT was also fed to another eight million children, mainly in Koprowski's homeland of Poland, in Switzerland, Croatia and Sweden, and (on a very small scale) in the United States—but, crucially, different vaccine pools were used in different places. More important still, there is evidence to demonstrate that even when the pool numbers were the same, different batches of vaccine were sometimes prepared in different substrates.

■ SUBSTRATE AT ISSUE

So what substrate, or substrates, did Koprowski use for making the polio vaccines that were fed out in Africa? The only certainty is that the tissue culture involved came from the kidney of a primate of some species or other. In 1991 and 1992, just before and after the OPV/AIDS controversy broke in the mainstream press, Koprowski gave various accounts of the substrate used for CHAT, including claims that his lab workers—such as Tom Norton—had used tissue from the African green monkey, the cynomolgus macaque and the rhesus macaque. In an interview with Tom Curtis, Koprowski said that the kidneys had arrived at the Wistar already excised from the host animal. Since then, the importance of the species has become apparent, and Koprowski now insists that he only used kidneys from Asian macaques (which, of course, are not naturally infected with SIV) (Koprowski, 1992). He has produced no evidence to support this claim.

The crucial importance of the CHAT substrate is highlighted when one examines the first appearances of HIV-1 and the early epidemiology of HIV-1-related AIDS. Outside Africa (in America, the Caribbean and Europe), we see no retrospective evidence of HIV-1 or its related disease prior to 1976. (The sole exception, the Norwegian sailor mentioned earlier, was infected—it has recently been revealed—with one of the minor variants, HIV-1 Group O, which has an apparent hearth in Cameroon and Gabon. Significantly, this man visited Douala in Cameroon as a 15-year-old deck-hand in the winter of 1961–62, and contracted gonorrhoea during the same trip, showing that he was already sexually active.)

By contrast, within sub-Saharan Africa, there are many retrospective traces of HIV-1 (beginning with the Leopoldville blood sample of 1959), and of HIV-1-related AIDS. The great majority of them pertain to the Congo, Rwanda and Burundi. Not only that, but a comparison of the specific towns, villages and rural areas where CHAT was fed, and those places where HIV and AIDS subsequently appeared, reveals some quite remarkable correlations.

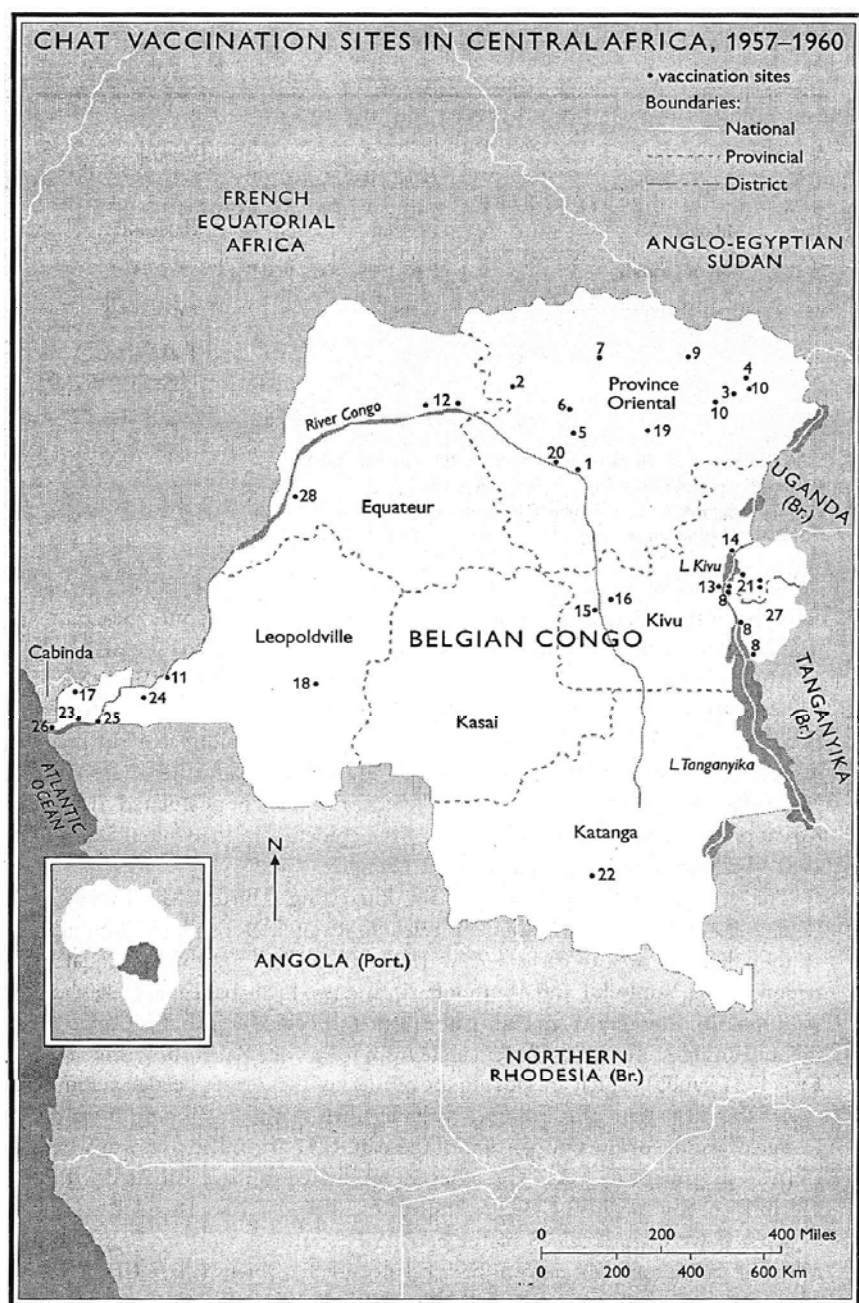
In the years up to and including 1980 (the year before AIDS was first recognized in America), there were 38 confirmed or probable cases of HIV-1-related AIDS from Africa, of which 31 pertain to these three countries, and another four to towns lying close to their

borders. We have an identifiable town of domicile (or else likely town of infection) for 28 of these early AIDS cases, and 64% of them come from towns where CHAT was fed, and 82% from towns within 175 miles of places where CHAT was fed. For a disease like AIDS with a long latency period (which allows more time for an infectee to move away from the site of infection), the synchronicity of time and place is remarkable.

If one looks instead at proven samples of HIV-1-positive blood taken in Africa in 1980 or before, the correlations with the Koprowski vaccine become even more compelling. Over 82% of the 46 positive African samples from 1980 or earlier come from towns where CHAT was fed, and 100% come from places within 140 miles of CHAT vaccination sites (see Figures 1 and 2).

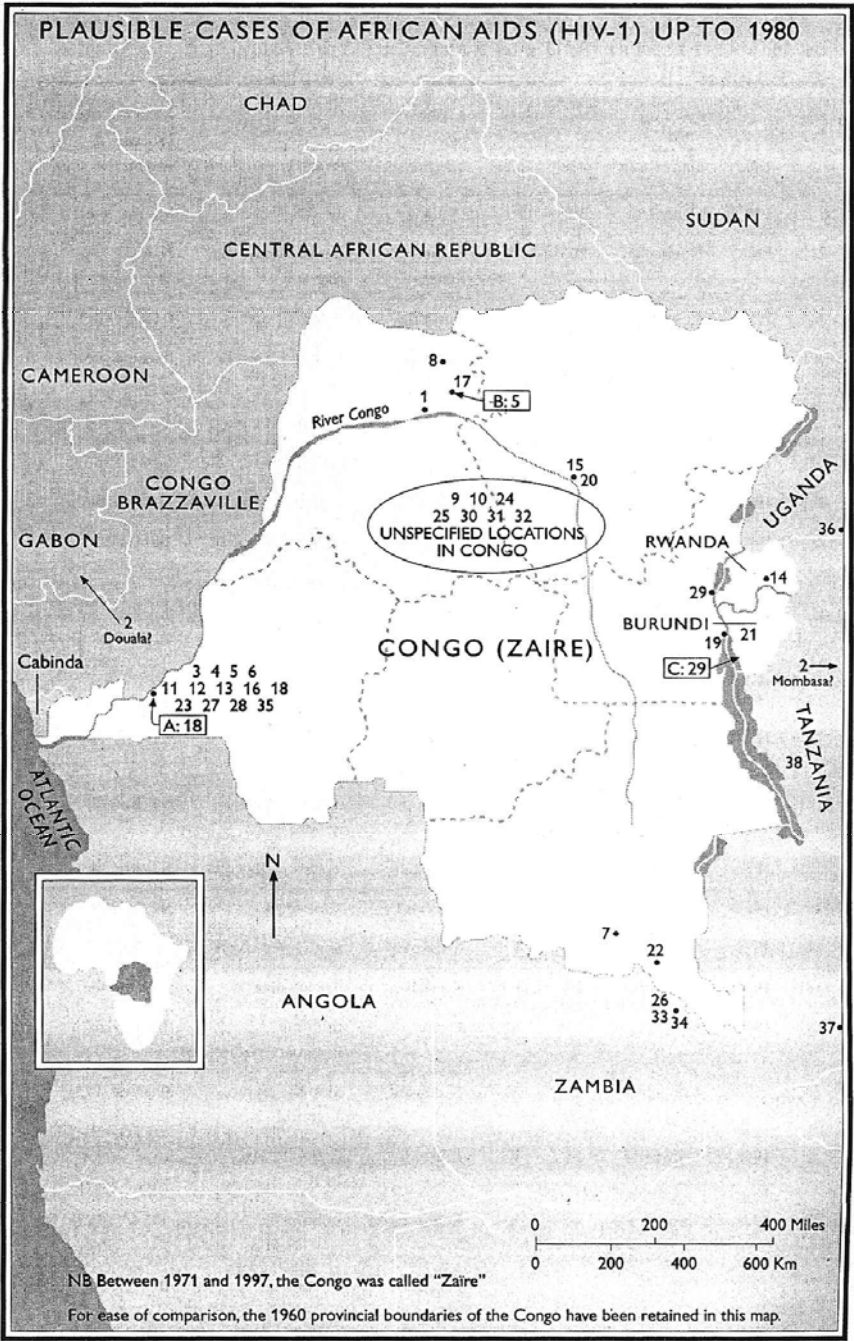
The negative correlations are important too. It seems that no CHAT vaccine was fed in the centre of the Congo, including the whole of one of its six colonial provinces, Kasai, and we see no early instances of HIV-1 infection or AIDS from that area. We can even postulate correlations with specific vaccination campaigns. In the 'Ruzizi valley' trial of spring 1958 (which actually included the shoreline of Lake Tanganyika, though this was not recorded at the time), only the western lowlands of Burundi were vaccinated. A second, more widespread CHAT vaccination took place in Burundi between December 1959 and March 1960, and this included the east and centre of the country. Virtually all the early HIV infections, however, were from the west, the area of the 1958 campaign. (Indeed, sera taken from here in 1980 and 1981 later demonstrated a remarkably high HIV-prevalence for so early in the epidemic: over 8% for the capital, Bujumbura, and nearly 12% for the small lake-side town of Rumonge.)

All of which brings us back to the question of the vaccine substrate, and here we must look again at Lindi camp, which seems to lie at the heart of the CHAT story. Various sources (including the Frenchman who organized teams of pygmies to capture chimpanzees from the surrounding rain forest) have confirmed that a massive total—of some 400 chimps—was involved in the polio studies that were staged at Lindi between June 1956 and February 1958 (Anon., 1958), and yet more chimps in other research conducted in the following two years. And yet nowhere is there anything approaching an adequate record of the experiments and other procedures that



Original drawings by Sally Griffin; these versions (*this page and right*) by Nigel Andrews.

(For full details of vaccination sites, and numbers vaccinated, see *The River*, pp. 742-43.)



(For Key, see p. 101.)

were carried out. Interested visitors from that era (such as a science journalist and a primatologist) say that the camp was shrouded in secrecy—and this secrecy continues to this day. Most of the Belgian doctors involved say that they can no longer recall the details of the research, and the Wistar apparently retains no relevant records. Koprowski, meanwhile, points out that Norton is dead, and says that his own records were lost in a move between institutions.

However, fleeting references in sources such as Belgian government archives, and the abstracts of contemporary polio conferences of the late 1950s, suggest that there may have been a total of three poliovirus experiments carried out at Lindi, involving just under 100 of the chimps. (In hindsight, most of the protagonists concede that these experiments were of questionable scientific value, in that they provided little relevant information that could not have been obtained by similar work in monkeys.) In addition, it would seem that a similar number died in captivity from ‘natural causes’. However, since we also know that virtually all of the 400-odd chimps were ‘used up’ during the period of polio experimentation, this still leaves approximately 200 apes unaccounted for.

Although there is no firm evidence of what happened to the 200 missing chimps, there are some highly suggestive clues. Between January and April 1958, Fritz Deinhardt, a virologist from the Children’s Hospital of Philadelphia (CHOP), was based at Lindi doing research into human hepatitis, and during this period he sent back several shipments of chimpanzee kidneys, so that further hepatitis research could be staged at CHOP in the unusual substrate of chimpanzee kidney tissue culture. Altogether, during and after Deinhardt’s visit, six shipments of chimp kidney were flown to Philadelphia, and all but one proved viable for tissue culture work on arrival (Deinhardt, 1962; Henle et al., 1958–59). The potential significance of this is illustrated by the fact that the Wistar and CHOP were collaborating on several projects during this period, including the polio vaccine research at Clinton prison.

■ CHIMP KIDNEY TISSUE CULTURE?

All this leads to the inevitable question: were chimp kidneys also used as a substrate for growing polio vaccines? In fact, several contemporary sources suggest that they were. The Hungarian who

was in charge of the Stanleyville veterinary laboratory from 1956 onwards, who helped tend to the Lindi chimps, believes that chimp kidneys were sent not only to CHOP, but also to Koprowski at the Wistar. This is apparently confirmed by Tom Norton's widow, who says that when her husband returned from the Congo in March 1957, he was carrying various biological materials including chimp kidneys, and that these were delivered to the Wistar (even though he and Koprowski were officially still Lederle employees).

Other evidence suggests that the Belgian doctor in charge of the Lindi research, Ghislain Courtois, sent chimp kidneys to Belgium in that same year, and that they were intended for tissue culture work. (Furthermore, we now know that roughly 75% of the CHAT vaccine fed in the Congo was made in Belgium, rather than America.) There is also circumstantial evidence suggesting that CHAT vaccine may have been further passed in chimp kidney tissue culture at the Stanleyville medical laboratory that Courtois headed either to amplify stocks or to boost viral titre. It is, in short, not unreasonable to propose that some of the CHAT batches fed in central Africa between 1957 and 1960 were prepared in chimp tissue—either in the US, Belgium or Congo—and that some of this tissue may have been infected with the simian precursor of HIV-1.

Those doctors who participated in the chimp research and who are still alive today speak about the polio experiments with varying degrees of lucidity—and, one suspects, candour. One, for instance, says that he did once try to make chimp kidney tissue culture in Stanleyville—but failed. Another admits that chimp kidneys were sent to Philadelphia for hepatitis research, but says he cannot recall which substrate was used for tissue culture work in Stanleyville (though he adds that it might have been baboon kidneys, which were also locally available). The only scientist directly involved in this work ever to state that CHAT vaccine had been produced in chimp kidney tissue culture (a Belgian doctor who was speaking English for my benefit), retracted a few minutes later, saying that he had meant to say *monkey* kidney tissue culture.

Thus, apart from Koprowski (who has changed his account several times) and his former deputy at the Wistar, Stanley Plotkin (who says that he cannot recall being involved with the CHAT trials in Africa before 1959), nobody is willing or able to state which primate species (singular or plural) was used to manufacture CHAT.

And none of those involved can offer any explanation for the absence of information about the Lindi research; instead, they merely express uneasy embarrassment.

There was a great deal more that slowly emerged in the course of my ongoing research into the OPV/AIDS hypothesis. For instance, the statistical likelihood is that at least a dozen (and maybe many more) of the 400 Lindi chimps involved in polio research would have been SIV-positive upon entry to the camp. We also know that Lindi housed both of the two major chimp species (common chimps and bonobos), and that it was common practice to cage chimps of the same and different species together. The potential implications for onward and cross-species transmission of SIV are obvious. Furthermore, the Lindi researchers recall that many of the bonobos effectively committed suicide by 'turning their faces to the wall' and refusing to eat when they arrived in the camp, and that the remainder were therefore quickly 'used up'. Soon afterwards, an epidemic of *Klebsiella pneumoniae* (nowadays recognized as one of the classic opportunistic infections of simian AIDS) began killing many of the common chimps.

One possible explanation could be that an SIV was transferred from one species to the other, and was then further transmitted within the camp, becoming ever more pathogenic in its new host. It must be added that nobody has yet isolated SIV from a bonobo, but there again very few have been tested. On the other hand, during the last year an increasing number of common chimpanzees have been sampled—and found to be naturally SIV-infected.

Earlier this year, however, a report was published in *Nature* which seemed, at first glance, to confound the CHAT/AIDS hypothesis. In February 1999 a paper by a team of American and British geneticists proposed that all three groups of HIV-1, including the major variant, Group M, had descended from the SIV of *Pan troglodytes troglodytes*, the common chimp sub-species that is found around Cameroon and Gabon, but not in the Congo, where the chimps are *Pan troglodytes schweinfurthii*.

On the other hand, the announcement was based on comparing three isolates of *troglodytes* SIV with just a single isolate of *schweinfurthii* SIV; the latter was slightly less similar genetically to HIV-1 Group M. It should be added that many geneticists are unpersuaded by these latest claims, saying that they are contradicted by strong

epidemiological evidence which suggests that the Group M hearth lies in the DRC, and that *schweinfurthii* SIV may well embrace a wide range of viral isolates, including viruses which are much closer to HIV-1 Group M. The hypothesis in *Nature* will not be disproved, however, until such time as a chimp SIV that is closely related to HIV-1 Group M is found in a *schweinfurthii* or paniscus chimp.

My own hunch is that such an SIV will be found, and that it will come from an animal captured in one of those places in the Congolese rain-forest where the French hunter, Gilbert Rollais, once captured chimps for Lindi. Monsieur Rollais is now dead, but I spent a day with him in 1995, and he gave me a comprehensive list of where and when he conducted his capture operations.

Of course, even if the kidneys of SIV-infected chimps *were* used to prepare certain experimental batches of CHAT, we still cannot be certain that SIV would have been present in the final vaccine. At least two scientific teams have investigated this question in the lab, and both found that SIV did not survive the vaccine-making process. It would seem, however, that the scientists in question used modern-day vaccine preparation techniques, and made no attempt to simulate the far more primitive methods of the 1950s. What we do know is that early tissue cultures were routinely contaminated with white cells such as lymphocytes and macrophages, which are the natural target cells for SIV and HIV. Clearly this aspect of the OPV/AIDS hypothesis could be further investigated, if and when a plausible Group M precursor is identified.

■ CHAT ABSOLVED?

When the OPV/AIDS hypothesis first came to widespread public attention, after Tom Curtis's 1992 article, the Wistar Institute (which had parted company with its long-time director, Hilary Koprowski, a year earlier) convened a committee of six expert scientists to investigate the hypothesis. Six months later, after three or four meetings, these scientists issued a brief, unreferenced report, which concluded that the likelihood of the hypothesis being correct was 'extremely low'. Since then, however, nearly all the arguments advanced by the committee as the basis for this conclusion have been scientifically disproved—most particularly the claim that SIV and HIV are not transmitted orally (they can be, readily), and that the so-called 'Manchester sailor', who fell sick in 1958 and died the

following year, had succumbed to AIDS; (the findings, it is now accepted, were actually based on a lab contamination).

But what of Professor Koprowski—how has he responded to the possibility that his CHAT vaccine may have been the source of the worst pandemic of modern times? At one stage, both he and the Wistar offered to release the one sample of CHAT virus that might be relevant to this period, and which they acknowledge is still present in the Wistar's freezers, for independent testing. However, they have never done so. Nowadays, it is claimed that the quantity is too small to test in two separate labs, even though the Wistar freezer records (of which I have a copy) reveal that there are five millilitres stored—more than enough for 50 such investigations. Not many people expect to find SIV in this sample of the attenuated poliovirus that was used as the basis of the CHAT vaccine, but it would at least be interesting to learn, by DNA analysis, the species used to grow the virus.

Instead of releasing the CHAT sample, Koprowski wrote a letter to *Science*, indignantly proclaiming his innocence—a letter so littered with sloppiness, error and inaccuracy that it has only fanned the flames of controversy. Sadly, instead of trying to provide some evidence to support his position, Koprowski's only other response has been to resort to the courts. He sued Tom Curtis and *Rolling Stone* for defamation, and eventually the publishers decided that it was safer to avoid the possibility of heavy damages by publishing a 'clarification'—a brief, placatory piece that did little more than restate their position that OPV/AIDS was a viable hypothesis. Koprowski likes to refer to this note as an 'apology'.

The AIDS pandemic, which officially began on 5 June 1981 with a brief medical report about an unusual cluster of illnesses among gay men in Los Angeles, is now more than 18 years old. My book on the origin and prehistory of AIDS is just half that age, but in August—after more than 9 years of research and writing—it will finally be published (Hooper, 1999). *The River* is 1100 pages long, and contains over 200 pages of footnotes. I feel proud of it—and, equally, amazed at where this line of research has led me.

At the end of the book, I reveal that other polio vaccines developed by the French virologist, Pierre Lepine, were also administered widely, both before and after independence, in the very areas of western and west-central Africa where the minor HIV variants

(HIV-2 and HIV-1 Groups N and O) seem to have originated. These vaccines were officially prepared in a substrate of baboon kidney, but we know that in the 1950s the French and Americans conducted experiments which involved growing polioviruses in the kidneys of many other African primates—including both chimpanzees and sooty mangabeys.

There is, in short, a real possibility that experimental polio vaccines made in the 1950s and 1960s and administered to populations across west and central Africa, were the agents which effectively introduced all four known variants of HIV to man. In particular, research undertaken in Kisangani in June and July 1999 has provided further evidence to suggest that certain batches of CHAT vaccine were made in chimpanzee kidneys. If these kidneys were indeed SIV-infected, this would help explain the sudden emergence of HIV-1 and AIDS, between the 1950s and the 1970s, in the very places where CHAT was fed in the former Belgian colonies of central Africa.

The family tree of HIV-1 Group M drawn up by geneticists shows a 'star-burst effect', which, according to leading British geneticist Paul Sharp, of Nottingham University, suggests that the virus arrived in humans some time in the mid-twentieth century, and that soon afterwards it suddenly subdivided into some 10 distinct subtypes. Professor Sharp calculates that the original transfer must have happened in around 1940. It is my belief that the star-burst effect has a different explanation, and that it was caused by the virtually simultaneous transfer of several different variants of chimp SIV into humans living in different parts of central Africa, via the CHAT vaccination campaigns. Paul Sharp is a proponent of the natural transfer theory, but he does concede that if several chimp SIVs were transferred (rather than just one), then the transfer event must have occurred rather later in time. Given the research which is presented in detail in *The River*, I would propose the likeliest date as 1957–1958.

I shall leave one final detail for the reader to mull over. Just one of the 10 Group M sub types, subtype B, was not found in Africa until recently, though it is responsible for almost all the HIV infections in North America, Europe and Australasia. So how and where did this Euro-American subtype originate? There is an intriguing possibility that the first HIV-infected person in America was a

promiscuous 16-year-old intravenous drug user who gave birth, in 1973 or 1974, to a baby who died of AIDS (confirmed retrospectively by HIV serology) in 1979. The mother, who was apparently immunocompromised at the time of the birth, lived in New Jersey, just 50 miles from Clinton. She herself was born between 1956 and 1958. Is it possible that she herself was a Clinton infant, who was fed an early version of CHAT? If so, is this the source of subtype B?

■ ENQUIRY NEEDED

There is not yet concrete physical evidence to prove the OPV/AIDS theory—even if the anecdotal and circumstantial evidence is now highly persuasive, according to many of those who have read *The River*. I and the publishers hope that the scientific establishment—and in particular its AIDS researchers and journal editors, many of whom have, until now, shown an unseemly desire to brush the theory under the carpet—will now be encouraged to initiate an independent investigation. Various possible lines of enquiry are suggested at the end of the book, and I have pledged to provide whatever assistance I can, if asked to do so. Among the items of documentary evidence, I have cassette recordings of all the key interviews.

Eighteen years have passed since the AIDS epidemic began—or since we knew it had begun. Perhaps now that much of the craziness and panic about AIDS is behind us, it is an appropriate time to return once more to that vital question about origin, and to see where the answers lead us. And perhaps this time we can examine the arguments without prejudice, without self-interest and without fear.

[Editors' note: The above was written in July 1999. The following text is an extract from an article which submitted to *The Lancet* in mid-September 1999, nearly three weeks after the release of *The River*, but rejected for publication.]

■ ON THE DIFFICULTIES OF RIVER EXPLORATION

Presenting a seriously challenging and controversial idea to the scientific community is not an easy process, especially when one comes, as I do, from outside that community. Over the past few weeks, since the publication of my book, *The River*, it has at times been a hard row upstream.

It is perhaps not surprising that many scientists react strongly to the polio vaccine hypothesis. Depending on experience and character, they tend to find it profoundly disturbing, challenging, threatening, or even offensive. Some are tempted to reject it out-of-hand.

Since *The River* was first released in late August, there have been several objections raised on and off the record by scientists, some of whom have not seen or read the book. It is worth reviewing these objections, and seeing whether they hold water.

- That CHAT vaccine was also fed to millions in Europe (for instance in Dr Koprowski's native Poland), without causing early outbreaks of AIDS there. Although this is correct, fewer than 5000 European children were fed with the same CHAT pools (10A-11, 13 and DS) that were fed to one million persons in Africa. Furthermore, it can be proven that different CHAT vaccine batches from identically numbered pools were produced in different laboratories and with different substrates.

- That the CHAT hypothesis fails to explain the other outbreaks of AIDS associated with HIV-2, and with HIV-1 Groups O and N. In fact, there are potential links between all three of these minor outbreaks and experimental polio vaccines which were administered in the former French colonies of west Africa and west central Africa (the apparent hearths of these minor outbreaks), starting in 1957. There is evidence that both chimpanzees and sooty mangabeys, the primate hosts to the immediate ancestors of HIV-1 and HIV-2, respectively, were present together with baboons (the species officially used for production of the French polio vaccines), in the monkey holding centres of Francophone Africa. Sometimes they were held in the same cages.

- That the CHAT hypothesis has fingered 'the wrong chimpanzee'. Early in 1999, an eminent group of microbiologists, led by Beatrice Hahn and Paul Sharp, announced that they had worked out the origin of AIDS (Gao *et al.*, 1999). They claimed that all three HIV-1s (Groups M, N and O) were descended from the SIV found in a particular chimp sub-species, *Pan troglodytes troglodytes*, the range of which embraces Cameroon, Gabon and Congo-Brazzaville, in west central Africa. They asserted that the SIV of *Pan troglodytes schweinfurthii* (the chimp sub-species found around Kisangani/Stanleyville) was only more distantly related to HIV-1.

However, several virologists and geneticists are known to dispute

this hypothesis. They feel that although Hahn's case is persuasive for the minor HIV-1 groups, O and N (which have a clear epidemiological hearth in west central Africa), it is anything but persuasive for the pandemic variant, Group M. For one thing, Hahn's team has based its case on phylogenetic comparison with the sole existing SIV sequence from a *schweinfurthii* chimp, the provenance of which is uncertain, and which may well be atypical. For another, the early epidemiology of HIV-1 Group M clearly suggests a hearth in the former Belgian colonies of central Africa. We need to sample further *schweinfurthii* chimps from the Congolese rain forest for SIV before leaping to conclusions about the origin of Group M. We also need to sample pygmy chimps (*Pan paniscus*) from the rain forests to the south of Kisangani, to see if this species also carries its own SIV—for *Pan paniscus* was the other primate species held at Lindi, often in the same cages as *Pan troglodytes schweinfurthii*.

● That the date proposed in *The River* for the iatrogenic introduction of the Group M precursor (1957–8) is too recent to explain the first human isolate of M, which comes from an African male bled in the Congolese capital, Leopoldville (now Kinshasa), in 1959. However, the Leopoldville sequence is clearly not far from the base of the Group M tree. Furthermore, after reading *The River*, a leading retrovirologist told me that he believes that both the routes of transfer proposed therein (either a single, or multiple arrival in humans from SIV-infected chimpanzee[s], via an oral vaccine) 'are indeed consistent with the phylogenetic evidence'.

● Some have opined that *The River* is too long: how can anyone be expected to read such a tome—of 1100 pages, including nearly 200 of footnotes? In fact, it was precisely because of the controversial nature of the central premise, and its far-reaching consequences, that the American and British publishers (Little, Brown and Penguin) agreed to publish a book of such unusual length. Knowing how provocative the theory would be for many scientists, it was felt to be vital to present the arguments comprehensively and clearly, and to include sources that could be verified and checked. This way, the publishers would still have the option of bringing out an abbreviated version, without footnotes, in a few months' time.

Some parts of the medical establishment may have been less than even-handed in their treatment of the polio vaccine hypothesis. Over

the last 12 years, a leading scientific journal, *Nature*, has rejected at least six articles on the subject submitted by different authors, many of them eminent in their own fields. These have included an 'extraordinarily eloquent' submission by the evolutionary biologist and Royal Society professor, Bill Hamilton. Various reasons have been given by the editors of this journal, ranging from '[the theory] does not seem to match the epidemiology of AIDS' (an extraordinary claim, even in 1987) to 'we have devoted considerable space to the topic you address'.

Meanwhile, Dr Koprowski's lawyers have threatened those who expound this hypothesis with litigation (Martin, 1996). Dr Koprowski, for his part, no longer advocates releasing the remaining CHAT samples for independent analysis, and neither has he offered to release any remaining papers which are relevant to the period. Despite his claim that all such papers were lost in a move, the circumstances of that loss appear to be confusing, and it is apparent from the materials provided to the investigating committee in 1992 that some documents, at least, do still exist.

It is important to emphasize that my analysis is not a witch-hunt against Dr Koprowski, the Wistar Institute, or the Belgian doctors and institutions who helped perfect CHAT. Back in the fifties, they were engaged in a race to produce a safe and effective polio vaccine—one that would save lives not just in America and Europe, but the world over.

But this *is* a call for an investigation into how the vaccine was produced. And it is also a call for greater transparency in science. For if this terrible, tragic mistake was indeed made, then how significant is it for scientific developments looming just over the horizon—for xenotransplantation initiatives, and for those who advocate testing live, attenuated AIDS vaccines in the open community? As Victor Grachev, one of the great Soviet virologists and polio vaccine researchers of the fifties told me: 'In Russia we have a very good [saying]. You should seven times ... check [if] it's good or not. And only one time cut. Because after you cut, it's impossible to [put it back together again]'.

■ POSTSCRIPT, ADDED BY THE AUTHOR IN FEBRUARY, 2000

In the end, there has been an interesting reaction to 'The River', and the debate—and controversy—seem to be growing as time passes.

Between September and November 1999, there was an escalating response to the book in the popular and the scientific press.

Most important were the five reviews in major scientific journals. The first of these, in *'Nature'*, was a huge disappointment, in that after praising the book in general terms, it attempted to destroy the hypothesis, but my misrepresenting several of the book's arguments. However, it was written by Dr John Moore of the Aaron Diamond AIDS Research Centre, who, just one month earlier, had been opining on the Internet that 'The polio vaccine theory of the origin of AIDS is something that is only believed in by the lunatic fringe ... It is sheer unadulterated nonsense, and not worth a moment of a serious scientist's time.' Moore further referred to the theory's adherents as 'madmen/madwomen'.

Fortunately, the four scientific reviews that followed (in *Science*, *Nature Medicine*, *The Lancet* and *New Scientist*) were a great deal more balanced (and positive), and had clearly been written by people who had taken the trouble to read the book, and examine its arguments. Whether or not the reviewers were themselves persuaded by the hypothesis, they all acknowledged that it was plausible, and needed to be put to the test. A very warm article in *The New York Times* followed, which sparked a fortnight of generally favourable US press coverage.

At around this time, I deterred a group of AIDS activists who had been planning to demonstrate outside the Wistar Institute and the NIH about the continued failure to test the CHAT samples, because I feared that sensationalising the issues would only deter scientists from examining them openly and fairly. This approach appeared to pay dividends. The debate broadened, and by the new year it had spilled onto the letters pages of *'Science'*. By this stage, the majority of English-speaking scientists and physicians, especially AIDS researchers, appeared to be familiar with the book and its central hypothesis. It had engendered a genuine debate, which was exactly what I had hoped.

In practical terms, there have been several repercussions. The Wistar expert panel has been reconvened in order to supervise the testing of CHAT poliovirus and polio vaccine samples (though certain details, such as which samples are to be tested, remain a topic of some concern). Several scientists have offered to help in other areas, by carrying out tests such as those suggested in the book's

appendices. Others, notably Oxford biologist Bill Hamilton, have been busy sampling from chimps and bonobos in the central African rain forest around Kisangani, to see whether there is evidence of SIV infection there, and—if there is—to evaluate how close the viral sequences are to HIV-1 Group M.

Perhaps most importantly, there is to be a two-day conference about the origins of HIV and AIDS which will be held at the Royal Society in London in May 2000. Scientists from all sides of the debate, and members of the great and the good from different scientific fields, have been invited, and there has already been a very good response. The proceedings and discussions will be published.

There have also been some important recent developments. Since the beginning of January, further articles have been published supporting Beatrice Hahn's claim that the AIDS pandemic started when a *Pan troglodytes troglodytes* (Ptt) chimp infected a human in French Equatorial Africa. These articles ignore the fact that there is still not nearly enough evidence about chimp SIVs for us to determine, with any degree of certainty, which chimp species or sub-species, or which group within that sub-species, was host to the Group M ancestor.

The debate about the timing of that mooted event has also heated up, following a presentation made by Dr Bette Korber at a conference on retroviruses at the beginning of February. She apparently used 'the world's fastest super-computer' to come up with an introduction date of 1930, plus or minus 20 years, which of course places it just before the African CHAT trials. However, her conclusions are once again predicated on the assumption that there was a single chimp-to-human transfer, and her calculations make no allowances for recombination, which is now known to be a crucial element in SIV and HIV evolution.

The alarming element has been the way in which these theories have been presented. When talking to the press after her presentation, Korber claimed that her findings rendered the OPV theory 'highly unlikely', which is a considerably different interpretation to that which she—and colleagues—had been indicating to me in private. Given the fact that her research (however painstaking) involves a purely theoretical approach which is based on various prior assumptions, her statement is—to my mind—both irresponsible and misleading. Hahn's assumptions about a *Pan troglodytes*

troglodytes source for all the HIV-1s represent a similarly regrettable over-statement, given our present state of knowledge. (This is widely conceded by other geneticists and virologists, but relatively few are willing to state their disquiet publicly.)

Later at the press conference, Stanley Plotkin, Koprowski's former deputy at the Wistar, told reporters that there were no records remaining about how CHAT vaccine had been made, but reiterated that no chimp tissues had been used. Again, given the fact that, by his own account, he was not involved with the early African trials of CHAT in 1957–58, and that he would not have had direct knowledge of vaccine preparation techniques in Belgium, where 75% of the African CHAT batches were produced, he would appear not to be in a position to provide such a sweeping assurance.

What I find disturbing about all this is that it represents science by press conference. In the bid to present the information in an accessible form for the media, statements get ever more simplified, claims ever more grandiose. This, I would propose, is not the best way to arrive at the truth. Shortly after the Korber speech, Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, the man effectively heading AIDS research in the US, was going several steps further, opining that Korber's findings would 'end any speculation about a link between the HIV-1 pandemic and the African polio vaccine initiatives, "... at least among scientists".'

A sweeping statement, and yet one which says a great deal more than it might at first seem.

Ed Hooper, 3 February 2000.

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Key to map, 'Plausible Cases of African AIDS up to 1980', p. 87.

Numbers 1 to 38 denote plausible and confirmed African AIDS cases up to 1980. For full details, see *The River*, pp. 746–47.

Seropositive for HIV-1 antibodies or antigens up to 1980/1:

A: Kinshasa (1959: 1; 1970: 2; 1980: 15)

B: Yambuku (1976: 5)

C: Burundi (1980: Bujumbura, 16; 1981: Rumonge: 8; Kihanga: 3; Muramvya/Ijenda: 2)

In addition to the 39 HIV-1-positive blood samples through 1980 detailed here, there are seven instances of HIV-1-Group-M-positive blood pertaining to specific locales detailed in the main AIDS table, from cases 6, 8, 14, 15, 18, 19 and 27. This makes a total of 46 HIV-1-positive samples by the end of 1980; all 46 come from within 140 miles of CHAT vaccination sites.