

# Appendix: Background

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Robert Silman (October 2018)

A long while back, right at the start of the AIDS epidemic in the late 1980s, I fancied I had a possible cure for AIDS.

There were three facts which underpinned the idea.

**Cause:**

*“AIDS is caused by a virus (HIV) infecting blood cells (T Cells) and destroying them.”*

**Prevention:**

*“AIDS is prevented by: i) stopping HIV entering the body; (e.g. non-infected sexual partners, non-infected blood transfusions, condoms, etc.); and/or ii) after HIV enters the body stopping it from infecting T Cells with an effective vaccine (not yet developed).”*

**Treatment:**

*“AIDS is treated by anti-viral drugs which slow down/stop the destructive activity of HIV on T Cells.”*

So what was my possible cure? It was the answer to a question which had been puzzling me, namely: “Why did HIV exist?”

I know you can ask that about anything; but in a scientific context, there was a good reason to ask it about HIV. HIV should not have existed because it killed its victims. It was such an effective killer, it should have ended up killing itself in the process. What I mean is that HIV was not like some common cold bug which leaves its victims alive, ready for reinfection at a later date. Nor was HIV like the syphilis bug which spreads slowly via sexual intercourse but which does not kill its victims during their reproductive life, thereby giving the victim time to transmit the bug to a new victim and the new victim to other new victims ad infinitum. HIV is more like the bubonic plague, a bug which kills its victims rapidly and which finally ceases to infect humans by running out of victims to kill through mass extermination or quarantine (e.g. the Black Death). But mass extermination/quarantine also kills the killer. If there are no further victims to kill, the killer has nowhere to live and therefore exterminates itself. In the case of bubonic plague, the bug continues to survive only because it has fleas and rats to prey upon until the time is right to reappear and strike a new human population (e.g. the Great Plague of London).

So my question “why does HIV exist?” needed to find its answer in wherever HIV was hiding before it struck and caused the AIDS epidemic of the 1980s.

In those early days there was speculation that HIV might have had its origin in Africa<sup>1</sup>, perhaps crossing species from monkeys to man, a Simian SIV to a Human HIV. But my thought was that if HIV had behaved in those early African populations as it behaved during the AIDS epidemic, there was even less chance that it could have survived. It would have killed its victims even more effectively in a small isolated African village population and therefore even more reason for it to be extinguished in the process.

My thoughts took me to the idea that HIV might be like Sickle Cell Anaemia (SCA). SCA is a severe blood disease which kills. Consequently the genetic mutation which gives rise to SCA should have been selected against and become extinct. However, the reverse is true. Instead of dying out, SCA flourishes to such an extent that in certain areas (Africa) the SCA gene is present in 10 to 40 percent of the population. And, the reason why SCA continues to exist is because individuals who carry the sickle cell trait are highly protected against malaria. This explains why a deadly mutation continues to survive, and why it is prevalent in areas where malaria is endemic. The SCA mutation is a pathogen in its own right but it is also a counter-pathogen to another disease; i.e. its pathology in provoking anaemia is outweighed by its advantage in combating malaria. So back in the 1980s I asked myself:

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“Was there some possible advantage to being infected with HIV?”

In other words, did HIV exist because it was a counter-pathogen to some other disease?

But what possible benefit could HIV confer? My childishly simple train of thought was: “If HIV exists because it is of benefit in countering the effects of another disease, maybe that other disease is one which multiplies T Cells.” My thinking ran something like this: if you have a disease (AIDS) which results from the destruction of T Cells and you have another disease (Leukemia) which results from the overproduction of T Cells, maybe (just maybe!) the two diseases hold each other at bay.

But what is this disease which multiplies T Cells? It is called adult T-cell leukemia (ATL), a disease characterized by an unregulated over-production of human T cells, first reported as a distinct clinical entity in 1977, and in the 1980s discovered to be caused by a virus. The virus was called human T-cell leukemia virus (HTLV) with each strain designated as HTLV-1, HTLV-2 etc. There are approximately 10–20 million HTLV-I carriers in the world. It is endemic in Japan, parts of central Africa, the Caribbean basin and South America etc. In the early years of AIDS research a prominent scientist, Robert Gallo (see later), believed that a variant of HTLV might be responsible for AIDS. This was finally disproved when it became evident that the true cause of AIDS was HIV, a totally different virus.

So here was my possible cure! In the late 1980s the treatment options for AIDS were not working; they only became truly effective in the late 1990s with the introduction of protease inhibitors. So before these effective treatments I was suggesting that if someone was dying from HIV, inoculate him/her with HTLV. (And/or if someone was dying from HTLV, inoculate him/her with HIV). I did say it was childishly simple. But, if true, one or two simple inoculations could in principle hold the disease(s) at bay indefinitely.

Though I was a medic and research scientist, working at St Bartholomew’s Hospital in London, even if I’d wanted to test the idea, it wouldn’t have been allowed. My speciality was neuro-endocrinology (hormones of the brain), I wasn’t a virologist or infectious diseases person. In science, you don’t swop specialities in mid-stream. Indeed I was straying over the boundaries just in thinking I might have had an idea in someone else’s terrain. I tried to plant the idea with some of my colleagues who were working in the AIDS area. Though they listened politely, I sensed they thought I was ignorant and/or mad (at best, eccentric).

So instead I decided to write this book. I wrote it with a co-author (that’s another story). We sent it to all the major agents and publishers. They all replied... Rejected!

I did make a discovery all the same. There is only one way to say “yes”, but hundreds of ways to say “no”.

The book lay dormant and unread in the backwaters of my computer until 2012 when a friend, who’d read a draft manuscript back in the early 90s, phoned me. The conversation went like this:

**Annick:** Robert, you remember the medical thriller you wrote about using the Leukemic virus to cure AIDS?

**Me:** Yes

**Annick:** Well I’ve just read that someone has used the AIDS virus to cure Leukemia.

And it was true in a way. It wasn’t exactly what I was proposing. In the clinical case which was being reported, it was a modified form of HIV that had been used and the Leukemia was not due to a virus. But it got me thinking again about my long lost cure for AIDS. In the late 1980s, I had suggested that you could easily test my idea with co-infection studies; i.e. studies on patients who were found to be i) infected with HIV alone; ii) infected with HTLV alone and iii) co-infected with HIV and HTLV. If I was right, the first group would be at risk of developing AIDS, the second Leukemia. However, the third group should be protected from both AIDS and Leukemia. The success of anti-viral treatment from 2000 onwards rendered co-infection studies of little use since it masks the effects (beneficial or otherwise) of co-infection. But, after Annick’s phone call, I decided to take a look at what had been happening in the area of co-infection and, to my amazement, I found there were studies which suggested I could have been right all along:

“HIV-1 and HTLV-2 co-infections have been linked in some cases to a long term non-progressor”<sup>2</sup>

A “long term non-progressor” is an HIV infected patient who maintains normal T cell counts and AIDS-free survival indefinitely. In other words, exactly what I was predicting. Of course if this is the case, i.e. if HIV is a counter pathogen for viral Leukemia and HTLV is a counter pathogen for AIDS, this could explain why the AIDS epidemic exploded like it did. In a remote African village, the occasional transmission of HIV without its partner HTLV to an individual might result in that individual’s early death but it would not adversely affect the local population if that local population was mostly co-infected, and therefore protected from a single virus disease. However, with modern means of mass travel allowing virtual immediate contact between continents, and with modern mores sanctioning sexual promiscuity,

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an occasional individual infected with HIV alone, without its partner HTLV, would be capable of setting off a train reaction of mono virus transmission from sexual partner to sexual partner in those parts of the world which have no exposure to the counter pathogen. It would spread like the Black Death of old, which is exactly what seemed to be happening in the last decades of the 20th century.

My conversation with Annick got me to resurrect my old manuscript; and, because printing technology and distribution had marched on in the interval, I found the means to publish the book myself. So, if anyone is out there and reading this, that's the reason why.

I also re-discovered that I had another good reason for publishing this particular medical thriller. I wanted it to deal with the much ignored issue that AIDS was a ruthless path to glory for research scientists.

Sometimes we make judgements about professions, such as “politicians are corrupt” or “scientists are altruistic”, without realising that they can be just as unmerited as a racist or sexist remark. Not all politicians are dishonest any more than all research scientists are motivated by the need to help mankind. Many of the best research scientists are motivated by ambition; i.e. the egotistical desire for fame and glory. I am not in the least arguing that this is immoral or even undesirable; on the contrary ambition is often a necessary attribute for the great achievers. Take the example of James Watson, one of our greatest scientists. He went after a project because he knew it was “a smashingly important problem”<sup>3</sup>. And he was right! By discovering the chemical structure of DNA, Watson and Crick are forever known as discovering the key which unlocks the genetic code. Watson's genius was choosing what to discover, sensing it was solvable and going for it. Of course he also had to be a very good chemist. But it is pretty certain that the structure of DNA would have been discovered at about the same time with or without Watson (Linus Pauling was hot on the trail), just like Mount Everest would have been climbed soon after Hillary and Tenzing. Fame comes from being first, and ambition fuels this flame<sup>4</sup>.

In the 1980s Robert Gallo (mentioned earlier) had picked the right project for an ambitious scientist. He was headed for the Nobel Prize and world renown. AIDS was the hottest medical topic of the time and discovering its cause was going to make headline news. And it was not only a question of fame. It was also about money. The first to discover the virus would also be the first to develop a test (because without the virus you wouldn't know what you were trying to test); and the first AIDS test would be patentable; and a patented AIDS test would be worth a fortune. So the stakes were immense: the winner in the race to discover the virus that caused AIDS

would have fame, fortune and the glory of a Nobel Prize. And Robert Gallo was the front runner!

But where Gallo's strength was his ambition, his weakness was possession. Unlike Watson and Crick who had no claim on any particular structure for DNA, just discovering its general structure was good enough for them, Gallo (as described previously) had already identified the retrovirus responsible for leukemia "Human T cell leukemic virus" (HTLV) and suspected that a variant of this virus was responsible for AIDS. The HTLV family of viruses had become, in a sense, Gallo's property. But a sense of possession can take on a life of its own, it can be a mischievous emotion ready to deceive and mislead in defence of what it owns.

We all make mistakes; one of the commonest is when we want one answer and fail to listen when presented with another. Gallo made just this mistake in early 1983, a mistake that forever compromised his subsequent career, and it was a mistake based on his "ownership" of HTLV. In early 1983 Gallo and his colleagues were about to have several papers published in the prestigious journal *Science*. These studies supported Gallo's theory that AIDS was caused by a virus linked to his HTLV family. On the other side of the Atlantic, the comparatively unknown Luc Montagnier and his team at the Pasteur Institute in France were isolating a virus from a French patient who would later die from AIDS (the Bruguère virus). Their investigations suggested it was different from HTLV. They purposely described it as "Lymphotropic" i.e. a virus attracted to lymphocytes, so as to make clear it was not like Gallo's "Leukemic" virus. In all likelihood, the French would have had great problems in getting their findings into a reputable journal. They had no track record and their English was poor, an important handicap when all the major scientific journals were being published in English. Gallo offered to help have their findings published in *Science* alongside his own. Montagnier sent the draft of his paper to Gallo but without an Abstract. (An "Abstract" is a summary of the paper's principal findings in a few sentences and is commonly the only bit of a scientific paper that is ever read). Gallo generously offered to write the Abstract for them and then passed the paper on to *Science* with his full endorsement. Now it turns out that the Abstract changed the meaning of the French paper<sup>5</sup>. Indeed the opening words of the Abstract read: "A retrovirus belonging to the family of recently discovered human T-cell leukemia viruses (HTLV) ... ." when of course it should have read "not belonging" (echoes of Thrump!). The French paper is now recognised as the first ever identification of what later came to be called HIV<sup>6</sup>.

It took months, even years, before the true meaning of the French paper was properly understood. There were suspicions that Gallo had deliberately "misunderstood"

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their findings, a sort of conspiracy by the powerful to suppress and distort. But I think it was the opposite. I believe Gallo's offer to write the Abstract was entirely in keeping with a spirit of collaborative science. However my guess is that Gallo made the mistake I am talking about; i.e. he didn't listen, he genuinely thought the French were confirming his theory about HTLV, not challenging it. I believe (this is pure surmise on my part) he thought anything in their paper which suggested it wasn't HTLV was probably because the French weren't as good as his team in their lab work. My guess is that he thought he was doing Montagnier a favour in emphasising the relationship to HTLV and underplaying the opposing evidence. If he was right (and I am sure his ownership of HTLV had blinded him to the possibility he could be wrong), his editorial changes would strengthen their paper not harm it.

If you don't listen, it's difficult to row back when the message finally gets through. Once you eventually hear what's being said and you discover that it does NOT correspond to what you want to hear, there is a natural disposition to denigrate the offending piece of news. So just as it took the scientific community time to realise that the French virus was not the same as HTLV, it took Gallo even longer to adjust to the possibility that "his virus" was not the virus that was causing AIDS. And in this he was egged on not by ambition, which would have led him to correct his mistake and move forward to almost certain glory, but by his sense of possession which led him to defend the indefensible. In January 1985, when Gallo and Montagnier's teams independently published the DNA sequence of the AIDS virus (Montagnier's in *Cell* three days before Gallo's in *Nature*) Montagnier called his virus LAV (Lymphadenopathy-Associated Virus) while Gallo was still maintaining his property rights by calling his HTLV-3B. Even though sequence data made it clear that the virus was unrelated to HTLV, Gallo was insistent in maintaining that HTLV-3 was "as accurate as innocuous and as consistent ... as any name possible"<sup>7</sup>.

Despite all the evidence which was piling up throughout 1985 that the AIDS virus was not a member of the HTLV family of leukemic viruses, Gallo continued to fight a rear guard action to force fit his name as if the name could alter reality, any more than if the word "communist" in the communist party of China alters the reality of a "capitalist" economic policy. Eventually, in the spring of 1986, a committee settled the issue between LAV and HTLV-3 by naming the AIDS virus "human immunodeficiency virus" or HIV. The French made no objection because for them the possession of a name was not the issue, they just wanted to make sure that it wasn't a misleading name. As Crewdson notes "Montagnier thought HIV a fine solution, since it amounted to a clear signal from the scientific community that the AIDS virus wasn't HTLV"<sup>8</sup>.

But the final and bitterest twist in the story is how the desire for possession turned on Gallo and became his fiercest enemy. It was almost as if the fates were playing a

game of poetic justice, as if they were saying “if you want to own something so much we’ll make sure you own nothing!” The story goes like this: despite his obstinacy over the name, Gallo was still in a strong position in his head to head race with Montagnier to identify the virus that caused AIDS. As of 1985/1986, it looked like a dead heat. Gallo and Montagnier’s teams had both, independently, identified and sequenced the AIDS virus. There were two sets of Patents for an AIDS test, one from the French based on Montagnier’s virus and another from the States based on Gallo’s virus. It looked as if fame and fortune were about to be shared equally between them. But the Gods of Possession had turned against Gallo and were determined to bring him down. As more and more AIDS viruses were identified by other researchers, it became clear that there were small differences between them, depending on the AIDS patient from which they’d been taken. All patient samples were slightly different... Except two! Gallo’s and Montagnier’s! Their sequence data were so alike that they had to have come from the same patient! But that couldn’t be true. Montagnier’s virus had come from a French patient in Paris, whereas Gallo’s virus had come from patients on the other side of the Atlantic. There were accusations of theft and lying, but the real reason was much less sinister. There had been an exchange of samples between the laboratories and through mislabelling and/or cross contamination Gallo’s team had ended up, without realising it, isolating and sequencing the French virus. The Gods of Possession had deprived Gallo of his right to his own virus.

It took many years before this was officially unravelled. At first Gallo tried to argue that the French patient might have left a blood sample in the States before making his way to Paris<sup>9</sup> or, later, that the amount of virus which Montagnier had sent him was too little to grow<sup>10</sup> or, even later, that the French had contaminated their sample with his virus!<sup>11</sup> And, of course, the Patents were a big problem. If Gallo’s AIDS test was based on the virus from the French patient and not his own, the division of royalties (which had been agreed between President Reagan and the French Prime Minister Jacques Chirac in 1987) would have to be altered in favour of the French. This eventually happened at a joint meeting of the French and American AIDS Foundation in July 1994 at NIH in Bethesda. The head of the Pasteur Institute announced “there is today an official acknowledgement by the US government... that the virus which was used to develop the American AIDS test kit was in fact a virus which had been isolated at the Institut Pasteur and sent to the United States”<sup>12</sup>.

The mix up surrounding who “owned” the virus robbed Gallo of his most prized possession. In 2008 Luc Montagnier and his colleague at the Pasteur Institute, Françoise Barré-Sinoussi, were awarded the Nobel Prize for their discovery of HIV. There was no mention of Robert Gallo. The Gods of Possession had succeeded in depriving Gallo of what he most wanted. Also what final irony if it turns out that Gallo had also, all along, possessed a potential cure (HTLV) but hadn’t noticed!

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### *Notes*

- Note 1:** The Origins of AIDS. Jacques Pepin. Cambridge University Press 2011 ISBN: 9780521186377. The early speculation that HIV might have arisen in Africa has now been substantiated by this outstanding study.
- Note 2:** Retroviral Co-infections: HIV and HTLV: Taking Stock of More Than a Quarter Century of Research Beilke MA AIDS Res Hum Retroviruses. 2012 Feb;28(2):139-47
- Note 3:** The Double Helix. James Watson. Phoenix 2010 ISBN: 9780753828434. This is a re-print of Watson's 1968 wonderfully well written, gossipy, informative and thrilling autobiographical account of the events that led to his discovery of the structure of DNA.
- Note 4:** A quest for fame is not the motivation for all great scientists. Amongst the greatest scientists of our generation was Frederick Sanger. He pursued problems that needed solving whether or not they captured the headlines and whether or not anybody ever heard of him. The first was a method to sequence proteins which led to his first Nobel Prize in 1958. The second was a method to sequence DNA which led to his second Nobel Prize in 1981. He is the only scientist to win two Nobel Prizes in Chemistry; but, as a person, he was self-effacing and shunned celebrity.
- Note 5:** Science Fictions. A Scientific Mystery, a Massive Cover-Up, and the Dark Legacy of Robert Gallo. John Crewdson. Little Brown & Co. 2002 ISBN: 9780316134767. This book is the definitive account of the scientific battle between Robert Gallo at the National Cancer Institute in Washington (who thought HTLV was the cause of AIDS) and Luc Montagnier at the Pasteur Institute in Paris (whose team discovered that HIV was the cause of AIDS). It is a must read for anyone interested in (to quote the author) "how scientists behave when the stakes are high" it is also a must read for anyone interested in one of the best pieces of investigative reporting on a scientific subject. Virtually all the history which I describe in this appendix is sourced from John Crewdson's masterly work. (The opinions are my own). For this incident see pages 56-57.
- Note 6:** Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for Acquired Immune Deficiency Syndrome (AIDS). F. Barré-Sinoussi; J. C. Chermann; F. Rey; M. T. Nugeyre; S. Chamaret; J. Gruest; C. Dautuet; C. Axler-Blin; F. Vézinet-Brun; C. Rouzioux; W. Rozenbaum; L. Montagnier. Science, New Series, Vol. 220, No. 4599. (May 20, 1983), pp. 868-871.
- Note 7:** See Note 5 page 179.
- Note 8:** See Note 5 page 236.
- Note 9:** See Note 5 page 180.
- Note 10:** See Note 5 page 211.
- Note 11:** See Note 5 page 394-395.
- Note 12:** See Note 5 page 521-524.

**Robert Silman** is a doctor/scientist, for many years Senior Lecturer and Honorary Consultant at St. Bartholomew's and the Royal London School of Medicine where he authored scores of research publications in the major scientific research journals, principally on the role of the pituitary hormones ACTH and endorphin in pregnancy and parturition, and the pineal hormone melatonin in growth and puberty. Before medical school he obtained a degree in Philosophy (Licence ès Lettres) at the Sorbonne where he co-wrote a political thriller, *Assassination*, under the pen name Ben Abro, published by Jonathan Cape in the UK and William Morrow in the USA. The book gave rise to a libel action with a celebrated French politician. The book was withdrawn during court proceedings and was republished in April 2001 by the University of Nebraska Press (ISBN: 9780803259393) with an extensive historical addendum on the accompanying libel action.

**Steven Froelich** is an actor/playwright. His first play, *They Offered Bob and Wilma Cash*, had Sylvia Miles in the lead with Steven playing opposite as her son. His second play, *Weekend In Rio*, was work shopped at the Steppenwolf Studio in Chicago with Laurie Metcalfe in the lead followed by public performances at the Edinburgh Fringe Festival where it received two Best Actress nominations.