

Michael Worobey's wobbly research into the early history of HIV

In late October and early November 2007 there was coverage in several media outlets (mainly in the US) of a newly-published study entitled "The Emergence of HIV/AIDS in the Americas and Beyond". The lead author was Michael Worobey, an assistant professor of ecology and evolutionary biology at the University of Arizona in Tucson.

Worobey's study focuses on the early spread of HIV-1 and AIDS out of Africa – and to the rest of the world. It concludes that, after it emerged from Africa, the first staging-post of pandemic HIV-1 was on the island of Haiti, and that it was from there that the virus later moved on to the United States and Canada. (The phrase "pandemic HIV-1" is used to mean the type of HIV that is found predominantly in North America and Europe: the so-called "Euro-American strain" of HIV-1, known officially as HIV-1 Group M, sub-type B.)

In itself this seems a reasonable hypothesis, one that was first mentioned in the non-medical literature as long ago as 1987, when it was proposed in Randy Shilts' seminal book on the AIDS epidemic, "And The Band Played On" [New York: St Martin's Press]. It is one of several hypotheses that seek to explain how the human immunodeficiency virus arrived on the North American continent, three of which are outlined below.

Hypothesis 1. The Africa – Haiti – North America transmission hypothesis favoured by Worobey is also supported by historical data, for it is known that thousands of Haitian teachers and technocrats worked in the Democratic Republic of Congo (the DRC, the former Belgian Congo) in the 1960s, after the exodus of Belgian officials in and after 1960, the year of Independence, left a critical vacuum. . (The DRC is now almost universally accepted as representing the initial hearth of pandemic AIDS.) Haitians were ideal replacements for the Belgians, being well-educated, French-speaking, black – and more than eager to leave a country dominated by the dictatorships of the Duvaliers.

Hypothesis 2. This hypothesis proposes that subtype B might have travelled straight from Africa to North America where it infected a gay or bisexual man who later infected a Haitian counterpart (probably a bisexual, and very possibly during a vacation). Again, there is some historical support, for during the 1970s gay cruises from the US were extremely popular, and almost all featured Haiti as one of the most favoured stopovers.

Hypothesis 3. In *The River*, I wrote about another possibility: that the virus was exported first from Africa to Europe (and in particular to West Germany), and thence to Haiti and the US. In support of this, the first two retrospectively diagnosed AIDS cases in West Germany date from 1976 and 1977, and thus predate the earliest recorded gay cases from the Americas; both were male patients who died in January 1979 (one of whom is known to have been an active gay/bisexual). A third significant early case was a gay German chef who died of AIDS in Manhattan in 1980, after spending the three previous years working in Haiti, where he first displayed symptoms. This man

apparently originated from Gelsenkirchen, the same city where Zaire (as the DRC was called from the 1970s to the 1990s) played two of its three games in the 1974 World Cup; thousands of Zairois came to Germany to support their team. Where, one wonders, was this man infected – in Haiti or Germany?

Hypothesis 4.

There is also a fourth possible hypothesis about how HIV-1 might have arrived in North America and Haiti, one that was tentatively advanced in my book “The River” in 1999. The clue that prompted this hypothesis was an apparently anachronistic historical detail. The earliest convincing case of AIDS in the United States involved a female baby born in New Jersey in 1973 or 1974 to a sixteen-year-old girl, who was identified as a drug-injector who had had multiple male sex partners. The infant died in 1979 after having shown the symptoms of AIDS for 5 years; her stored tissues later tested positive for HIV-1. Because the baby’s case of AIDS predates any other known AIDS case in North America by at least four years, it would seem to have real significance.

The strong indications are that she was infected perinatally by her teenage mother, who must have been born at some point between 1956 and 1958. Might it be, I wondered, that 16 years earlier, the mother had been one of the infants born to women prisoners at Clinton State Farms in Clinton, New Jersey in the ten years beginning 1955, nearly all of whom were experimentally vaccinated with Hilary Koprowski’s oral polio vaccines?

From late 1955 onwards, Koprowski and his team used Clinton Farms as a convenient North American testing-ground for their early OPVs, and it is therefore eminently possible that they tested not only batches of vaccine that had been produced in the US, but also vaccine batches that had been prepared locally in the Belgian Congo.

Former Koprowski aide Stanley Plotkin has reported that this Clinton hypothesis has been disproved, but I can demonstrate that his claim is incorrect.

There is considerably more to report on this subject, but I feel that this is not the right time to place these matters in the public domain.

[However, more detailed information about the early history of HIV-1 and AIDS in North America, Haiti, and West Germany may be found in chapters 3 to 5 of *The River* (pages 55 to 88), and more about the Clinton hypothesis appears on pages 692-700 and 778-779.]

The inherent bias of Worobey’s paper.

In his Americas paper [PNAS; 2007; 104 (47); 18566-18570; official e-pub October 31st, 2007; formal publication November 20th, 2007], Dr Worobey states that his analysis of the sequences of 122 persons infected with HIV-1 Group M subtype B indicates a 99.8% probability that Hypothesis 1 is correct,

and that the subtype B virus travelled from Africa to Haiti to North America, and not by any other route.

On the face of it, the conclusions of Worobey's paper seem reasonable enough. But there is a huge caveat about this work.

The 122 subtype B sequences on which the work is based consist of five sequences from early Haitian AIDS patients tested in the USA, and 117 subtype B sequences selected from the HIV/AIDS Sequence Database, (after attempts were made to exclude atypical strains and strains which suggested that they might be recombinant in origin). The five early Haitian sequences all apparently came from a Florida doctor, Arthur Pitchenik, who had gathered samples from Haitian men who had emigrated to the US in or after 1975, and whose blood was taken in either 1982 or 1983, after they had first displayed symptoms of AIDS. (It would seem, therefore, that some of these men may have been living in the US for 7 or 8 years before they fell sick.)

As additional historical background (not considered by Worobey), the first plausible case of AIDS from Haiti itself was a retrospectively identified case from 1978, and 7 further plausible Haitian cases have been identified from the years 1978 and 1979. Four of these eight cases from the 1970s were from Haiti itself, and four involved Haitians living in Canada and the US.

Save for the intriguing paediatric AIDS case from New Jersey mentioned above, the first *American* to show symptoms of AIDS did so in the first quarter of 1978. A total of 12 US cases (11 in gays/bisexuals) were retrospectively identified from 1978 and 1979 (one of whom may have been Haitian; [Selik RM, "Acquired Immune Deficiency Syndrome (AIDS) Trends in the United States, 1978-1982"; *Am. J. Med.*; 1984; 76; 493-500.] (However, in other papers the first Haitian with AIDS in the US is documented as presenting in early 1980.)

By the end of 1981 there were hundreds of American AIDS cases, and Haitians were one of four risk groups who were indiscreetly described by certain CDC scientists as "The 4 Hs": homosexuals, heroin injectors, haemophiliacs and Haitians.

Of course, this historical background begs a question. Where are the viral sequences from the early AIDS cases from the US – the cases that did not involve Haitian immigrants?

The earliest US HIV-1 sequences included in Worobey's study are eight sequences dating from 1981 and one from 1982. Although the eight 1981 sequences predate the earliest Haitian sequences in the study by one year, this may not be very significant. This is because, as far as I can determine, all nine of these early US sequences are from gay/bisexual men, and the epidemiological evidence suggests that HIV-1 only entered the hothouse atmosphere of the gay bath-houses in 1977-8, after which the virus spread like wildfire. (The fact that the first people in the world to be identified with AIDS were gay American men was probably a function of the fact that multiple

partner exchange, especially in the bath-houses, allowed a large number of gay men to become infected with HIV very rapidly. Partly because of the weight of numbers, and partly because multi-partner gay sex also encourages a wide range of other infections, it was almost inevitable that some of these gay men became “fast progressors”, and progressed rapidly to showing symptoms of AIDS. We now know that roughly 1% of HIV-infected persons display frank symptoms of AIDS in less than a year.)

It is therefore apparent that many of the US AIDS cases who provide the 1981 and 1982 sequences in Worobey’s study may only have been infected with HIV since 1978-1980. By contrast, the five Haitian AIDS patients tested in 1982-3 may not have been fast progressors, and may well have been HIV-infected before leaving Haiti as early as 1975. (It is worth noting that 1975 represented the peak year for “boat people” – Haitians who escaped to the US by sea.)

In short, Worobey finds that the five Haitian sequences are more ancient (set deeper in the phylogenetic tree) than the US sequences, but this may merely, or mainly, be a function of the fact that the Haitian patients were infected in an earlier year, as in all likelihood they were. So what he may actually be recording here is the year of initial infection.

To guard against this possibility, he surely needs to include in the study some sequences from US citizens who were infected back in the 1970s.

And indeed, there is no obvious reason why earlier US HIV-positive serum samples were not also studied. Huge numbers of serum samples were taken from gay and bisexual American men for many different studies throughout the 1970s. In particular, starting in 1977-8, sera were routinely gathered from hundreds of gay and bisexual men in five different North American cities (including New York, Los Angeles and San Francisco), as part of the Five Cities Study. The earliest retrospectively proven HIV-positive serum sample comes from a gay man tested in New York on September 6th, 1977 – but within the next 27 months a viral explosion took place, for both the San Francisco and New York cohorts referred to above were retrospectively found to have levels of HIV-positivity of above 10% by the end of 1979!

Yet as far as I know, there has never been any molecular analysis of HIV-1 viruses from these 1970s sera, or from the stored tissues or sera of US AIDS cases from the 1970s.

What, I wonder, would be the result if the US sequences included in Worobey’s study had included sequences obtained from the very beginning of the gay epidemic, or from one or more of the seven HIV-positive babies (all born to drug-injecting mothers in New York and San Francisco, many of whom may also have been prostitutes) in 1977? [See *River*, pages 71-72.] Or what if his study had included a viral sequence from the HIV-infected baby born to a drug-injecting New Jersey mother in 1973-4 (alluded to in Hypothesis 4 above)?

I believe that if sequences from early US AIDS patients (or, indeed, early German AIDS patients) had also been included in this study, the outcome of the molecular analysis might have been different.

For instance, such a study might conclude that HIV-1 travelled first from Africa to the Americas, and was then exported via a US infectee to Haiti, where it first entered the gay/bisexual community, and was then re-exported back into the US and Canada a few years later, perhaps via a gay cruiser, or else one of the boat people, thousands of whom fled Haiti for Florida from 1975 onwards. Or else such a study might conclude that the virus had actually travelled from Africa to Germany to Haiti to the US.

In short, it may well be that the findings of Worobey's study were almost inevitable, given his choice of samples. Under these circumstances, I would propose that his conclusions (that HIV-1 arrived in Haiti before it came to the US) cannot be relied upon. When a study is biased in its selection of samples, it is hard to draw any meaningful conclusions.

The strange dearth of early molecular data from the US.

The lack of any molecular studies of early HIV-positive stored sera and tissues from the United States is remarkable, and deserves further comment.

It would seem that North American doctors are keen to do molecular analysis on potential AIDS cases and HIV infectees from Africa (many studies); the UK (the famous case, apparently later refuted, from 1959: the so-called "Manchester sailor") and the Caribbean (Worobey's research), yet there is apparently a total lack of studies of early US and Canadian HIV-infected sera and tissues, and thus no molecular analysis of early North American HIV sequences.

This great gap in the published research also extends to epidemiological studies of the US epidemic. Beginning in 1990, I conducted interviews with doctors from the CDC and elsewhere who were involved in the early days of the American AIDS epidemic. In retrospect, one thing I repeatedly noticed was that nobody from the CDC was willing to talk about the earliest cases.

People such as Jim Curran, the epidemiologist who was the first head of AIDS research at the CDC, and who was the last author of the aforementioned "AIDS trends in the US, 1978-82" paper, were notably reticent about these crucial cases. I was asking for details such as dates, places and symptoms, and not for the names of patients, so there was no need for excessive confidentiality. Despite this, I met with a wall of silence. The only witnesses who were more forthcoming on this topic were a couple of doctors who had left the CDC, and with their cautious help (allied to information obtained from Shilts's epic book, "And The Band Played On"), I managed to reconstruct a fair part of the early US epidemic (see Chapter 3 of *The River*).

Many questionable decisions were made in those days. For instance, Shilts relates that the notebooks of the epidemiologist who had single-handedly

tracked the early spread of AIDS in San Francisco were shredded by the local public health department within two months of her retirement, with patient confidentiality apparently cited as the reason. These days, such wilful destruction of vital epidemiological data would appear breathtakingly irresponsible.

For studies of ancient sera and tissues, the names of patients or serum donors are *automatically* withheld, which removes the risk of compromising patient confidentiality. This makes it truly remarkable that no virological studies of early US samples, and no molecular analyses of early US HIV-1 viruses, have yet been carried out (or at least reported in the medical literature).

Is it possible that these vital ancient samples have been autoclaved (just as that early epidemiological data from California was apparently shredded)? I very much doubt it. But in that case, why the dearth of early HIV-1 studies from the US itself? Is it possible that there are concerns that such analyses might reveal some inconvenient or embarrassing information?

The unique prehistory of Subtype B.

There is one further strange historical detail that needs to be mentioned. From the late 1970s onwards, HIV-1 Group M Subtype B experienced epidemic spread in North America and Europe (and indeed in the rest of the world outside Africa). In fact, in many parts of the world outside Africa, it quickly became the dominant strain of HIV.

And yet in Africa itself subtype B apparently either never existed, or else quickly died out. Indeed, until the last few years, the only strains of HIV-1 subtype B ever detected in Africa came from three or four blood samples obtained in the 1990s, which in all likelihood represented viruses that had been re-imported to Africa from the West.

The only plausible candidate for a genuine *African* subtype B virus was one that was retrospectively reported in 2001. It came from a serum sample from a Congolese woman from Kinshasa who was originally tested at some point between 1983 and 1985. Some 15 years later, her virus was among a group of HIV-1 viruses from the DRC that was sequenced by Tom Folks' retrovirology team from the CDC with the results published as: M.L. Kalish, T.M. Folks et al., "Evidence for the Presence of all Known HIV-1 Group M Subtypes and Some Unclassifiable Strains in Kinshasa, Zaire, in the Early to Mid-1980s"; 8th Conference on Retroviruses and Opportunistic Infections; 2001; Abstract 268.

Every single one of the major subtypes of pandemic HIV-1 (ten, in those days) had been found in this early sampling of the city of Kinshasa – a unique and hugely significant result.

The presence of a subtype B virus in that city was especially fascinating. In 2002 I e-mailed Folks, asking whether he thought that this 1983-5 subtype B

had been a local virus (ie one originating from Zaire, now called the DRC) or a Western re-import, and he e-mailed back: “Only a hunch, but I would guess home (local) infection.”

I found this implausible, in that it was his own team that had sequenced the virus, and yet we then heard nothing more about it – as we surely would have done, if this had been the only genuine sample of *African* HIV-1 subtype B in existence.

Five years later I asked Folks (now retired from the CDC) the same question, and on December 16th, 2007 he e-mailed back a different answer: “Yes, I agree, it would be strange to find it [the subtype B sequence] there [in Kinshasa] if it were not reimported, but of course, no proof.”

It appears, therefore, that (alone of all the subtypes) the molecular biologists have found no genuine examples in Africa of HIV-1 subtype B.

Of course, the ancestor of all subtype B viruses could still have existed in the DRC back in the 60s, and could have caused onward spread to Haiti, the US and the rest of the world, before dying out in the DRC itself.

Alternatively, the OPV theory (and in particular the Clinton sub-hypothesis outlined above) clearly provide another possible explanation.

This sub-hypothesis would beggar the following questions:

- a) What if the original subtype B virus existed in a vaccine batch that was prepared in the Belgian Congo in the 1950s, but was either never given to humans in that country, or else used only on a limited scale in the Congo, causing only sporadic infections that were insufficient to spark a full-scale subtype B outbreak in that continent?
- b) And what if this same batch was among those sent back to the US for laboratory testing, and was also tested *in vivo* on an infant or infants from the women’s prison in Clinton, New Jersey?

Depending on one’s beliefs about origins, this scenario may or may not seem far-fetched. But I believe that it is no more far-fetched than the scenario proposed by Michael Worobey, which is based on a whole series of assumptions, none of which are scientifically proven.

When one examines the information (including historical details) available from a number of different sources, rather than making a theoretical analysis that is solely based on a phylogenetic dating theory that has been shown to be inherently flawed, it is revealed that Worobey’s near-certainties are actually based on rather flimsy ground.

Hypothesis 1 (the Africa-to-Haiti hypothesis favoured by Worobey) is a perfectly plausible hypothesis, and may indeed reflect what actually happened historically. However, I firmly believe there is nothing in Worobey’s paper that disproves Hypotheses 2, 3 or 4.

Worobey's wobbly dating analysis.

In a press release dated October 29th, 2007, Professor Worobey also proposed some dates to flesh out his transmission scenario. He suggested that HIV-1 arrived in Haiti from Africa in “about 1966”, and that the first American was infected with a Haitian version of the virus in “about 1969”. This was sexy stuff, and it engendered coverage in several newspapers.

The latter date is somewhat earlier than many previous estimates, such as those which placed the arrival of HIV-1 in the United States in the early to middle 1970s, mainly on the basis of epidemiological analysis. It requires HIV-1 to have been circulating in the US for 12 years before AIDS was first recognised and reported (in Los Angeles in 1981). I find this rather implausible, but it is certainly not impossible.

What is far less plausible, and in fact highly controversial, is the use of phylogenetic or molecular analysis to try to date the age of HIV-1 isolates.

A brief aside. The early molecular analysis of immunodeficiency viruses by people such as Beatrice Hahn, Paul Sharp and Bette Korber was incredibly useful. It illustrated, for instance, that a simian immunodeficiency virus (SIV) discovered in a Tanzanian baboon had been acquired from a local African green monkey (perhaps one that the baboon had attacked or eaten); this was one of the earliest proofs that cross-species transmission of SIVs occurred in the wild.

And the systematic surveys of SIVs in primates that these and other doctors are currently conducting in different parts of Africa (which have recently discovered an SIV in the gorilla, one that is related to – and probably derived from – chimpanzee SIV) continues to this day to provide dramatic and important new information.

But unfortunately, as the activities of these researchers have grown and their grants have multiplied, some of them have over-reached themselves and have started to make exaggerated or misplaced claims.

Their attempts to *date* the events on their family tree of SIVs and HIVs is perhaps the best example of science that is based on assertion, rather than on solid scientific principles.

I strongly believe that their research into the “molecular dating of HIV” is inherently unscientific, because it is based on a false premise. This premise is that HIV-1 mutates at a constant rate, according to a molecular clock that beats like a metronome – and that this mutation rate can be measured and used to calculate the dates of significant events in the virus's early history.

Or to put it in Worobey's own words, from an interview he did with National Public Radio on November 12th, 2007: “Because viruses mutate at a relatively constant rate, you can actually calibrate what we call a molecular clock, and

when we did that we find [sic] that the US epidemic basically – all of it – traces back to what looks like a single migration event of the virus, somewhere around 1969, plus or minus a couple of years.”

In reality, this molecular clock approach is a reasonable approach for dating DNA-based viruses like smallpox, which evolve almost exclusively through mutation. However, it begins to fail for RNA-based viruses, and in particular retroviruses, where a substantial degree of evolution occurs through recombination. Recombination occurs when two different viruses meet inside a cell, and exchange portions of each other’s genomes (much as a male and female human have sex and produce a baby with the genetic characteristics of both parents).

Recombination is a totally different form of evolution from mutation, and it cannot be measured by a molecular clock.

HIV-1 is the most *recombinogenic* human virus (ie the human virus most prone to recombination) known to medical science. A study published back in July 2002 spelt out just how recombinogenic this virus is. In its title it referred to “massive recombination” and it revealed that recombination is four to ten times more common than mutation in both HIV and SIV. [S. Wain-Hobson et al., “Network analysis of human and simian immunodeficiency virus sequence sets reveals massive recombination resulting in shorter pathways”; J. Gen Virol.; 2002; 84; 885-895.] This important paper also revealed the direct implication of this finding: that HIV sequences were in reality younger (ie closer to the present) than had been anticipated by molecular dating analysis.

A commendably fair-minded commentary on this “really interesting and beautiful study” written by *Science* staff writer and AIDS specialist Jon Cohen (himself no friend to the OPV theory in the past) concluded that it “raises significant questions about phylogeny trees that attempt to date the origin of HIV, all of which intentionally discard suspected recombinants to make the data interpretable”. [*Science*; 2002; 297; 312-313.]

As Wain-Hobson and Cohen highlight, all that geneticists such as Michael Worobey can do in their dating attempts is to exclude *obvious* recombinant HIV-1 sequences from their analyses, so that what they are left with are sequences that have supposedly evolved only through mutation.

In reality, however, HIV-1 sequences that recombined early in their evolutionary history can no longer be identified or recognised, and therefore cannot be excluded from the geneticists’ analyses. In short, there is no way of knowing whether or not any given HIV-1 sequence features ancient recombination.

What this means in practice is that evolutionary dating analysis of HIV-1 is inherently flawed, and that it tends to promote dates of origin that are (a) unreliable, and (b) too far back in the past.

Perhaps the best-known example of HIV-1 phylogenetic dating was published in 2000 by Professor Bette Korber's team at the HIV Sequence Database at Los Alamos. This was a paper published in *Science*, which proposed that the Most Recent Common Ancestor (MRCA) of pandemic HIV-1 existed in about 1931 (plus or minus 10 or 15 years). [Korber B. et al.; "Timing the ancestor of the HIV-1 pandemic strains"; *Science*; 2000; 288; 1789-1796.] Effectively, Korber was proposing a date of origin for the HIV-1 virus in Africa, and thus a start date for the global AIDS pandemic.

The publication of the paper was promoted by a huge press conference, and it naturally garnered world-wide headlines. The science it proposed was elegantly presented, but it was essentially fantasy.

It is noteworthy that Michael Worobey stresses that his dates for the arrival of HIV-1 in Haiti and the US are broadly consistent with this 1931 start date.

In reality, the principal HIV-1 molecular daters turn out to be quite a small group of American, British and Belgian scientists who tend in practice to come up with dates that are consistent with Korber's ancestral date of 1931. This in turn may mean one of two things:

- a) That the work of all these scientists from Korber onwards is remarkably accurate, even though they are using a molecular clock to try to measure the mutation rate of a virus that evolves mainly through recombination, or
- b) That the findings in Korber's original study were dubious, and that all HIV-1 molecular dating studies since then have been equally dubious, as they have strived for internal consistency with Korber. In short, that these researchers' results tend automatically to be self-confirming.

I personally favour scenario (b), and I am not alone. Many scientists with whom I have spoken and corresponded, including molecular biologists and population geneticists, believe that in reality, the molecular dating studies of HIV-1 represent a 21st century version of alchemy, the medieval science which claimed that base metals could be "transmuted" into gold. In the Middle Ages, alchemy was an accepted science. Nowadays, alchemy is viewed with gentle amusement, since it is recognised that the basic premises and assumptions underlying that "science" were wrong.

With the molecular dating of HIV-1 so many different parameters are possible, most notably the selection or rejection of different HIV-1 sequences and the choice of the specific model used to create the molecular clock, that one can arrive at any one of a rather wide variety of dates in the final results column. It therefore becomes relatively easy to come up with dates of origin that tie in with one's preconceptions, and to convince oneself that one is producing great science when all one is actually doing is reflecting and repeating dubious science of the past.

The latest type of model that the HIV-1 molecular daters (including Worobey in his "Americas" study) like to use is called a "relaxed molecular clock", which allows the mutation rate to vary among the various HIV-1 sequences. In lay

terms this means a clock that does not always act like a clock. With such a clock, it is not so difficult to bend time.

However, a recent key paper from this school of phylogenetic daters (Anne-Mieke Vandamme's group from the University of Leuven, a seat of learning which was a major collaborator on Koprowski's 1950s CHAT vaccination trials in Africa) contains rather revealing information about the limitations of these procedures. It concedes how difficult it is, even among the major HIV-1 subtypes, to identify recombinant sequences, and states the following: "As current phylogenetic methods are not capable of accurately reconstructing the evolutionary histories of highly recombinant strains, it may never be possible to correctly assign for all strains which one is the recombinant and which one is the parent." [Abecasis AB, Vandamme AM et al.; "Recombination confounds the early history of human immunodeficiency virus type 1; subtype G is a circulating recombinant form"; J. Virol.; 2007; 81 (16); 8543-8551.]

(Finally, it is worth pointing out that Vandamme's group at Leuven is not unique, for nearly all the American, British and Belgian phylogenetic daters mentioned above are either from labs which collaborated directly with Koprowski in the CHAT trials in Africa in the 1950s, or else are scientists who are known to have had contacts in the recent past either with Koprowski's former deputy Stanley Plotkin, or Plotkin's group of anti-OPV collaborators. Whether this is significant or coincidental is not yet apparent.)

Possible explanations for the phylogenetic dating mumbo-jumbo.

Outside the heady atmosphere of the molecular dating labs, an increasing number of scientists have over the last seven or eight years realised that molecular dating analyses for HIV-1 are unreliable. The fact that relatively few have spoken up about it is mainly a factor of the way Science is conducted today.

The origins-of-AIDS controversy is one of the most politically-loaded debates in Science. Over the years many scientists (some of whom are generally regarded as eminent) have spoken to me off-the-record, on the basis that I never mention their names. There is widespread concern that getting involved in this debate on the "wrong" side could turn out to be injurious to your health (ie to your funding and career prospects).

This fear may seem incredible, or exaggerated. If you think so, then cast your mind back to the 1930s, when millions of Germans (and indeed, Britons and Americans and others) found it acceptable, or possible, to cast a blind eye to what the Third Reich was doing in Germany. Let me be absolutely clear: I am not suggesting that the HIV-1 geneticists are Nazis! I am merely underlining that there are many ways in which (and levels on which) beliefs, whether or not they are sincerely held, can be transformed into dogma. I am also stressing the fairly obvious fact that because the man and woman in the street (and indeed, the scientist in the lab) don't have the time to investigate every scientific issue for themselves, they tend in practice to accept much of what they are told by scientists who *have* spent years studying those particular

issues, and who are perceived as experts. In reality, it is not that easy to question the expertise of “experts”.

The dissenting scientists referred to above all expressed deep-seated scepticism about the molecular dating of HIV-1, but insisted that I treat their words as either unattributable or off-the-record. Of course, I have respected their wishes. However, there are also some highly experienced scientists who have spoken up *on the record*. I am keeping some up my sleeve for now, but two who have come out publicly are professors Gerry Myers and Mikkel Schierup.

In 2000, Professor Myers had recently retired from his job as head of Group T-10 at the Los Alamos National Laboratory (the group responsible for compiling the HIV Sequence Database), where he had been Bette Korber’s boss. Despite having health problems at the time, Myers wrote an intelligent and powerful critique of Korber’s HIV-1 dating work. Gerry Myers was not well enough to fly to London to present this paper at the Royal Society conference on “Origins of HIV and the AIDS epidemic”, but it was presented instead by a young statistician who had co-authored the paper, Tom Burr. [T. Burr, G. Hyman and G. Myers, “The origin of AIDS: Darwinian or Lamarckian?”; *Phil. Trans. Roy. Soc. (London) B*; 2001; 356; 877-888].

However, five months earlier I had flown to Los Alamos to meet with Myers (for the second time) in order to discuss the molecular analysis of HIV-1. A classicist by training, Myers is a logical and independent thinker, and during our April 2000 meeting he gave me a clear sense of the extent of the disagreement and uncertainty that had existed among the HIV phylogeneticists about how best to undertake the dating of ancient HIV-1 isolates.

In his Royal Society paper, Professor Myers found Professor Korber’s dating approach inherently flawed and questioned some of the specifics of her work. However, as he has told me and others on several occasions, he feels constrained from presenting a more sustained critique, partly because Korber is a personal friend of himself and his family.

Another open critic was the Danish population geneticist Mikkel Schierup, whose paper entitled “Recombination and Phylogenetic Analysis of HIV-1” was first presented at the 2001 meeting on HIV origins at the Lincei Academy in Rome; [*Atti dei Convegni Lincei*; 2003; 187; 231-245]. Schierup’s paper ably dismantled the molecular dating approach for HIV-1 by using deliciously understated scientific language. Sadly, the closing speaker at that conference (Robin Weiss) together with Paul Sharp (who also spoke at the conference, but who later withdrew his paper from the published proceedings) and his fellow HIV daters have found it easiest to ignore the import of Schierup’s paper.

So why is misleading research based on the molecular dating of HIV-1 promoted and published in the pages of the major scientific journals? The answer may be fairly simple. It ties in with the vague but non-controversial

bushmeat hypothesis of origin of AIDS, which proposes that the AIDS pandemic arose through Africans eating or butchering chimpanzees in or around the 1930s. Moreover, it appears to refute the Oral Polio Vaccine (OPV) hypothesis of origin, which proposes that AIDS arose through the experimental vaccination of some 900,000 Africans in the Belgian Congo (now the DRC), and what is now Rwanda and Burundi, with vaccine grown in chimpanzee cells in the late 1950s.

Unfortunately, Michael Worobey now appears to be a committed molecular dater, just like his mentors, molecular biologists Bette Korber and Paul Sharp. As a result, he tends to come out with sweeping and unreliable statements. For instance, in his November 12th, 2007 interview on NPR, he said the following: “[T]here’s a lot of evidence that [the HIV-1] virus was circulating in central Africa for many, many years before it emerged elsewhere in the world.” Worobey went on: “That evidence comes in part from” the fact that similar viruses are found in African apes and monkeys, and that these primates are sold as bushmeat in African markets.

That was all the explanation he gave. In reality, this constitutes no *evidence* at all, merely a hypothesised mode of transmission which has never been supported by a single compelling piece of evidence.

I believe that Worobey’s claim (that HIV-1 had been circulating for “many, many years before it emerged elsewhere in the world”) is unreliable. Even if one accepts Korber’s date of 1931 plus or minus 10 or 15 years for the emergence of HIV-1 in Africa (which, remember, is an entirely theoretical calculation), this would place emergence in Africa only some 25-35 years before Worobey’s date of export to the rest of the world. This is hardly “many, many years before”, especially when one considers that Africans must have been killing, skinning and eating SIV-infected primates for hundreds of thousands of years!

Given the premises and vague assumptions of the bushmeat school, I would have expected HIV-1 to have emerged in Africa not in 1931, but in 1931 BC....or perhaps 1931000 BC!

The question that the molecular daters prefer not to ask.

I often wonder how these HIV phylogenetic daters can avoid asking themselves what seems to me to be the key question. The question is this. Why is it that, according to them, ten separate transfers of SIV from African primates to man have all occurred during the recent past (in fact, during the middle part of the twentieth century), whereas Africans have been eating and butchering chimps and other monkeys since time immemorial?

According to their own analysis, these ten primate-to-human transfers comprise seven transfers of sooty mangabey SIV to make HIV-2 Types A to G (only two of which, Types A and B, have spread further among humans to cause actual human outbreaks), and three transfers to humans of chimpanzee

SIV to make HIV-1 Group M (causing pandemic AIDS), Group N and Group O.

I believe that these geneticists are actually caught in a cleft stick. On the one hand, they cannot argue that HIV and AIDS existed as far back as the early 19th century, because it is easy to prove that those millions of Africans who were forcibly taken to the Americas during the Slave Trade were not infected with any of the HIVs. So this is where their much-vaunted phylogenetic dating analysis comes in. This allows them to argue that those ten proposed transfers of SIVs to *Homo sapiens* occurred during the 20th century, *but only during the first half of the twentieth century, a few vital years before the polio vaccination campaigns of the 1950s and 1960s!*

The molecular biologists contend that the index case of the AIDS pandemic, the very first HIV-1, existed in 1931. So why, according to them, was no AIDS seen in Africa *before* the 1960s or 1970s? They argue that it must have been there, but went unrecognised (a) because the numbers infected were smaller, and (b) because these early cases were instead diagnosed as one of the typical AIDS indicator diseases, such as tuberculosis.

To my mind (and here I am confident of the support of many Africa-based clinicians), this rather jesuitical argument actually demonstrates a basic misunderstanding, or misinterpretation, of the clinical presentation of African AIDS. In reality, AIDS very rarely presents as just a single disease such as TB. In reality it usually presents with a striking range of opportunistic infections (such as oral thrush, and certain specific – and untreatable – dermatological, respiratory and enteropathic complaints) which allows it to be recognised surprisingly quickly. (In the years before AIDS was identified, such a case would have been recognised as striking and unusual; from the 1980s onwards it would have been recognised as AIDS.)

Indeed, this is a key point about AIDS, one that I tried to make in the opening chapters of *The River*. Even to inexperienced observers, the condition of AIDS is readily recognised as something that is different and new. For instance, the first cases in the Rakai district of southern Uganda were seen in 1982, and by 1984 the local people had given this apparently new disease a new name: “Slim”. (This was even before Slim was recognised by Western doctors in Africa as a presentation of AIDS.) The Sharps and Worobeys, by contrast, apparently believe that thousands of Africans must have been infected between the 1930s and the 1960s, but that nobody noticed that anything new was going on!

In any case, even if one were to accept their 1931 start date as accurate, there is another possible explanation, one that is I believe far more compelling. As I have reported since year 2000, experimental polio vaccination campaigns that used vaccines grown in the kidneys of (a) chimpanzees; and (b) baboons and “other monkeys” (including sooty mangabeys) were staged in Africa in the 1950s and early 1960s, in the very places which are now known and accepted as the geographical hearths of HIV-1 and HIV-2.

The geneticists assume that the various outbreaks of AIDS all evolved from a single index case of HIV infection. However, their molecular dating approach cannot distinguish between one single HIV infection in, say, 1931, and a small cluster of index cases infected via the African vaccines used in the late 1950s. This is because, according to their model, their 1931 index virus would, over 25 or 30 years, have evolved genetically to the same extent that would obtain if multiple HIV-1 variants were introduced to humans in the late 1950s via different batches of vaccine.

To put it another way, the geneticists believe that the nine or so genetically divergent subtypes of HIV-1 group M (pandemic HIV-1) all evolved from that one index case between the 1930s and the 1950s, whereas I believe that the different HIV-1 subtypes represent the different viral strains that were transferred to humans via the different vaccine batches. (It appears that the OPV batches given to humans in Africa were produced in series, one from another, so there is the potential for new chimp viruses to have entered the "soup" and recombined every time that new chimp tissue cultures and chimp sera were employed to grow a new batch of vaccine.)

In short, despite the two very different scenarios for first transfer proposed by the bushmeat and OPV hypotheses, the epidemiological (and phylogenetic) patterns from the late 1950s onwards would be exactly the same.

Has there been a cover-up?

Major scientific journals such as *Science*, *Nature*, and the *Proceedings of the National Academy of Sciences* continue to publish the impressive-sounding (but ill-supported) scientific research of researchers such as Bette Korber and Michael Worobey, while refusing all submissions that contain material or analysis supportive of the OPV hypothesis, even submissions from men as eminent as Bill Hamilton.

Why are these leading scientific journals showing such apparent bias? I believe that the reasons are partly financial and political, and partly ideological.

The Belgian Congo vaccination campaign was master-minded by American and Belgian scientists, and they and their successors can be imagined to be far from happy at the prospect of being sued for billions by large numbers of AIDS patients, for instance in a class action suit.

The governments of the USA and Belgium, both of which backed the trials financially and administratively, may feel very much the same way, and be every bit as defensive.

As for the ideological reasons, vaccination is the Holy Grail of Modern Medicine, and is the process on which most public health interventions are based. It is therefore also the process that can never be allowed to be seriously questioned or criticised in the public domain.

Never mind that I repeatedly emphasise in my writings that most vaccination campaigns are safe, and that I am simply questioning the safety of one experimental campaign conducted in the 1950s. From the perspective of many (far too many) of those in the public health fraternity, it's a case of never mind what happened in the past: OPV/AIDS is a "dangerous theory" that could adversely affect popular confidence in the vaccination campaigns of the future.

I believe that the bias, as evidenced in part by the censored coverage in major scientific journals, is so extensive that it amounts to an implicit cover-up. Unfortunately, many scientists do not have the time or inclination to investigate these matters themselves, and they therefore tend to accept what *Nature* and *Science* have already pronounced on the subject. In practice, this means accepting the assurances of well-known scientists such as British retrovirologist Robin Weiss, who is, I believe, one of the principal architects and promulgators of the "official" bushmeat version of how AIDS began.

In response to my book *The River* in 1999, Professor Weiss wrote a cautious, but basically positive, review in *Science*, and then helped organise the Royal Society meeting on "Origins of HIV and the AIDS Epidemic" in September 2000. He skilfully arranged and co-ordinated that meeting so that it highlighted the establishment response to the OPV hypothesis, a response that was based on (a) the bushmeat hypothesis, (b) phylogenetic dating analysis, and (c) the testing of samples of CHAT vaccines obtained in the US and UK.

The latter samples of vaccine had never themselves been used for vaccination in Africa, and they clearly represented different batches of vaccine from those used in Africa (although Weiss and others tried to argue otherwise, mainly by obfuscating the issue). Of course, all these vaccine samples from the US and UK tested negative for SIVs and for chimpanzee DNA.

Apart from promoting and favouring such misleading research, several speakers at the Royal Society meeting deliberately tried to confuse and obfuscate the history of what had actually happened during the OPV campaigns in Africa. And then came the *coup de grace* in the form of Professor Weiss's closing speech. His comments were quite blatantly biased, favouring only the bushmeat theory, and these were the comments that got reported in the press and in scientific journals the world over.

Weiss was also present at the second major origins of AIDS conference, held at the *Accademia Nazionale dei Lincei* in Rome in September 2001, where, strangely, he was once again appointed to deliver the final summing-up. This time he was even more flagrantly biased, in that he managed to ignore virtually every bit of the new evidence that I and others (such as Luisa Bozzi and Mikkel Schierup) had presented. This time I was so disgusted that I surprised myself by getting up and walking out, shouting at the podium as I did so: "This speech is a disgrace."

[Michael Worobey's past and future research.](#)

The author of the “Emergence of HIV in the Americas” study is the young Canadian Michael Worobey, a Rhodes Scholar who first worked under molecular biologist Eddie Holmes (another bushmeat proponent) at the Department of Zoology at Oxford University, and who a few years back was appointed head of his own evolutionary biology lab at the University of Arizona in Tucson.

Worobey actually has a significant history of involvement in the origins-of-AIDS debate. Furthermore, he would appear to be the man who is being promoted by kingmakers such as Robin Weiss to become the new “star investigator” of the bushmeat lobby.

The Haitian research may therefore be part and parcel of a continuing process designed to position Dr Worobey in the public eye, and to lend kudos to his work. In reality his Americas paper was not an especially ground-breaking study, but it is one that garners easy headlines – especially when allied to his estimates of when HIV may have arrived in the United States.

And what comes next? This is revealed by the last line of the press release, which states: “Worobey’s next step is following the trail of HIV-1 even further back in time using older archival samples”.

Some clues about what he is actually looking at are provided by Worobey’s 2005 grant proposal to the National Institutes of Allergy and Infectious Diseases (part of the NIH). This ended with his promise to “illuminate the remarkably unstudied early phase of HIV evolution (from around the time of discovery of AIDS, back to 1955 or perhaps even earlier)”.

I consider the fact that Worobey specifically mentions the year 1955, which immediately predates the polio vaccine trials, to be very telling – and in a companion essay to this one I shall explain why such responsible-sounding work is in reality a cause for considerable concern.

Edward Hooper. First version written November 1st, 2007; this updated version written January 20th, 2008; minor changes made and posted on March 19th, 2008.

[See also the essay on “Michael Worobey’s possession of 1950s tissue samples from Stanleyville”, which leads on from this one.]

Michael Worobey's possession of 1950s tissue samples from Stanleyville (Kisangani)

Michael Worobey's first active participation in the origins-of-AIDS debate is believed to have occurred in late 1999, when Professor Bill Hamilton (a highly-respected evolutionary biologist, then rated by many as the "star" of the Royal Society) was seeking someone to accompany him on his second trip to the Democratic Republic of Congo (DRC) to test the SIV of wild chimpanzees.

Some background. Since I first met him in 1993, Bill Hamilton had been my mentor, and he wrote a powerful and highly supportive foreword to "The River". In July 1999, after the book was completed but before it was published, Bill and I spent just over a week in the DRC, but we had some quite serious disagreements during the trip, which focussed on whether I was there mainly to help him with the collection of samples from local chimpanzees, or was also there to conduct my own historical research into Lindi Camp and the *Laboratoire Medical de Stanleyville*. We had obtained visas from the rebel government based in Kisangani (formerly Stanleyville) that were good for six further months, and Bill in particular wanted to return there to do more research. Since he and I were, by late 1999, still going through a cooling-off period (and since I was busy dealing with the response to *The River*, published in September 1999), Bill looked around for a companion in his own Department of Zoology at Oxford University, and came across a young Rhodes Scholar, Michael Worobey, who suggested that they also bring along a Canadian friend of his, Jeff Joy, who had practical skills and experience of living in the wilds.

(Bill and I spoke regularly by phone in the final weeks of 1999, and good relations were restored between us. I had intended to drive up to Oxford to see him the day before his departure for the DRC, but was prevented when my car broke down. However, we did speak once more together when he called briefly by satellite phone from Africa.)

Hamilton, Worobey and Joy set off for Kisangani in early January 2000. The expedition enjoyed success in terms of locating faeces from wild chimpanzees, but worked less well on a practical level. While on safari Worobey got a scratch on his thumb which became infected, but instead of returning immediately to Kisangani, he stayed out in the bush with the others. This nearly turned into a bad judgement call, because by the time they got back to the city, the thumb was almost gangrenous. Bill, meanwhile, declined to take any malaria prophylaxis, and promptly got a serious bout of what appears to have been cerebral malaria (just as he had done during our safari in July 1999). He became seriously ill as they were about to leave Kisangani, and although the Canadians managed to get him on board a flight to Entebbe, Uganda, he was then confined to a hospital bed for several days. Eventually he appeared to have recovered, and the three men flew back together to London. However, after one night spent at his sister's house, Bill again felt unwell, and was taken to University College Hospital in London. While waiting for blood tests, he experienced a massive intestinal haemorrhage, which was probably sparked by a pre-existing condition – and may possibly have been

exacerbated by the aspirins he is believed to have taken to cope with the malaria. He fell into a coma from which he never recovered, and he died six weeks later.

While Bill was lying comatose, Mike Worobey flew back to Nairobi to get hold of the samples of chimp faeces which had for some reason become entangled in Kenyan customs. Later, at Bill's memorial service, Worobey was praised warmly by Richard Dawkins for the role he had played in the expedition. At that service, Dawkins maintained that Bill was a fair-minded neutral who had gone to Africa to test an unpopular and controversial theory (the OPV theory).

This was misleading, in that by 2000 Bill Hamilton and I had been collaborating on OPV/AIDS research for seven years, and Bill was strongly persuaded that the OPV theory was correct. That the Dawkins account did not gain further credence was largely due to the efforts of Bill's partner of his last six years, the Italian science writer Maria Luisa Bozzi. She read a paper at the *Accademia Nazionale dei Lincei* conference on "Origin of HIV" in 2001 in which she quoted from one of Bill's letters to an Oxford colleague, which stated "I rate the chance at about 95%....[that] the OPV theory is right".

From the start, I recognised Worobey as someone who was committed to his work, but was less sure about what to make of him on a personal level. He was a member of Eddie Holmes' evolutionary biology group in the Department of Zoology at Oxford University, which broadly supported the bushmeat analysis and molecular dating claims of Bette Korber, Paul Sharp and Beatrice Hahn. Worobey, however, claimed to be a fair-minded neutral who was not convinced by either theory (bushmeat or OPV). On several occasions he told me that the molecular dating of HIV-1 was a "dog's dinner" because of its failure to take recombination into account. (He seems now to have set aside these reservations, although his reasons for doing so are not apparent.)

On the other hand, Worobey did not appear to be someone who was inclined to rock the boat. Indeed, he seemed to be in awe of certain leading figures in the origins debate, notably Beatrice Hahn and Robin Weiss, and he defended them vigorously against my charges that they had at times acted unscientifically. Broadly, his response to this seemed to be: "So you think you know more about this than they do, do you?"

At one stage in early 2002, I visited Oxford three times to discuss a possible collaboration with Mike Worobey involving the testing of samples from Africa, but I always made it clear that I was not going to put anything in writing in advance about the source of the samples that I might be able to help to provide. Despite this, I was eventually asked to contribute some paragraphs to his grant proposal, which I declined to do. Worobey apparently took umbrage, for he ignored a series of six e-mails I sent him over the next six months, and then when I challenged him to reply within 48 hours if he wished the collaboration to continue, he sent an inappropriately angry and defensive reply.

Soon after this, Worobey was appointed head of his own lab in Arizona, quite a coup for someone so young. And then in 2004, he published his brief communication in *Nature* (co-written with Beatrice Hahn, Paul Sharp and others) about obtaining an SIV sequence from a single *Pan troglodytes schweinfurthii* chimpanzee from the Parisi Forest, some 110 kilometres from Kisangani. In summary, they claimed that the chimp faecal samples gathered during the January 2000 safari with Bill Hamilton had not provided any evidence of SIV, but that urine samples gathered at the same time had given intriguing indications of SIV antibodies. Because of this, Worobey had returned to the Congo in 2003, and had obtained a single SIV sequence from a chimp faecal sample from the Parisi Forest. The SIV in question was apparently similar to pandemic HIV-1, but about 10% less similar to it than the SIV commonly found in *Pan troglodytes troglodytes*, the chimp sub-species originating from Gabon, Cameroon and Congo Brazzaville in west central Africa, a few hundred miles to the west of Kisangani/Stanleyville. The authors then claimed that the Lindi chimps (which by then I and others had identified as having been involved with the preparation of Koprowski's OPVs) had originated only from "the vicinity of Stanleyville". Without more ado they asserted that this one sequence of chimp SIV therefore constituted "direct evidence that these chimps were not the source of the human AIDS epidemic" – and went on to claim that they had "refuted" the OPV theory.

Their claim of having refuted OPV/AIDS was complete nonsense, but as usual *Nature* (where AIDS coverage is allegedly more or less controlled by Robin Weiss) did not publish my brief and pertinent letter of response.

Amusingly, this was the third or fourth time that claims alleging that the OPV theory had been disproved had been published in *Nature* and *Science*, all of them false.

There are several reasons why the claims made in Worobey et al's "brief communication" of 2004 were incorrect, of which I shall itemise just three:

- a) The 400 or more chimps that were used in the polio vaccine research at the LMS and Lindi camp were not just gathered from around Stanleyville/Kisangani (as they claimed), but from right across a region spanning some 200,000 square miles of rain forest, which included areas such as Coquilhatville (now Mbandaka), where there is documentary evidence that *Pan troglodytes troglodytes* chimps were being collected and sold.
- b) It is true that most of the chimps the LMS scientists used came from the *Pan troglodytes schweinfurthii* subspecies of common chimpanzee and *Pan paniscus* (pygmy chimps or bonobos). However, there is documentary evidence that the LMS scientists also used *Pan troglodytes troglodytes* chimps in their research.
- c) There is also documentary evidence that chimps and bonobos at Lindi were frequently housed two to a cage, and that up to ten apes at a time used to be placed inside a large play-cage. Onward transmission of SIVs is known to occur when different species are caged together, so clearly there was potential for onward transmission of a *Pan troglodytes*

troglydytes strain of SIV to either *Pan troglodytes schweinfurthii* or *Pan paniscus*.

Maria Luisa Bozzi was especially indignant and upset about the partisan conclusions that Worobey and his group had drawn in this *Nature* paper, which she considered a betrayal. She apparently sent Worobey a courteous note, in which she commended him for publishing something which related (albeit indirectly) to the work done on that final research trip with Bill. However, she also spoke with me twice on the phone during the days that followed, and here she was much more forthright. I still have the notes from one of these conversations. Dr Bozzi said she had always known that the young Canadian was ambitious, and that he had quite clearly been a supporter of the bushmeat theory from the very start, from even before the time of his safari with Bill Hamilton. (If *she* had always known this, it seems likely that Bill Hamilton would also have been aware of Worobey's leanings in the debate.)

She also told me that Worobey had been telling people in Oxford (including Richard Dawkins) that Bill had "changed his mind" about the OPV theory during the January 2000 trip. The supposed evidence for this was contrived and flimsy in the extreme, and both Luisa and I concluded that Worobey might have been telling certain people what they wanted to hear.

By an unhappy coincidence, Luisa Bozzi died a few days later, after an unusually severe asthma attack. She was aged 64, almost exactly the same age that Bill had been at the time of his death.

The possibility of impropriety.

I am reliably informed from an anonymous source (with information that is largely confirmed by another source) that the one really old sample of HIV-1 that Worobey has managed to locate dates from 1960, and was allegedly provided by a patient from Leopoldville, Belgian Congo. It appears that he intends to make a molecular comparison between this HIV-1 sequence and that of the famous ZR59 sample of HIV-1 (obtained from a Leopoldville male, allegedly in 1959), and then argue that this "proves" that the HIV-1 epidemic must stretch back to before the time of the polio vaccine trials.

If so, then his analysis will once again be highly contentious. We know that virtually every Leopoldville child aged up to 5 years was vaccinated with Koprowski's OPVs (the Type 1 polio vaccine, CHAT, and sometimes the Type 3 vaccine, Fox) in the months between August 1958 and April 1960. Older people, including adults, were also vaccinated with these strains of OPV in Leopoldville (Leo) during this period; (I have primary evidence of several such vaccinations). Besides this, a significant proportion of the adults vaccinated with Koprowski's strains elsewhere in the Congo would be expected to have moved to the capital in the years around Independence, since (a) Leo experienced a huge population influx during those years, and (b) people tended anyway to head for Leo, where there were far better medical services, when they fell sick.

I believe it to be highly significant that (if Worobey's alleged 1960 sample proves to be genuine) the two earliest samples of HIV-1 come from a place that was so extensively vaccinated with CHAT, and date from the years immediately after the start of the vaccinations.

Worobey's 1960 sample apparently came from an adult, and many people (myself included, in the past) have concluded that the ZR59 sample must have come from an *adult* male. However, this is not necessarily so, for other sera coming from the same series of blood samples (also described in the original literature as having been provided by "adults") have in fact turned out to have come from children as young as 3 years! Given the mass-vaccination of Leopoldville's entire population of 0 to 5-year-olds between 1958 and 1960, this is potentially relevant.

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In 2004, Worobey published his first major origins-of-AIDS article (the infamous "Contaminated polio vaccine theory refuted" communication in *Nature*) from his new lab at Arizona. Now in 2007 come the further inadequately-supported claims (especially those based on phylogenetic dating theory) in his latest article about the arrival of HIV in the Americas, and in his press interviews.

After publishing two major articles featuring exaggerated assertions about the age and origins of HIV-1, Worobey is now revealed to be a committed member of the bushmeat lobby. Furthermore, it is known from several different sources that he is closely linked to the Koprowski/Plotkin/Desmyter/Korber/Sharp/Hahn support group described below.

Worobey's undeclared research.

What is most worrying, however, is the other work that Professor Worobey has been doing behind the scenes.

I am reliably informed that in the last year or two he has obtained the remainder of the ancient tissue samples (preserved sometimes in the form of paraffin wax blocks and microscopic slides, and sometimes in formalin, with or without another preservative known as *buin*) from the basement of what was formerly the *Laboratoire Medical de Stanleyville* (LMS), which served as the headquarters lab for the CHAT vaccinations in Africa in the late 1950s.

On the basis of the OPV theory, if there is one place in the world where one would expect to find samples of early HIV-1, it is Stanleyville.

But we now know that the people investigating this possibility also have a considerable vested interest in the results. In past publications, every one of them has shown significant bias towards the bushmeat theory, a theory that

would fall apart if significant clusters of early strains of HIV-1 were found in Stanleyville in the late 1950s.

In April 2001, when I returned to Kisangani, this time accompanied by a film crew, I made a spirited attempt (with the help of the film-makers, who spoke far more fluent French than I) to ensure that at least a portion of the LMS basement samples would get tested at an independent laboratory. However, every submission we made to the then-Rector of the University of Kisangani (who was effectively custodian of the samples) was roundly rebuffed, and it soon became clear that shortly before our arrival the University of Leuven (represented by the then-head of virology, Professor Jan Desmyter), together with an arm of the Pasteur (where former Koprowski aide Stanley Plotkin occupied an executive position at the Aventis Pasteur pharmaceutical house) had both been in touch with the Rector to make formal requests to obtain access to the samples. It was also clear that the University of Kisangani, and in particular certain senior figures at the University, stood to profit significantly if they agreed to these requests.

Both Plotkin and Desmyter clearly had vested interests in these ancient samples: Plotkin because he had helped mastermind the development of CHAT vaccine and the planning of the African vaccination campaigns, and Desmyter because he had taken over the chair of virology at the University of Leuven, the same Belgian university that had collaborated with Koprowski and Plotkin in the African CHAT trials of the 1950s.

An attempt by a Belgian professor who was present in Kisangani at the time of our visit to illegally smuggle some of these samples out in his suitcase was foiled. It later turned out that this professor, who had been born in Kisangani and visited there annually dispensing Belgian government aid, was also directly collaborating with Plotkin and Desmyter.

This Plotkin/Desmyter collaboration began in late 1999 or early 2000. Together with Dirk Teuwen (an Aventis Pasteur employee who was put on secondment on full pay, and given to Plotkin to help him in his efforts to refute the OPV theory) and Abel Prinzie (a Belgian researcher who had worked on CHAT vaccine in the 1950s at the Rega Institute, a semi-independent commercial offshoot of the University of Leuven), they produced a vigorous defence of the CHAT trials, which they presented in the form of a postscript that was added retrospectively (and under conditions of great secrecy) to the published proceedings of the Royal Society meeting on "Origins of HIV and the AIDS Epidemic". [S. Plotkin et al., "Postscript relating to new allegations made by Edward Hooper at the Royal Society Discussion Meeting on 11 September, 2000", *Phil. Trans. Roy. Soc. (London) B*; 2001; 356; 825-829.]

I had a chance meeting in Antwerp in 2004 with Professor Paul Gigase, a Belgian doctor who had done research in the Belgian Congo and whom I had twice interviewed in the past. He told me that he also had played a role in Plotkin and Desmyter's effort to obtain the LMS basement samples. Gigase said that in 2001 or 2002, at Desmyter's request, he had flown to Kisangani with another Belgian professor, Francois Stepman (the head of VLIR, the

Flemish aid organisation to the Congo) and acted as a sort of go-between. Among other things, he apparently persuaded the Kisangani professors to release at least some of the basement samples to the Desmyter/Plotkin group. The samples were apparently flown to Europe shortly afterwards, and Gigase told me that “a large number of blocks” were examined at the Pasteur, (presumably at the directions of Plotkin). Gigase clearly believed that Plotkin was bank-rolling the entire investigation (including the parts played by Desmyter and Teuwen) through Aventis Pasteur, and he expressed surprise that since the samples had arrived in Europe there had been no announcements about them, but only deafening silence. He indicated that he was beginning to regret the helpful role he had played.

Gigase also apparently interviewed one of my witnesses, an ex-worker from the LMS, on Desmyter’s behalf. However, Gigase apparently had not taken notes, and at different times he gave me differing accounts of what this man had allegedly said to him.

This is fascinating, because later, after “The Origins of AIDS” documentary was released, two Congolese professors from Kinshasa apparently flew to Kisangani to interview some of the other witnesses featured in that film. I have since discovered that during this process at least two of these witnesses were pressured – one of them through a financial inducement – to change their testimony on key issues. It is not known how successful this attempted cover-up may have been; all I can say is that one Stanleyville witness, at least, appears to have changed his testimony on one key issue after receiving a bribe. However, I have filmed evidence that this man spoke very differently when first interviewed.

But back to the LMS basement samples. In the last year or two, the remainder of these valuable ancient samples from the LMS have apparently been obtained by Michael Worobey, who has clearly taken over the work of testing them from Plotkin and Desmyter. Since Worobey is also dealing with ancient samples gathered from Leopoldville and elsewhere, one hopes that he is being scrupulously careful about the provenance and labelling of the samples.

What’s the worst that could happen?

There are now huge stakes involved in the outcome of the origins of AIDS debate. Under these circumstances, can one be absolutely confident that men like Plotkin, Desmyter and Worobey will issue accurate reports about the presence (or lack of presence) of HIV-1 in the ancient samples from the basement of the Stanleyville lab?

Alternatively, can one be absolutely confident that an HIV-infected slide or block originating from Stanleyville in 1958 will not end up being misreported as having come from, say, Leopoldville in 1955, or perhaps another place and time entirely (perhaps Ouessou in Congo Brazzaville in 1937, or some other place and year that ties in nicely with the bushmeat theory)?

The bottom line is that it only requires the participation of one unprincipled researcher (not necessarily one of the aforementioned persons) to effect a crucial change to the results.

In April 2001 the team that made “The Origins of AIDS” documentary and I did our best to make sure that at least some of the priceless LMS basement samples were distributed to different labs, and there independently tested. Because of the pressures and inducements from the Pasteur and the University of Leuven, we failed to persuade the Rector and his senior colleagues at the University of Kisangani to collaborate. I personally have continued these efforts since 2001, but apparently without success.

The fact that the LMS basement samples have, since 2001 at latest, been effectively under the control of scientists who have already shown that they are committed to one specific outcome (an outcome based on bushmeat theory) in the origins-of-AIDS debate means that there has been – at the very least – an opportunity for impropriety.

Because there is prima facie evidence that the origins of AIDS was a subject that was all but ignored by the medico-scientific community for nearly two decades, and that since 1999 a number of incorrect claims have been promulgated in the scientific literature, even the fact that there has been an opportunity for impropriety is of great concern.

What should have happened, of course, is that all the LMS samples should have been placed under the control of a neutral body (some might suggest a lab run by the WHO), and then aliquots from those samples should have been distributed to a variety of different labs to test. Instead, they have fallen under the control of Stanley Plotkin and his allies.

The fact that these samples were not placed under the control of a neutral and independent body means that there will always be the suspicion that the results may be skewed.

For instance, key early HIV-1 results from Stanleyville/Kisangani may have already been suppressed, and indeed, may never be published in the future.

Furthermore, there have clearly been potential opportunities for mislabelling of samples during the transportation and testing process.

This means that there will now be legitimate doubts about the authenticity of any other early HIV testing results that may be announced in the future.

Afterword.

For the record, I have received an anecdotal report from an unexpected source about the results of the HIV testing of some of these archival materials from the LMS basement, and I am currently trying to obtain confirmation of this information.

Ed Hooper. First version completed November 1st, 2007; this update version completed January 20th, 2008; minor changes made and posted on March 19th, 2008.

- My sincere thanks to the four scientists from different disciplines and the one “armchair expert” who have read and made helpful comments on the text of this and the accompanying essay, “Michael Worobey’s wobbly research into the early history of HIV”. I have adopted many of their suggestions, but any mistakes that might exist are my responsibility alone.
EH