NARROW ROADS OF GENE LAND

The Collected Papers of
W. D. HAMILTON

VOLUME 3

Last Words

Edited by
Mark Ridley

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Editorial Preface

The Narrow Roads of Gene Land is W. D. Hamilton's title for his collected papers. This book is Volume 3, and completes the set. In the previous two volumes, however, Bill (as I'll refer to W. D. Hamilton here) did much more than simply reprint his scientific papers. For each paper, he also wrote an autobiographical introduction, and those amazing introductions were for many readers the most immediate attraction of the books, notwithstanding the scientific fire-power of the papers themselves. Bill died in the year 2000. He had seen Volume 1 through publication (it came out in 1996). He left almost-publishable manuscripts for Volume 2, together with all the decisions about which papers were to be included. After some editorial work, and guess-work, Volume 2 was published posthumously in 2001; it included papers published up to 1990. Bill intended to produce a Volume 3, but when he died he had done no work on the introductions nor left any indication about which papers would be included.

The editor at Oxford University Press, Michael Rodgers, who had dealt with the publication of Volumes 1 and 2, spoke round and corresponded with a number of people about how to publish Volume 3. I am not sure who exactly invented the form that the book has taken; Luisa Bozzi and Marlene Zuk may have been particularly influential, along no doubt with Michael Rodgers himself. Anyhow, a plan was somehow devised in which Volume 3 would include the papers from Bill's final years, together with more-or-less personal introductions written by Bill's co-authors. The introductions would work rather like Bill's own autobiographical introductions in Volumes 1 and 2, taking the reader somewhat closer to Bill's extraordinary personality and intellect. I was subsequently (though by then Michael Rodgers had retired from the OUP) invited to edit the volume, according to that plan. I accordingly encouraged Bill's collaborators, in their chapters, to write personally about Bill (if they wished to do so) as well as introducing the science. These introductory sections now provide, I believe, another way to get to know one of the great scientist's of the twentieth century, through the eyes of his collaborators. And the papers themselves enable readers to find out about, or remind themselves of, Bill's scientific output for 1990–2000

(though papers continued to be published until 2003). In addition to the co-authored papers, Volume 3 also contains several papers of which Bill was the sole author, and these are reprinted without introduction.

Volumes 1 and 2 both had leading themes. Most of the papers in Volume 1 were about social behaviour, and most of those in Volume 2 were about the evolution of sex. The themes are identified in the subtitles that Bill gave the volumes. By the time Volume 3 begins, Bill's research was moving into a more diversified phase. Bill continued to be interested in sex, and particularly its relation with parasitic disease; several of the chapters in this book are on this topic or something close to it. But he was also thinking about a huge range of topics, and often collaborating with someone else who worked on a particular topic in more detail. Some of the co-authors who have contributed introductions here have remarked how they had little idea that Bill was also working with half a dozen other people on disparate research topics at the same time as he was collaborating with them. I initially hoped to provide a subtitle for Volume 3 that would link its diversified papers into an identifiable theme; but I failed to find one and fell back on chronology. Olivia Judson invented the particular subtitle I have used, 'Last words'.

Bill's thinking ranged from highly imaginative abstract theory, to exact mathematical and computer modeling, and he liked to relate the theory to abstruse natural history, particularly from entomology. Volume 3 shows him at work in all these ways. He began the decade doing parasitically revved up computer simulations of genetic algorithms with Brian Sumida (Chapter 1); he ended it doing simulations of 'pacemakers' in spatial models of host–parasite coevolution, with Akira Sasaki and Francisco Ubeda (Chapter 18). In-between, he helped some astonishing work on antiobiotically cured parthenogenesis into print (Chapter 2); wrote about gender with Laurence Hurst (Chapter 4), the weird habits of Strepsiptera with Jeya Kathirithamby (Chapter 6), virulence with Dieter Ebert (Chapter 10), and diversity with Pete Henderson (Chapter 16). He backed the controversial hypothesis that the AIDS pandemic had accidentally originated in the polio vaccination campaign in Africa (Chapter 14). He had some wonderful flights of Bill-style theorizing about Gaia (Chapter 15) and the colours of autumn leaves (Chapter 17). Moreover, the co-authors who have contributed introductions here are by no means the only who collaborated with Bill in these years, though they are a good sample. Bill's sole authored papers look at models of sex (Chapter 7) and—again with some characteristically imaginative thinking—at inbreeding (Chapter 8).

Volume 3 contains almost all the published papers that appeared with Bill's name on after the end of Volume 2. Bill excluded a few minor publications from Volumes 1 and 2—publications such as letters to the editor, and short book reviews (though one more substantial book review made it into Volume 1); he also excluded at least one co-authored paper from the chronological period covered by Volume 2. For Volume 3, I have followed similar principles, though Bill's changing work-mode has suggested some slight modifications. I have again excluded short book reviews, letters to the editor, and minor abstract-length publications, though I encouraged co-authors to quote from and cite sources of this kind (as well as correspondence) in their introductions if they thought it appropriate. I also excluded a posthumous paper that had Bill's name on but that he knew nothing of—the posthumous papers included here are ones that Bill had worked on, contributed to, and knew were destined for submission. Finally, I excluded one or two manuscripts, of conference lectures, that Bill had worked on before he died, and probably would have been published; they seemed to me to be too incomplete for most readers to be able to follow.

On the other hand, I have included some papers that Bill might just not have included—either because he made only small contributions to them, or because he might have judged them too minor. Bill made little contribution to the Wolbachia paper (Chapter 2) or the second Gaia paper (Chapter 15), but they provide interesting sidelights on the way Bill was working now that he was famous. I also included a couple of lecture-addresses (Chapters 11 and 12), given when Bill received major prizes. They only just make it past the 'published' criterion—technically, they were published, but privately by the foundations concerned. Part of the reason to include them, along with Bill's bravura personal eschatology (Chapter 3), a bibliographical piece (Chapter 9), and a preface to a book on paper wasps (Chapter 13), is their autobiographical interest. Volumes 1 and 2 were rich in Bill's autobiography, and I inclined to stretch the net to admit some autobiography here too. In the end, about 90% of the decisions about inclusion and exclusion were straightforward, but there was a residue that was inevitably arbitrary. The book also includes a chapter by Jeremy Leighton John on the Hamilton archive—'Bill's last great work'—complete with irresistible pictures (Chapter 19), and Alan Grafen's biographical memoir (Chapter 20) by way of overview of Bill's life and work.

Finally, the book is necessarily missing the largest part of Bill's writings from his final decade: the autobiographical introductions to Volumes 1 and 2

of *Narrow Roads of Gene Land*. They amount to more than the length of the papers included in this volume. As Alan Grafen says (Chapter 20), Bill had invented an original way of writing autobiography, and one that is peculiarly appropriate for a scientist. Any one who wants a full picture of Bill's activities in the 1990s will need to add them to the publications reprinted here. If, by some paradox, those autobiographies had been included in this volume, I'd have offered as subtitular theme for Bill's final decade 'collaborations and autobiographies.'

Mark Ridley
Oxford, December 2004

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1959 MANCHESTER CASE OF SYNDROME RESEMBLING AIDS[†]

EDWARD HOOPER AND WILLIAM D HAMILTON

Bailey and Corbitt's letter to *The Lancet* about the 25-year-old man who died in Manchester Royal Infirmary, UK, in August, 1959, with a clinical syndrome resembling AIDS[1] is welcome but it leaves several points unresolved, including some raised by a science journalist in March, 1995.[2]

A particular puzzle is that the original polymerase chain reaction (PCR) study[3] was claimed to be of a randomised double-blind design. Properly applied, such a design makes it difficult for an interpretative bias to generate a false positive or negative result, and impossible for random contamination to do so. On application of Fisher's exact test to the results of 1990, the probability that random contamination of the test and control samples would produce four positive results in six test samples and none in six controls is 1 in 33. Occurring in 1990, before the dangers were fully appreciated,[4] accidental contamination in the first PCR study of a potential early case of AIDS would be understandable. However, the subsequent failure to address the statistical anomaly above and the neglect of other anomalies is not. We wish to highlight not only the mystery of how random contamination could have led to the results but also five more questions. For the third and fifth and partly for the fourth we suggest possible answers; the other two remain open. The questions are:

(1) How did the original tissue samples from the patient come to be found HIV-1 positive by PCR when these results cannot now be repeated?

(2) How have archival human tissues, which were apparently well enough preserved in 1990 to allow human and viral genetic analysis after 30 years in storage, apparently ceased to be so in the past five years?

(3) Accepting contamination,[1] what is its likely source?

(4) How have four (and possibly five) different human genotypes been reported for HLA-DQα in tissue samples claimed to be from one cadaver?

(5) What was the patient's fatal disease?

[†] *The Lancet* **348**, 1363–1365 (1996).

Contrary to speculation mainly, but not wholly, in the non-medical press, investigations by EH have shown no evidence to suggest that 'the Manchester sailor' (MS) was either homosexual or bisexual, or that he ever visited Africa. In early 1957 his ship did dock in Gibraltar for a fortnight. A day trip (well recalled by members of the ship's company) was made by about a dozen sailors to Tangier in Morocco, but a member of that party has no recollection that MS was present. Even if he was, or there were other day trips to Tangier, and even if (as has been hypothesised) he had sex in a brothel during such a visit, this can hardly be characterised as a high-risk episode. HIV prevalence varies widely across Africa and the seroepidemiological evidence suggests that Morocco has always been among the least affected countries. The earliest evidence of HIV infection in the country pertains to 1984–87, when seven of 8161 individuals (0.086%) tested positive, all from Casablanca. Six were in high-risk groups (gay men, male prisoners, and female prostitutes), the seventh was one of 3577 blood donors. None of 283 blood donors and pregnant women tested in Tangier in 1991 proved to be HIV-1 positive.[5]

Questioning MS's fiancée, family, friends, colleagues, and doctors suggests that he was neither sexually adventurous nor very experienced, and that he was not an intravenous drug user and had received no blood transfusions. Clearly one sexual encounter could have been enough, but everyone who knew him rates him as an improbable candidate for HIV infection. Those closest to him were saddened, indignant, and (rightly as it now appears) near to incredulous at the suggestion that he might have died of AIDS.

That incredulity is now borne out by Bailey and Corbitt,[1] who have joined Zhu and Ho[6] in concluding that the posthumous AIDS diagnosis was unsound, and that certain of the archival tissues made available to them may have been or have become contaminated with a modern (subtype B or 'Euro-American') strain of HIV-1. They suggest contamination 'sometime from sectioning onwards', and that the most likely source 'would be from within our own laboratory'.

The following scenario might go some way towards explaining the facts. The positive control used during the PCR work on MS was a CEM cell line infected with CBL-1.[1] In 1991, Weiss reported that CBL-1 had 98.0% identity with LAV-1 BRU (or, as it is now referred to, LAI) and 97.8% identity with HTLV-IIIB in *env, tat*, and *nef*.[7] An accompanying commentary on this 'remarkable similarity' cited laboratory contamination as the possible cause,[4] and reported that Gerry Myers of the HIV Sequence Database in Los Alamos considered that up to 3% divergence in *env* usually indicated different isolates from the same person, whereas, at the other extreme, genuinely unlinked isolates usually diverged by more than 10% in the envelope gene.

The earliest versions of LAI are the French patent application sequences bearing the Genbank/EMBL acquisition numbers A04321 and A07867, and Fergal Hill, of the MRC Laboratory of Molecular Biology in Cambridge, has characterised A04321 as 'apparently the most similar sequence to the Manchester isolate sequence currently known—at approximately 90% identity

over large tracts, including the envelope gene'. Hill concludes that 'this high degree of sequence similarity, and the fact that CEM/CBL-1 was grown in Manchester, *strongly* [his emphasis] suggest that the Manchester isolate is . . . derived from LAI via its derivative CBL-1'. Clearly Hill believes that repeated passaging of CBL-1 (for instance in Corbitt's laboratory) could explain the 10% divergence between this positive control and the MS isolate. Myers is less convinced, considering that 'the contaminant may have been a lab strain, or . . . another patient sample'.

We have already mentioned that only MS's tissues came to be contaminated in spite of their random interspersion with the controls. Thus conventional significance points either to earlier contamination, before the coding and dispatch of the samples to Corbitt's laboratory (in which case considerations of the last paragraph suggest that the CEM cell line might also have been present in the source laboratory) or to error during the breaking of the codes. Sections were cut 'with separate knives for case and control and with careful cleaning, with alcohol soaked swabs, of knives between blocks'.[3] If we accept that the procedure was as stated, the best scenario at this point would seem to be that a knife cleaned neither before nor between section cutting happened to be contaminated with modern HIV-1-infected tissue and thus passed not only HIV-1 DNA but also appreciable human cell material to the first four sections, which happened to be from MS. By the fifth and subsequent cuttings the knife supposedly had wiped itself clean. As discussed below, however, there are still many problems.

The hypothesis of prior contamination might be clarified by a detailed description of the storage and location of the two sets of tissues, and of how and where sectioning was undertaken. EH learned from one of the doctors involved that for at least a part of the period of the PCR investigation the blocks were being stored in Williams' home, and Williams later confirmed this.

Both Corbitt and Williams told EH that the code had been broken during a telephone call, in which Corbitt read through the list of numbered samples, indicating for each whether or not the presence of HIV had been demonstrated, and Williams then broke the codes, indicating which samples had come from MS and which from the control patient. Corbitt states that nobody else was in the room at the time; Bailey was waiting outside. A more appropriate method might have been an exchange of sealed envelopes and the presence of witnesses when the envelopes were opened.

Further examination of the original MS tissues and of the PCR products from Corbitt's laboratory is needed. In the past, Williams has stressed that there was little tissue available and that he had been keeping a judicious eye on what remained to ensure that not all was used up.[8] But he acknowledges that about 40 blocks were taken at necropsy. These originated from a wide variety of skin lesions, together with bone marrow, heart, lung, and central nervous system, and abdominal viscera (including liver, kidneys, pancreas, and spleen), and even

if most of the tissues are not ideal for finding lymphotropic virus, some DNA from an overwhelming virus infection should be detectable. Extraction of human DNA should be feasible from any of the samples. Perhaps the Central Manchester Health Care Trust could reveal exactly what tissue remains and perhaps some of the blocks could be examined by another laboratory. One laboratory, experienced in PCR and in sequencing lentiviruses, made a written offer to test tissues from the patient in March, 1995, in response to Williams' statement[2] that he would 'be quite happy to supply tissue to anyone who would take it on'. This offer was apparently forwarded to the Trust but was neither acknowledged nor accepted.

Five human genotypes for MS have been mentioned.[1,6] Zhu and Ho found that three HLA-DQα genotypes had been sent to them, with traces of a fourth. In material from Corbitt they found type 1.2,4 'with traces of 2,3' in kidney and 1.2,3 in bone marrow. In material from Williams, on the other hand, they found 3,4 in thyroid, liver and kidney. Bailey and Corbitt now report that, working on samples received from Williams in 1989 (those from 1995 having been found unusable), they detected 2,4 in liver and brain. They also found human type 2,4 in the CEM line that was their HIV-positive control in 1990. The frequency of 2,4 in Britain is likely to be well below 5%.[9]

If Zhu and Ho's interpretation of their bands was at all equivocal and '2,4 with a trace of 1.2,3' for kidney and bone marrow is a possible alternative to their stated '1.2,4 with traces of 2,3' the inconsistency of the New York and Manchester accounts would be greatly lessened: 2,4 could then be due to the contaminating CEM cells, and Zhu and Ho's technique, perhaps more sensitive than that of Bailey and Corbitt, could be revealing the underlying tissue type 1.2,3, exactly as found by Zhu and Ho in bone marrow which had seemingly escaped contamination.[3] MS would then have a puzzle of only two genotypes; a third would be due to the CEM cells.

Perhaps both DNA and proteins of the wax block material were so degraded that they provided weaker and sometimes undetectable signals relative to those provided by a recent cell contaminant, when present. This is further suggested by the partial and wholly negative results obtained, respectively, by Bailey and Corbitt and by the UK Forensic Science Service.[1] However, the idea that contaminant CEM cells explain all the genotyping and viral results since 1989 still involves many difficulties, whether that contamination arose in the laboratory where sectioning took place or in Corbitt and Bailey's laboratory.

Turning to the nature of the patient's disease, Bailey and Corbitt express themselves puzzled and reiterate that the symptoms were, retrospectively, very suggestive of AIDS. We believe, however, that the diagnosis has become the least of the problems of the case. It would be flippant to suggest that a patient with five HLA genotypes—more diploid combinations, it may be noted, than are known for any chimera apart from a few Panamanian strangler fig trees[10]—would of necessity be a simmering cauldron of autoimmunity and

immunocompromise. Let us propose two plausible alternatives. MS may after all have had Wegener's granulomatosis. This was the working diagnosis for the final two months of his life and for more than seven weeks after his death the gross post-mortem findings were being described as 'consistent with [this] diagnosis'. Only when the microscopic findings revealed cytomegalovirus and *Pneumocystis carinii* was this diagnosis abandoned.

A second possibility is CD4+T-lymphocytopenia (CTL). This condition was christened 'AIDS without HIV' when its existence was first announced at the Eighth International Conference on AIDS in 1992.[11] Other publications quickly followed (e.g. Laurence *et al*. in 1992[12]). Rezza *et al*[13] mention a 39-year-old man without HIV infection who died as a result of a wasting syndrome, *P. carinii* pneumonia, disseminated cytomegalovirus infection, and neurotoxoplasmosis. Apart from the *Toxoplasma* infection, the clinical profile matches that of MS.Dr T B Stretton, one of the MS physicians in 1959, now leans towards this retrospective diagnosis.

If MS did die from AIDS it is vital to our understanding of the early history of primate immunodeficiency viruses that an authentic sample of HIV DNA from such an archival case be made available for sequencing and phylogenetic analysis. Besides the controversial postmortem tissues, biopsy specimens were taken from sternal marrow, scalene region (including a lymph node), and ulcers and skin lesions. Perhaps these are still available at the Manchester Royal Infirmary.

If, however, as we believe, this patient did not have AIDS, and if there was either substantial contamination with modern HIV DNA or tissue samples from other patients came to be included in the PCR investigations, then this man's family and fiancee are owed an apology for the distress which this episode has caused them.

Unsourced information in this article is based on tape-recordings and notes of interviews between EH and the various scientists mentioned, personal letters from some of these scientists, and medical records of the patient, viewed with permission of his next-of-kin.

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FOREWORD TO E. HOOPER, *THE RIVER*[†]

W. D. HAMILTON

Every time two people put their heads together, Truth suffers; when many put their heads together, she suffers more. A major point of this book is that when the heads are great ones and have owners with much to lose (employed perhaps in giant companies or government departments), Truth can be made so ill that we should all shiver.

Evasion and untruth have long been known to be beneficial at many levels and useful to people in many ways. They can be presented as virtues—the little bads that add to a greater good, with a proviso, of course, that the good is of a kind that the colluders believe only they know how to attain. 'Don't we have faith in ourselves?—let's keep it simple for their—for all our sakes.' Even for God's sake: this version has been abundantly illustrated by religious leaders ever since Christianity became official in the Roman Empire, with disastrous effects upon other faiths—and a fiery impact upon a myriad of free-thinking 'witches,' as well as the occasional literary loner like Giordano Bruno. Once there is acceptance by an 'establishment,' there is often no need to whisper about it anymore: in those who have jointly suffered to win, say, the Queen's Commission in the British armed forces, or the privilege of saying the Hippocratic Oath, a solidarity springs up automatically, and with it a deep conviction that the purpose of the discipline, whatever it be, must be good. And yet, knowing the untruths that emotions arouse, especially in groups, Plato amazingly denied roles even for poetry and music in his ideal Republic.

Most of the daily untruths communicated need not be taken too seriously: we have become accustomed to them and in a sense self-vaccinate. However, when eminent rivals in an ancient profession are seen to be uniting to crush an outside critique, and when the best-funded branch of science, to which the rivals belong, draws almost all its practitioners into line behind them (as Louis Pascal and then Tom Curtis in the case treated in this book had already experienced, even

[†] In E. Hooper (ed), The River: A Journey Back to the Source of HIV and AIDS, pp. xxvii–xxxiii (Harmondsworth: Allen Lane, The Penguin Press. Boston: Little, Brown, 1999).

before Hooper), and when an expectant and immensely wealthy international industry is also seen marching in step with the profession in question, it is time for the rest of us to wake up.

The thesis of *The River* is that the closing of ranks against inquiry may, in this case, be preventing proper discussion of an accident that is bidding to prove itself more expensive in lives than all the human attritions put in motion by Hitler, Stalin, and Pol Pot. Furthermore, essentially unwarned by what we have recently done, we may be moving rapidly toward further and perhaps even worse disasters of the same kind. Some aspects of genetic engineering may indeed be dangerous, but a situation in which the general public has greater concerns about mystical subversion of the chemicals in soy sauce than about the risk of viruses in live animal products that are already administered, almost compulsorily, to our bodies, is near to absurd. In parallel to this, our doctors' Hippocratic Oath warns them of various temptations and dangers, but it says nothing of how they need to guard themselves, and their profession, against the effects of the millions of profit that dangle before the nascent industry proposing to transplant organs into humans from other species.

These are the foreground dangers emphasized by Hooper in this book. Its background has another danger, which is still more insidious. Litigation has been used to suppress the publication of discussions about a hypothesis; litigation is again being used as a threat to Hooper. In the same vein and equally unsettling, we have seen the best known and seemingly most independent science and medical journals join forces on the side of the countercritique, while generally avoiding publishing details of the original issue. Again it is time for us to wake up and consider what is happening to freedom of discussion and to the spirit of science.

It is the foreground, the potential repercussions in the next thirty or so years, which will probably most arouse the reader of this book. Perhaps something is being tardily seen by the establishment. A few months ago, the British Medical Association announced revisions to the Hippocratic Oath British doctors must take; then just a week ago, as I write, the Association's organ, the *British Medical Journal*, published for the first time an admission of a likelihood that Simian Virus 40, established as an infection in millions of humans by the Salk polio vaccine, is causing human cancers. 'Salk,' it may be remembered, is the 'dead' and therefore safer polio vaccine—safe supposedly not only from reversions to virulence but from the possibility of 'extraneous agents.' It is quite different from the type focused upon in this book—the type we now all receive. On another front, committees in recent months have enjoined slowness and caution with xenotransplants, but not before the first baboon liver transplant into a human was attempted—an operation that perhaps fortunately failed. Meanwhile heart valve implants from pigs, a species known to harbor retroviruses that can live in human tissue cultures, are in trial and application.

All this is why the world still very much needs lone researchers like Edward Hooper. They reach truth faster than committees. Shortly after I first knew him, I introduced him to someone as a journalist, knowing he had formerly been

one in Africa. Later he asked me, pained, 'Why journalist? Couldn't you call me a *writer?*' I did so from then on but stayed puzzled. Weren't journalists supposed to be the guardians of our free world, the para-predators ranging our savannah and making even the most lordly lions take care of their actions? Weren't they (the best at least) even cousins to us scientists, ferrets setting themselves to bolt the most willfully concealed and elusive truths of history where we scientists deign only to chase the immobile targets, such as atoms and missing links? Why should one not want to be a journalist? After reflection and listening to the talk of 'paparazzi' and the like that came after Princess Diana's death, I think I see better now the perspectives that journalists dread—but just as hyenas do less scavenging and far more primary predation than was once thought, so also do the best journalists.

Whatever, this book, with its almost 2,500 footnotes, demonstrates how Hooper has finished up. Not only is he the kind of predator that all in Big Science should fear, but he is a writer and historian as well. Even that is not all. He has self-taught his way to 'honorary' status in several branches of science—to be almost virologist, almost geneticist, almost evolutionist. To most of us, however, these achievements just provide the reassurance that he is writing sense in his diverse fields; in contrast it is the writing itself and the history—dare I say even the first-class journalism?–that will keep us bent over the pages that follow. What scoops, what personalities, what landscapes, what far places! Above all what enigmas, what awful inexorable tragedy (tragedy at its deepest, gnawing within millions of homes—a scale perhaps grander than any ever before described) stand there behind!

In 1995, in Africa for another purpose, I tried to help Ed by looking for some of the Ugandan friends who had helped, nearly a decade earlier, with the research for his first book, which described the AIDS disaster in that focal area close to the shores of Lake Victoria. There were two men in particular whom he wished to contact and to thank. As I discovered after some questioning, both had died. I was led to the father of one, and he in turn took me to a neat private graveyard in his *matoke* plantation and showed me the newly heaped mounds, six in all. They were for his wife and all his children. One mound, with a stone slab, was for the son Hooper knew, a local government official (who had been, perhaps, a little more important locally than the others). The old man sat on a corner of the slab and read the letter Ed had sent, while two grandchildren, come into his care after the last death, watched from nearby. The children were lively and healthy but very quiet, and I hoped the infection was going to miss them. Such graveyards, I found, were everywhere in the district, though they are not much seen from the roads. Orphans, too, were everywhere: a generation had been scythed out from between those who were too young and too old to be readily infected. I saw children in groups ranging from teens to tots seemingly loose and self-foraging in the countryside, which included as it happened trying to forage from me, the passing foreigner. Presumably these were the children

not lucky enough to have grandfathers and grandmothers who were still alive. Both in the robust elderly and in these youthful gangs I felt I was seeing how Africa would survive, if only after a period of great suffering. Yet it may end up less changed, it seemed to me, than will the continents of the First World, in spite of our lower expected mortalities.

After that brief experience in southern Uganda—a few days only—I understood better what had been driving Hooper to follow up on the lighter and more emotional book he had already written about the epidemic in Africa. I suspect he had no idea, at the start, of the magnitude of what he was undertaking, nor of the nine-year odyssey of research and travel it would require. Even before he read Louis Pascal's extraordinary paper 'What Happens When Science Goes Bad . . .' and had realized the full tragic possibility about the origin that it raised, he had been aroused by personal indignation to far more energy over the epidemic than had most of the rest of us. In the late eighties in Nairobi and Kampala, he had seen friends sicken and die around him. Despite this, in the nineties he was still finding Westerners who claimed it was all untrue, and that there was no epidemic. Instead, false trails and absurdities were glibly promoted; hypotheses were floated that seemed aimed, even from the first, to lead into impenetrable bush. At the same time, as he found later, much better hypotheses about the epidemic were studiously ignored and had needed tortuous paths to achieve any public notice at all. The ideas and research of New York-based Louis Pascal, for example, had to be published in Australia, and the investigations of science journalist Tom Curtis went perforce to an outlet in a popular magazine, *Rolling Stone*. Neither piece was much followed up.

Without question it is science that will shape the human world of the Third Millennium. Even if science can only direct us back to a dark age it will still be our cause and our guide. But it could be made to do better or worse. There is a risk that science is going to lose its fertility and change radically away from that spirit of free inquiry and exchange that first inspired the Greek and then later the Renaissance experimenters and philosophers. Indeed, this process seems to be starting already; patenting and secrecy about gene sequences are perhaps one symptom. Science may bring on us not so much a dark age in the old sense, via some spectacular collapse, but rather a super-technological state whose monstrous futures—if they could be shown to us dearly through the present smoke of excitement about more and ever more technology—would only arouse our dread. While still working its miracles on the outskirts, science may already, at its center, like a great city, be slowly dying of its very success. Dictators and businessmen everywhere want to use all the technical products of science and, if possible, to control the rights and the how-tos for creating more. They would also like to be free to hide the results of their unsuccessful or disastrous experiments.

After reading Pascal's paper, it was a great shock to me that when I passed out copies to others whom I thought would be interested, including a journalist

who had written on AIDS for a major popular science magazine, I met with exactly the wall of silence Pascal had described. From being at first impressed mainly by his theme about the origin of AIDS, I thus began to believe his arguments about scientific integrity as well—arguments that at initial reading had seemed to me just overreactions generated in a sensitive, frustrated man. Only one person (from the medical fraternity, surprisingly) replied to my mailing with any sign of taking the paper seriously. Even my old mother, a doctor, told me, 'You are going to be very unpopular if you pursue that one—polio of all things, that one is sacred! Anyway, if it's true, it's all happened and what could you do?' Well, personally I didn't pursue anything very far; after several tries with the editors of both *Science* and *Nature*, I lapsed back again into the general silence. Overall I have left it to Pascal, Curtis, Julian Cribb, and now Hooper. I have simply watched from the sidelines as each in turn has held aloft his blazing but strangely unregarded torch. However, I have become, with each new revelation, and particularly with the discoveries of Hooper, which you can now read about for the first time, more and more a convert to the underlying theme. The new facts in the case still tend to be widely separated and none by itself amounts to a proof; however, taken together the steady trend and accumulation has become very impressive. At the very least the OPV theory of the origin of AIDS now merits our acute attention.

I have pondered very much about what sorts of people should be encouraged to try which sorts of tests: Hooper also in the book gives his list. There are some that could be decisive. However, the factual case was already quite strong after Pascal, and the present situation adds up to reiterating that Pascal was also right in his other theme, and that very major questions need to be asked about why supposedly 'free' science has been so slow to listen to what should have been taken very seriously from the first. If the topic had somehow been far from Big Science and had lacked any implications touching on issues like politics and professional pride, I have little doubt that its questions would have been much more discussed and investigated by now. I very much hope this book will cause the questions to be asked and the tests to be undertaken, and that it will also stimulate a lot more of the kind of sociology and science critique which Brian Martin in Australia promoted during (and supportative to) the building of the present story. How much more useful his effort is than so much that is done under the name of the sociology of science!

Forensic high-tech analysis has been enthusiastically applied to the hair of a historic corpse, Napoleon, in order to try to separate the natural events, accidents, and malfeasance that might have played a part in his death. He was a great man by any standard and also, looked at a bit more sourly, was instrumental in causing hundreds of thousands of deaths. Most would agree that these attributes of Napoleon justify the considerable interest historians have in how he died. But this level of interest makes it all the more remarkable that another historical issue with already far more deaths to its tally, and its Waterloo not

even in sight, receives currently only a single historian's effort. Vaccine vials, which are surely much more accessible than samples of Napoleon's hair, stay untested in the Wistar Institute freezers. Through turning a blind eye to the OPV/AIDS hypothesis, our establishment actively avoids testing and hearing about the plentiful though scattered evidence that the AIDS epidemic may have had a medical accident at its origin—an accident possibly compounded, more recently, by a desire by certain protagonists to conceal the evidence.

In getting together the materials for his book, Hooper has worked harder and for much longer than any of his forerunners. Several times he has countered my plea for a start on the writing by saying there just had to be this further trip to Belgium or that one to the United States. His work has amounted to more than six hundred interviews in all, he tells me, and this says nothing of the library research. I believe no one, not even a person 'speaking as a scientist,' is going to call this book 'the wildest of lay speculation'—the criticism that was leveled, even then unfairly, at Tom Curtis's much briefer accounts in *Rolling Stone*. If the OPV theory of AIDS origin comes to be proved, I think the new standards of *evolutionary* caution in medicine that their publications will eventually engender (especially regarding all treatments that use live products from other animals on humans) should merit for Hooper and Pascal jointly a Nobel Prize. As a species we ought to have known somehow in our culture, or even genes, that intimate invasions of live animal products, especially those coming from closely related species, are inherently dangerous. I have conjectured elsewhere that these dangers may be the main reason why separate species exist generally. That notion and what happens next in the present case are all in the lap of the gods. There are as stated, however, tests which can prove convincingly whether or not AIDS was our medical mistake. Meanwhile, Hooper deserves great praise for having so tenaciously carried through his investigation and for bringing to light so many more facts affecting the main question—facts that are almost all further challenges to the null hypothesis of 'coincidence only.' Even if the OPV theory is eventually rejected or remains permanently in limbo, he has done a great service in putting so many details of the early spread of AIDS on record. He has in fact given us the best history of the epidemic.

I have seen the cost the task has had for him manifested in many stages of tiredness, illness, and despair, which however he has always managed to overcome. Truly it has been like watching an explorer—Burton or Livingstone—making his halting progress toward some center of mystery that is far inland from the obvious coastal hills which we have all been seeing. Most strangely, as it may seem at first, his story wends toward exactly the same center of Africa as those Victorian explorers sought. This comes to seem a little less strange, however, once we reflect on our evolutionary origins. What dramas on all scales have been played out in the human population in the same geographic region, around the spine of Africa and in those places where the savannah and the forest meet. Almost all of these things were happening long,

long before there was anyone who could write or even speak about them. Upright we became . . . trying for new social structures, for tools, for speech, for fire . . . Finally out of Africa, our home, there came this new disease and on its heels, in this case, a *written* drama of *how* it came. Both themes are gravid with our future, and the written one is like Sherlock Holmes, Professor Challenger, Augustus Caesar, and Mark Antony all rolled into one.

Everyone should read this book, both for its story and in order to think hard on all that it implies—all this before Truth, more white and sick even than with AIDS, quietly rejoins us through another door.

CHAPTER 14

BILL HAMILTON'S INVOLVEMENT WITH THE OPV THEORY

'Medical Science's most Hated Hypothesis'

EDWARD HOOPER

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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