CHAPTER 14

BILL HAMILTON'S INVOLVEMENT WITH THE OPV THEORY

'Medical Science's most Hated Hypothesis'

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I knew Bill Hamilton for the last six years of his life, and our relationship was almost exclusively based around a mutual interest in how the AIDS pandemic began.

It was also, however, an intensely personal relationship–so much so that after his death, I was for some time unable even to mention his name without weeping. The reasons for that are many, but in retrospect, I believe they mainly involve certain qualities of his which I find both exceptional and moving—his lack of hubris, his searing honesty and his intellectual generosity.

By the time Bill and I first met, in September 1993, I had been working on AIDS for seven years, and researching its origins for three. By 1992 I had done enough literature research into the earliest evidence of HIV-1 and AIDS to know that the pandemic epicentre was located in the African countries formerly administered by Belgium—the Democratic Republic of Congo, Burundi and Rwanda, rather than in Uganda, Gabon (and even Haiti), as was then being proposed in scientific journals.

I also knew that almost all of the theories about the origins of AIDS were unsustainable. The only apparent exception was the hypothesis that the virus had entered humankind when African hunters or market-sellers had killed, or butchered, an animal infected with the simian immunodeficiency virus (SIV)

that was directly ancestral to HIV-1. By 1990, it was known that the probable host of this immediate ancestor was the common chimpanzee, *Pan troglodytes*. The main problem with this 'cut hunter' or 'bushmeat' hypothesis of origin involved the timing. A second AIDS virus, HIV-2, had been discovered in West Africa, and the absence of these two viruses from North America and the Caribbean before the 1970s strongly suggested that neither virus had existed in Africa during the time of the Slave Trade. So why had two AIDS epidemics evolved since that trade ended in 1865, when Africans had been eating chimps (and sooty mangabeys, the ancestral host of HIV-2) for millennia? It seemed possible that the Hand of Modern Man might have been involved.

In 1992, I first heard about another theory, one initially proposed by Louis Pascal, an armchair philosopher from New York. Pascal had been amazed to learn that polio vaccines had been routinely grown in primate kidney cells, and further research revealed an oral polio vaccine (OPV) called CHAT, developed by the Polish-American scientist, Hilary Koprowski, which had been tested on a million 'volunteers' in the Belgian colonies in the late 1950s.[1] Pascal came to an amazing conclusion—that CHAT vaccine was responsible for the arrival in *Homo sapiens* of the precursor virus of HIV-1, and therefore for the birth of AIDS. He sent carefully written papers to many eminent scientists, most of whom didn't reply, and to several scientific journals, all of which rejected them. His powerful essay, 'What Happens When Science Goes Bad',[2] eventually had to be published as a 'working paper'.

The only considered response to Pascal had come from Bill Hamilton, and I decided to seek an interview with the one major scientist who seemed to take the OPV theory seriously. Bill lived up to my vision of the eccentric genius—a shock of white hair; a house littered with papers; a shy, self-effacing manner; and a gift (when he did speak) of describing important ideas in accessible language. By that stage, I had interviewed several hundred scientists, and immediately recognized that here was someone special, in terms of both breadth of knowledge and clarity of reasoning. I told him about my research, and he made his responses, sometimes simple and sometimes profound, but always based on a bed-rock of sound judgement. That first meeting lasted eight hours, and a bond was forged between us. We became partners in pursuit of the putative iatrogenic event at the source of AIDS.

There were many factors that fired this search, but one was key. Koprowski had been testing CHAT at Camp Lindi, a huge colony of chimpanzees and bonobos sited just outside Stanleyville (now Kisangani). To Bill and me, the coincidence between the world's first mass trials of OPV,

its earliest cases of HIV-1 and AIDS, and perhaps its largest chimpanzee colony seemed too significant to ignore.

By the end of our second meeting, on New Year's Eve, 1993, I felt I knew Bill well enough to ask a sizeable favour. Knowing that he had recently won several major scientific prizes, and having finally exhausted both my own savings and the largesse of my parents, I asked him whether he could lend me the money to make the two remaining research trips (to the US and Belgium) that I felt were needed before I could start writing my book. Bill asked for a breakdown of the costs and then, without further hesitation, wrote me two cheques totalling £2,000, adding that he would like me to consider these as a grant, rather than a loan. (Much later, after the deaths of my parents, I tried to repay Bill—but my letter was found in his papers after his death, with the cheque still inside. He had decided to ignore it.)

The next month we visited Stockholm to see Hans Wigzell, the head of the Karolinska Institute, where I had discovered that some unopened vials of 1958 CHAT vaccine were stored in the freezers. Professor Wigzell agreed to our request to have them tested for the presence of HIV and SIV, but declined to release any portion of the samples to us, to test for the mitochondrial DNA of the primate cell substrate.

Later that January, Bill prepared a long letter to *Science*, in which he sought a fairer hearing for the OPV theory. The letter was rejected, so Bill wrote a follow-up letter to the editor, Dan Koshland, further pleading his case. He was told that he was 'superbly qualified to comment' on this issue, but still *Science* declined to publish. Bill was sent copies of sections of the referee's reports, which revealed that one referee had highlighted 'the possibility of local contamination [of OPV] by chimpanzee tissue in Central Africa', an eerily prescient suggestion. Nevertheless, he voted against publication, and against the testing of CHAT samples (on the grounds that even if found positive, they would only prompt a lawsuit—and that scientists were already well aware of the dangers of potential iatrogenic disasters). Details that feature in this referee's report reveal that the author can only have been the eminent British retrovirologist Robin Weiss.[3,4*]

Bill then submitted a similar, but stronger, letter to *Nature*, which was also rejected.[5] I have recently learned that for many years, major AIDS submissions to *Nature* have been routed through Robin Weiss, so it seems that he may have been involved in a two-fold rejection of Hamilton's plea.

* See section 5(b) in reference 4.

In January 1995, the Karolinska faxed Bill their findings: the CHAT vials were negative for immunodeficiency viruses. However, one intriguing detail was highlighted, for both the original 1958 vaccine from the Wistar, and further vaccine that had been prepared therefrom in cynomolgus cells at the Karolinska in 1963, were described as 'CHAT pool 10A-11'. The truth dawned slowly. Pools (or lots) of OPV represent material prepared at a certain level of attenuation, but it is the specific batches prepared from those pools that are homologous—not the pools themselves. Different batches of CHAT pool 10A-11 had been prepared at different times, in different labs and (it seemed) in different substrates. It was the history of the batches, not the pools, that was crucial. It was therefore not legitimate to argue—as some had—that a pool of CHAT fed in Africa must have been uncontaminated, because the same pool had been fed without problems in Europe.

Over the next four years, Bill and I were in contact by phone or letter every few days. In addition, about once a month I would drive up to Oxford, or else (more occasionally) he would visit me in West Sussex, and later Somerset. It did not then strike me as remarkable that whenever I called, he always had time for me. But amidst all the serious talk, we also had the odd bit of fun. When I told him that one of the Belgian doctors recalled vaccinating along the eastern shore of Lake Kivu, and remembered seeing the clouds changing colour to russet when they passed above the volcano of Mount Nyiragongo, Bill spent some hours analysing maps and the curvature of the earth, to try to determine where my witness might have been.

In 1996, we collaborated on a letter to the *Lancet* that attempted to unravel the mystery of the so-called 'Manchester sailor' (an apparent AIDS case from 1959). There seemed to have been lab contamination, but we were still unable to explain how four of six tissues from the case, and none of six from the control, had tested HIV-positive in the original double-blind study.[6]

Bill also helped greatly as I began writing *The River*, providing not only a fine foreword, but also some suggestions for the opening sentences of text, inspired by the book's title. They show something of his love of the natural sciences, and of his clarity of thinking, and I adopted them almost wholesale.

> What is a source? Where does a river begin? In this valley is a spring, but higher up the hillside lies a dripping rock. . . . . That ultimate source on the ground is almost never easy to identify, and some would say the search is meaningless. But the resulting geography—the nick in the hillside, the steep-edged valley, the mature river, the floodplain, the estuary—although it never ceases to evolve, remains firm enough to allow description on maps. These features are the visible consequences of that tiny source, and it is these that make their immense impact on humanity.[7]

What I found most remarkable about the foreword he wrote for *The River* was the extent to which he was prepared to allocate responsibility for the genesis of AIDS. From the opening words ('Every time two people put their heads together, Truth suffers . . .'), he weighed in against his fellow-scientists, against pharmaceutical houses, and against governments.[8] He spoke with conviction and quiet anger, and went further than I was then prepared to go.

Not all his peers liked the foreword. Shortly after Bill's death, Robin Weiss told me he considered it 'bullshit'. At that stage I too had some misgivings, partly about Bill's range of targets, and partly because of the praise he had lavished on me. Now, however, in 2005, I find his central argument a marvellous piece of reasoning, one that shows the fearlessness and foresight that evolved from his years of lonely study of biological processes.

Shortly before *The River* was published in September 1999, Bill and I made our one and only safari together, spending ten days in the breathless humidity of Kisangani, Democratic Republic of Congo (DRC), where the *Laboratoire Medicale de Stanleyville* (LMS) had coordinated the 1950s CHAT trials, and ten miles from Lindi camp, where some 400 chimps had been utilized as the scientists 'put the finishing touches' to CHAT vaccine.

The journey was a success in terms of research, but a personal disaster, for we had three volcanic arguments. In the end, Bill largely concentrated on collecting faeces from pet chimpanzees to test for SIV, and I on trying to discover more about the history of the LMS and Lindi camp. Yet I have many fond memories of his Congolese exploits. Bill rushing, vortex-like, across the hotel courtyard to greet a fresh arrival of banana leaf-wrapped chimp shit, with passport, notes and money spinning in his wake. Bill astonishing a large crowd beside the Congo ferry crossing, by whipping out a butterfly net and executing a series of startling manoeuvres in pursuit of an especially glorious specimen. Bill, surrounded by children, inventing a drawing game in his notebook which prompted whoops of delight. And the two of us returning in a huge motorized dug-out from the site of Lindi camp, now overgrown by rain forest, but still heavy with significance and collective memories. We sit in facing plastic armchairs, watching the banks of the Congo idle past, as he explains the evolutionary similarities between the strangler figs of the Amazon and Congo basins. The common denominator of all these memories is the sometimes unworldly, but always single-minded, scientist.

Bill's uncompromising approach to travel included an unwillingness to rely on pharmaceutical products, and he refused anti-malarial prophylaxis; not surprisingly, he contracted the disease. (He felt that the best way to fight illness was to experience the worst, and build up natural immunity, but

there was also something stubborn and old-fashioned here: a true explorer does not complain. I found his disregard for his personal safety quite at odds with his professionalism as a scientist.) The last image I have of Bill as an active player in life is of an ashen man standing alone at the baggage belt at Heathrow, awaiting the emergence of his battered rucksack.

The trip scarred us both, but the months that followed eased the hurt. Bill was as happy as I about the burgeoning, and largely positive, response to the publication of *The River* in the UK. At the end of November, after three months of silence in the US, the *New York Times* published a lengthy article,[9] and suddenly all the news media were phoning. At my request, Bill did an interview with CNN,[10] in which he once again stated his position on OPV/AIDS . . .

> It's not only the origin of AIDS which is in question here, it's also the conduct of Science towards this hypothesis, which has been one of almost paranoid rejection . . . I think I would not exaggerate to describe it as medical science's [most] hated hypothesis.

Sadly, I was never again to speak with Bill in person. I planned to see him just before he flew back to the DRC in January 2000 (this time to collect faeces and urine from wild chimps), but my car broke down. He called once briefly from Kisangani by satellite phone, but the next news I heard was that he was comatose in a London hospital, having collapsed from a massive intestinal haemorrhage the day after his return. Once again he had contracted malaria, this time the cerebral variety, and although he had apparently recovered by the time he returned home, it may be that the strain which this placed on his system exacerbated a pre-existing gastric condition. Whatever the precise cause of death, those who loved him were incredulous. I spent half a day with him in hospital, holding his hand, and telling that great still body the latest news on the debate. But this time, when I paused, there was no quiet, reflective response, no impish smile.

All February I was racing to complete a new postscript to the book, and it was arranged that once I finished, I would come up to see him one final time. I was working on the penultimate footnote on the morning of March 7th when the phone rang, and his long-time partner, Maria Luisa Bozzi, told me the sad, but not unexpected news.

At the funeral and the remembrance event there were tears, but also power struggles taking place in the wings. Some of Bill's former colleagues, embarrassed by his involvement with the OPV theory, began to propose that

he was merely an open-minded scientist seeking to test a rather far-fetched hypothesis. It was largely because of Luisa Bozzi that this position was unable to take hold. She read through his personal and professional letters, and at the Lincei conference in September 2001 gave a moving and powerful speech in which she confirmed that Bill was '95% persuaded' that the OPV theory had merit.[11] In reality, during his final years, Bill was intensely involved with OPV/AIDS research, and he effectively risked his life in order to collect more of the hard data which, he felt, would support the hypothesis.

Shortly before that final safari, Bill had persuaded both the Royal Society and the *Accademia Nazionale dei Lincei* (in Rome) to stage conferences at which the origins of AIDS could be debated. The co-organisers of the London conference, Robin Weiss and Simon Wain-Hobson, took over sole responsibility after Bill's death. They managed to keep the conference on track (not an easy thing, since while Bill was still comatose a campaign had been waged, mainly by American scientists, to declare the debate one that damaged Science, and to persuade others not to attend. Two of the principal supporters of the bushmeat theory, Beatrice Hahn and Bette Korber, simultaneously withdrew, while Koprowski's former deputy at the Wistar, Stanley Plotkin, implied that he and Koprowski might join them.) After Bill's death all these scientists came back on board, but at a price. Two extra speakers were allowed to the anti-OPV camp, while I was refused the chance to nominate a full speaker to replace Bill.

Many attendees felt that the conference was far from the level playing field that had been promised, but instead afforded a prepared stage for an official refutation of the OPV theory, focusing on the half dozen samples of CHAT vaccine that Koprowski's Wistar Institute had belatedly released for independent testing—which were found negative for HIV, SIV and chimpanzee DNA. But there was more. A team led by Stanley Plotkin had approached many of the scientists I had previously interviewed, and obtained signed statements from some that contradicted their previous, tape-recorded statements on key issues. (Later I discovered many instances of improper approaches being made, including one case in which a witness was badgered to sign a prepared statement which was patently untrue.)[4*] Robin Weiss also played an unwelcome role, for his closing speech was frankly biased. He implied that the theory had been fatally wounded, and not unexpectedly, the press followed his lead.[12,4†]

* See section 5(e) of reference 4.
† See section 5(d) of reference 4

Seven months later, the world's two leading scientific journals, *Nature* and *Science*, took the unusual step of reporting simultaneously on what was termed new phylogenetic dating 'evidence', and test results from another sealed vial of CHAT, again originating from the Wistar. Weiss claimed incorrectly that this CHAT material was from the same batch that had been used in Africa (when it was merely from the same pool),[4*] and concluded his *Nature* commentary: 'Some beautiful facts have destroyed an ugly theory'.[13] *Science* headed its commentary 'Disputed AIDS theory dies its final death'.[14] This blanket rejection of the theory had an enormous impact, and most neutral scientists and lay persons now seem to believe that the debate is settled.

But on what grounds have the OPV sceptics reached their conclusions? They have five main arguments: that local chimps are not infected with SIV; that local chimps are not infected with 'the right SIV'; that chimp tissues were never used to make the vaccine; that phylogenetic dating indicates that HIV-1 predated the OPV trials; and that there is anyway no correlation between the CHAT feedings in Africa and the first appearances of HIV-1 and AIDS.

I believe that each of these arguments is flawed, and that recent scientific and historical findings actually offer very strong support to OPV/AIDS.

Simon Wain-Hobson, who had agreed to collaborate by testing the samples of chimp faeces and urine that Bill collected on his two trips to Kisangani, has sadly never reported the details or results of his SIV testing. Furthermore, he has failed to make any sensible response to the five detailed e-mails I have written to him over the last four years, requesting feedback on his findings, or else that he release the samples so that others can do the work. Given how much Bill invested in this research, I think that Wain-Hobson's performance has been disappointing. Beatrice Hahn, another committed opponent of the OPV theory, was given aliquots of these samples in 2001, and she repeatedly found protein bands typical of SIV. However, she did not report these findings (which ran counter to her general hypothesis) until 2004, when they appeared in a brief communication in *Nature* entitled (misleadingly, to my mind) 'Contaminated polio vaccine theory refuted'.[15,16]

Hahn's findings indicate that chimps from one of the very sections of the DRC rain forest where Lindi chimps were collected are SIV carriers, and Paul Sharp has also reported that 13% of a single wild troupe of this same subspecies were SIV-infected.[17] If that percentage applied to the 400 chimps used during the Lindi polio research, then approximately 50 would have

[*] See section 4(a) of reference 4.

been naturally SIV-infected before arriving at the camp, where co-caging of pairs and groups was routine. However, Hahn and Sharp also argue that the Lindi chimps are from the 'wrong subspecies', pointing out that the very closest HIV-1 relative discovered to date comes from a *Pan troglodytes troglodytes* from Cameroon or Gabon, rather than a *Pan troglodytes schweinfurthii* from DRC.[18] This is true, even if relatively few chimpanzee SIVs have so far been sequenced, and even if it leaves Hahn having to postulate an infected chimp-hunter who failed to spark AIDS in Cameroon or Gabon, but who migrated hundreds of miles southwards to spark infection in the HIV-1 epicentre in the DRC. However, one of the 54 Lindi chimps for which there are surviving records came from Mbandaka territoire in the west, which is as near to the range of *troglodytes* as *schweinfurthii*. This animal spent over two years at Lindi, and clearly could have introduced a *troglodytes* SIV to the camp. But perhaps it didn't need to. Because exactly the same genes are found in HIV-1 and in chimp SIV (whether *troglodytes* or *schweinfurthii*), a recombination event looks to be the most parsimonious explanation for bridging the genetic gap between the chimp and human viruses.

The official reason for Lindi camp was to test the susceptibility of chimps to orally administered poliovirus, and to safety test the Koprowski vaccines by intraspinal inoculation, but Koprowski's group mentioned these tests in conference discussions in 1959, revealing that only 89 chimps has been involved.[19] In reality, the chimps served other purposes too, as I discovered during a second visit to Kisangani in April 2001, when I conducted further interviews with the surviving Lindi 'caretakers'. They confirmed that almost all the chimps had been sacrificed, with blood and organs frequently being obtained from anaesthetised chimps, just before sacrifice. (The significance is that the best method for preparing tissue culture, for instance for vaccine cultivation, involves removing organs from living animals.) I also interviewed several technicians, former workers at the LMS, who reported that tissue culture had been mainly prepared from chimpanzees, and that the head of the virology department had been 'making the polio vaccines' in his lab, namely propagating vaccine in locally prepared tissue culture, to boost both vaccine titre (concentration) and quantity.[4] These African testimonies have since been confirmed and enlarged upon by Belgian sources, including one eminent doctor who stated that the principal purpose of the Lindi chimpanzees was for 'the preparation of the vaccine'.[20]

This unique aspect of the Congo CHAT trials (making fresh batches of vaccine locally in chimpanzee cells) is the key detail that is missing from

The River, albeit largely because of the denials of the Belgian and American vaccinators. Over the last three years, every stage of the local preparation process has been multiply confirmed by different sources.[21] The vaccinators continue to issue strenuous denials, but these are often self-contradictory, and their attempts to explain away the counter-evidence are increasingly implausible.[4*] For example, they stress that the LMS annual reports mention nothing of chimpanzee tissue culture, or of local polio vaccine propagation. This is true, but it merely highlights that the use of chimp cells was a secret, even back in the 1950s.

Further research has revealed that propagating OPV locally (either from a sample of vaccine or from a seed pool) was routine practice in the 1950s; it happened with the vaccines of Sabin and Lepine, as well as Koprowski, and in places as far apart as Switzerland, the USSR and South Africa, as well as the Congo. This demonstrates that the CHAT batches that need to be tested for SIV and chimpanzee DNA are not those produced at the Wistar Institute, but those that, uniquely, were administered (and also prepared) in central Africa. Robin Weiss believes that samples of the vaccines used in Africa no longer exist.[22] I suspect that they do, but doubt that they will be released for testing.

The geneticists have a different 'disproof'. Those who favour the concept of 'phylogenetic dating' for HIV-1 argue that the most recent common ancestor (MRCA) of all the AIDS viruses seen today existed in 1931, plus or minus 15 years—namely, before the OPV trials. But their calculations are based on a constant molecular clock, and they ignore recombination, which, according to the OPV theory, could have occurred in a tissue culture based on chimp cells. Documents prove that primitive chimpanzee tissue cultures prepared at the LMS in 1958 also contained 'isologous serum' (serum from other chimpanzees) as a nutrient medium,[23] suggesting that these chimpanzee cultures were effectively pooled, which further increases the likelihood of *in vitro* recombination.

Immunodeficiency viruses are inherently recombinogenic. Recent studies indicate that the intrinsic recombination rate of HIV-1 is some ten times greater than its mutation rate (which is what phylogenetic dating measures). They also show that ignoring recombination would lead one to place the MRCA too far back in time.[24] At the Lincei meeting, Mikkel Schierup highlighted the evidence not only for substantial recombination, but also (crucially) for substantial *early* recombination, even before the virus diversified

* See sections 4(b), 5(d) and 7 in reference 4.

into subtypes. But whether or not early recombination occurred, the phylogenetic dating of HIV-1 is invalid, being based on a false premise.[25]

Finally, there is the epidemiological argument. I am pleased that Bill Hamilton's friend (and first post-grad student), Peter Henderson, has agreed to co-author a statistical study that compares several different hypotheses of AIDS origin (including the ranges of different chimp subspecies; and proximity to transport routes, major towns, and centres of health delivery). His analysis detects a significant link in only one instance: when the early foci of HIV-1 infection are compared to places where CHAT vaccine was given in Africa in 1957–1960. The correlations are highly significant both on a macrocosmic scale, across central Africa, and on a microcosmic scale, in Burundi alone.[26] This study substantially undermines the one full epidemiological paper that was presented at the Royal Society, which inexplicably ignored the CHAT vaccinations in Rwanda and Burundi (over half of the African total), and then concluded that there was no association between CHAT and AIDS.[27]

This new evidence (especially about local vaccine preparation) is revelatory. I would argue that every one of the alleged 'disproofs' of the OPV theory presented at the Royal Society and in *Nature* and *Science* has been intrinsically flawed.[28]

Bill, who realised long before I that several of his peers were more interested in disposing of an ugly theory (with frightening implications) than in examining that theory in a cool, dispassionate, scientific manner, would have derived great pleasure from these latest developments. I suspect he would also have been pressing for those individuals, institutions and governments that staged and backed the trials to be brought to book, and (if found culpable) to be made to accept some degree of responsibility for the terrible aftermath.

To him, there was only one way to practice Science, and that was with absolute integrity—and his pessimism about our 'human future' was at least partly based on his growing belief that integrity is a vanishing virtue.

Many have commented on the beauty of Bill's 'last testament', which describes his body being laid out in the jungle and consumed by Amazonian beetles, and through them borne aloft beneath the stars.[29] It seems that Bill may have wanted to die in the field, in such a way that his work and his spirit lived on, and I believe that metaphorically, at least, this final wish was granted.

NB Many of the Royal Society and Lincei articles are accessible on http://www.aidsorigins.com.

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