

Immunologia. — *Non è Vero, è Mal Trovato: Polio Vaccine is not the cause of HIV.*

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ABSTRACT. — A journalist has proposed that an oral polio vaccine tested in the early 1960s in the then Belgian Congo was contaminated with chimpanzee SIV, and that this was the source of HIV-1 Group M for humans. Although this idea was thoroughly evaluated in scientific forums and literature, and was found wanting in factual basis, the journalist continues to plead his case in various publications. This article replies to those recent publications, and refers to the body of accumulated information.

KEY WORDS: HIV; Oral polio vaccine; Virus.

RIASSUNTO. — *Non è vero, è mal trovato: il vaccino antipolio non è la causa dell'HIV.* Un giornalista sostiene che il vaccino antipolio orale testato agli inizi degli anni 60 nel Congo Belga fu contaminato dal virus SIV degli scimpanzé, e che questo fu la causa dell'HIV-1 Gruppo M per l'uomo. Benché quest'ipotesi sia stata rigorosamente esaminata in molti convegni e nella letteratura scientifica, e sia stata considerata carente di valide basi, il giornalista continua a sostenere la sua tesi in varie pubblicazioni. Questo articolo risponde a tali recenti pubblicazioni, e fa riferimento alle informazioni esistenti.

Mr. Edward Hooper was recently afforded over 200 printed pages in the proceedings of this society [1] to support his previously published allegations [2, 3] that oral polio vaccine (OPV) tested by us in the former Belgian Congo in the late 1950s was contaminated by chimpanzee immunodeficiency virus (SIVcpz) and served as the source of the HIV-1 group M epidemic. A document of this size is quite extraordinary for a scientific publication and if Mr. Hooper had any proof of his allegations he would not have needed 200 pages.

Nevertheless, we will first respond to substantive arguments found in the document, and then discuss some of the speculations that are larded throughout. For the reader who is unfamiliar with the story, Mr. Hooper is a British journalist who published a book in 1999 [2] that made numerous accusations against the current authors, which have been supplemented in the Italian article and are listed in table I. A meeting was held in 2000 in London at the Royal Society, where investigations refuting the accusations were presented. The negative evidence is summarized in table II and the reader may wish to refer to several previously published responses [4-8].

Mr. Hooper's principal accusation is that the type 1 attenuated polio vaccine strain called CHAT, which was developed in the United States at the laboratory of Hilary

(*) Nella seduta del 14 maggio 2004.

La Nota è presentata d'ufficio dal Socio Pignatti, in qualità di Direttore del Comitato consultivo dei Rendiconti Lincei: Scienze Fisiche e Naturali, su proposta a maggioranza del Comitato Scientifico (presieduto da Edoardo Vesentini) della Tavola Rotonda sul tema: «Origin on HIV and emerging persistent viruses» tenutasi presso l'Accademia Nazionale dei Lincei il 28 e 29 settembre 2001.

TABLE I. – *Hypotheses Proposed by Edward Hooper Relative to Putative Introduction into Humans of HIV-1 Group M viruses by SIVcpz Contamination of CHAT strain Type 1 Oral Polio Vaccine [2, 3].*

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- First evidence of HIV-1 is in former Belgian Congo.
 - CHAT OPV was tested in the Congo between 1957 and 1960.
 - Early AIDS cases were reported where CHAT was tested.
 - A camp for captive chimpanzees was associated with the polio work.
 - Chimp SIV (SIVcpz) is genetically closest to HIV-1 Group M.
 - Chimp kidneys must have been removed and used as cell substrate for production of OPV (allegedly in Philadelphia, Belgium, or numerous places in the Congo).
 - New publication fixes blame on Paul Osterrieth, Belgian virologist, based largely on quotations from Congolese technicians some of whom are anonymous or dead [1].
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TABLE II. – *Summary of Evidence Against Hooper's Hypothesis.*

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- Many «early AIDS cases» chosen by Hooper were never confirmed [4].
 - Geographical correlation disappears when a few critical examples are found to be false, and when account is taken of urban agglomerations where cases are numerous and medical diagnostic facilities available («looking for keys under light syndrome») [35].
 - No documentary evidence that chimp cells were used in American, Belgian or Congo labs [4-8, 21].
 - Negative documentary evidence for cultivation of chimpanzee cells in Congo virology labs [4-6, 17].
 - PCR of CHAT OPV lots used in the Congo negative for SIV RNA, negative for chimpanzee DNA, positive for macaque monkey DNA [4, 36-38].
 - Same lots used in the United States and Europe without causing HIV-1 infection [4, 39].
 - Molecular evolution analyses suggest crossover from chimp to humans in 1931, well before introduction of OPV [5, 28, 40, 41].
 - Abundant virological and sociological evidence that Congolese hunt, butcher and eat chimpanzees, allowing for exposure to SIV [42, 43].
 - Evidence that HIV-2 crossed from sooty mangabeys to humans in 1940, and that there are numerous other documented natural lentivirus crossovers [5, 29].
 - Osterrieth denies cultivation of chimpanzee cells or vaccine production [21].
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Koprowski [4, 9], was «amplified» locally in Kisangani (then called Stanleyville, Belgian Congo) by Dr. Paul Osterrieth, a Belgian virologist, in a clandestine manner. An earlier hypothesis, that the vaccine was contaminated by HIV-1 in the United States or in Belgium [3], seems to have been abandoned, presumably for lack of supporting evidence. Hooper argues that «amplification» of vaccine sent from the US was performed in Stanleyville in chimpanzee kidney cells. He seeks to show that the CHAT type 1 live attenuated vaccine used in early trials in Europe was made in European laboratories and that therefore the same practice of local manufacture was followed in the Congo. This would negate the fact that the same pools tested in Africa were also used in Europe without introducing HIV infection [4]. Although the literature is quite clear that the early trials (late 1950s) in Poland, Sweden, Switzerland and Croatia were done with vaccine furnished from Philadelphia, [4, 10-13] it is true that an additional lot was made in Belgium in 1959 [4], and that later both Poland and Croatia undertook local manufacture of the CHAT virus [14, 15], but that was far too late to be responsible for introducing HIV, and in any case it was done in macacus monkey kidney cells. Here Hooper confuses vaccine production by experienced vaccine laboratories with an alleged uncontrolled *ad hoc* manufacture, which he refers to as «amplification».

To support his hypothesis, Hooper points out that the titer of lot 13 of CHAT was $10 > 7.3$ TCID₅₀ in Philadelphia, but the same lot is recorded as having a titer of $10 > 8.25$ in Warsaw. This he considers evidence for manufacture of a new batch of lot 13. Although the text of the paper states that the vaccine used was produced in Philadelphia and thus does not support the idea of local manufacture [4, 10], there is a prosaic explanation for the discrepancy. In Philadelphia, when calculating titers from serial dilutions of vaccine in tubes of monkey kidney cell culture, we used the Reed-Muench formula [15], which is based on statistical considerations. In Warsaw, as late as 1960, one of us (SP) observed that titers were calculated by averaging the arithmetically computed titers at each serial dilution. For example, by chance a pool might calculate to be $10 > 7.8$ TCID₅₀ at one dilution (5 of 8 tubes positive at the $10 > 7$ dilution) and $10 > 8.2$ at a higher dilution (1 of 8 tubes positive at the $10 > 8$ dilution). The average would be $10 > 8.0$ TCID₅₀. By the Reed-Muench formula, however, the titer calculated from the same distribution of positive tubes would be only $10 > 7.3$ TCID₅₀. Moreover, most scientists would agree that the margin of error of viral titration is $0.5 \log$ TCID₅₀. Thus, the discrepancy disappears.

The evidence adduced by Hooper for local manufacture of OPV in a diagnostic laboratory in Kisangani, Congo, consists of statements obtained in interviews from Africans whose jobs did not allow them first-hand knowledge of what was being done in the laboratory, or hearsay by certain Belgians who were also not in the laboratory. In contrast, statements contradictory to Hooper's were also obtained by us from Belgians, including several of those interviewed by him [6]. Most recently, Dr. Lise Thiry of the Pasteur Institute of the Brabant stated «When I was in Stanleyville in May 1958 ... we visited the beautiful premises of the new laboratories and animal house. To my recollection cell culture was not yet being practiced there, but that figured in the plans» [16].

Hooper contends that the Kisangani (Stanleyville) virology laboratory routinely cultivated chimpanzee cells. The major evidence against this idea is the repeated strong denials by Paul Osterrieth [21] (the sole scientist working in that laboratory), the absence of evidence that the laboratory was capable of cultivating cells before mid-1958, and the fact that no mention of cultivation of chimpanzee cells or production of polio vaccine is made in any written document. Indeed, the crucial 1958 Annual Report of the Stanleyville Provincial Laboratory [4, 17] makes no reference to attempts to culture cells from chimpanzee organs or to vaccine production. Indeed, the report says specifically «tissue culture was done *exclusively* from baboon kidney (*italics ours*)». Hooper finds it suspicious that the 1958 Annual Report refers only to baboon cells, and suggests a prescient cover-up! Incidentally, the Report specifies that the baboon cultures were used for diagnostic studies.

Osterrieth was replaced in November 1959 by Dr. Ludo Verbist. His testimony is worth quoting verbatim:

«The virology department was rather rudimental: simple incubators (no control of humidity or CO₂), a locally fabricated safety hood without air filter, a small kitchen for the preparation of culture media and cleaning and sterilisation of laboratory materials. The only written laboratory procedures mentioned preparation of culture media,

maintenance of the HeLa cell lines and procedures for isolation and identification of enteroviruses from stools. There was no mention of procedures to obtain cell cultures from animal tissues. It was my task to maintain and transfer HeLa cells and to perform isolations of viruses on demand of the clinic.

«In the virology lab there was only one local technician (Assistant Médical) to clean and sterilize bottles and tubes, and to prepare culture media. The only laboratory work he was trained for and allowed to do was to neutralize the pH in bottles with growing cell cultures every two to three days.

«The only research in animals that was going on in April 1960 was on Arboviruses (Chikungunyavirus, Buniavirus). Both viruses were maintained and transferred on baby mice» [18].

Hooper repeatedly questions why the Lindi chimpanzee camp was organized. In 1956, Ghislain Courtois visited one of us (HK) at Lederle Laboratories to discuss doing research at a chimpanzee colony he had recently organized. Courtois was familiar with our research on live oral polio vaccine, and chimpanzees appeared appropriate to study the immune responses to oral polio vaccine. Challenge studies also could be done in chimpanzees using virulent poliovirus. Courtois returned to the Congo to complete the arrangements, and Thomas Norton and HK came to Lindi camp in 1957. Of interest, the 1958 Annual Report alluded to above mentions the use of chimpanzees for studies of polio pathogenesis and attenuation, viral hepatitis, allergic encephalitis, arteriosclerosis, blood groups and transfusion, measles and distemper. Unfortunately, the late Dr. Courtois, who was supposed to publish reports of the work, had to leave the Congo precipitously at the time of independence in 1960, and never managed to complete the task, perhaps for lack of records left in the Congo.

Comments on other specific allegations made by Hooper are as follows:

It is stated (p. 28) that the only vaccine made in Philadelphia and sent to the Congo were 2000 doses in capsules and that vaccine was made at Kisangani in chimpanzee cells from 1956 to 1958. This is contradicted by the mass vaccination carried out by Jervis and Flack in the Ruzizi Valley in 1958 [4, 19] and the mass vaccination in Léopoldville (Kinshasa), using liquid vaccine brought from Philadelphia [4, 20]. Moreover, eye witnesses and letters of the time mention shipments of CHAT vaccine from Philadelphia to the Congo. The vaccine was then diluted locally to obtain the desired concentration for mass vaccination. In pages 37-41, Hooper attempts again to correlate early cases of HIV-1 infection with sites of CHAT vaccination. As explained previously, there is no statistical or epidemiological basis for such a correlation [4, 5] which derives from impressions based on the localized availability of medical diagnosis in the Congo.

Hooper quotes an African assistant to the effect that Paul Osterrieth performed autopsies on chimpanzees, and went to Camp Lindi each Saturday (pp. 45-46). Apart from the fact that even if true, this would not constitute proof that chimp tissues had been used for cell culture, Osterrieth denies this statement in an article in press elsewhere [21]. Moreover, a testimony from Joseph Limbaya [22] (2002) confirmed that «he [Joseph] stated it was not possible to know what the whites did after the organs and

the blood was being collected». The testimony also refers to the fact that Mr. Edward Hooper had documents and photos with him, that he [E. Hooper] read the answers and begged him [J. Limbaya] in a repetitive way to remember that it was this way [Il dit que Mr. Edward Hooper avait sur lui tous les documents et les photos, il lisait les réponses, et le priait d'une manière répétitive de se rappeler qu'il en était ainsi]. In addition, Joseph also confirmed he had no further contacts with Paul Osterreith since the latter returned back to Belgium. This is in contrast to the statement of E. Hooper that Paul Osterreith has recently contacted a former co-worker.

On page 54, Hooper claims that another African assistant stated that Courtois had made cell cultures from chimpanzees in his own laboratory, and quotes from Courtois who wrote that monkey kidneys had been sent from the Congo to Belgium [23]. From this he infers that the kidneys were from chimpanzees. No other evidence is presented to show that the kidneys were truly from chimpanzees, that Courtois had the competence to do cell culture, or that cell cultures were ever prepared in Belgium from kidneys sent from the Congo.

In trying to deal with the published 1958 Annual Report of Stanleyville Laboratory in which only baboon cell culture is mentioned, Hooper says that in 2000 Osterreith acknowledged doing chimpanzee cell culture and that he would have had difficulty to obtain baboon kidneys (pp. 59-60). The first statement is simply untrue, as in his article [7] Osterreith clearly says that he only minced chimpanzee tissue for dispatch to a laboratory studying hepatitis and that he did not attempt cell culture, and the second is answered by Dr. Osterreith who says that baboons could easily be purchased at Stanleyville [21]. On page 91, Hooper offers an explanation of why Koprowski did not mention «amplification». He argues that Koprowski did not want anyone to know that vaccine «to vaccinate millions» could easily be made from a few ml. of seed vaccine. Of course, seed virus is used to generate individual lots of vaccine, and such an obvious fact is true for any live virus vaccine, including that of Albert Sabin. Thus, it is absurd to suggest that Koprowski wished to hide what everyone knew. Moreover, any new lot of vaccine must be tested for potency and safety in cell cultures and in animals, which requires extensive facilities not available in Stanleyville.

On page 97, Hooper makes much of the idea that Koprowski SM-N90 strain was being tested in chimps at Camp Lindi in 1956. He implies that SM-N90 was made in chimpanzee cells locally available in Stanleyville. Considering that SM-N90 had previously been prepared in Philadelphia, and was only tested in 227 subjects [9, 24], what reason would there be to make new virus locally? Once again, there is no evidence for Hooper's assertion.

On page 164, Hooper draws inferences from a bacteriological study done by Osterreith concerning strains of *Klebsiella pneumoniae* recovered from patients in a Stanleyville hospital and from chimpanzee autopsies [25]. Hooper attributes these to human and simian immunodeficiency infection; however, this ignores the facts that *klebsiellae* are frequent pathogens in human pneumonias and urinary infections [26], and are only the fourth cause of opportunistic bacterial infections in AIDS patients [27].

On page 171, Hooper dismisses the molecular evolution evidence that dates the

passage of chimpanzee SIV to humans in 1931 (leading to HIV-1 Group M) [28], and of sooty mangabey SIV passage to humans in 1940 (leading to HIV-2) [29], because of the possibility of recombination events in their lineages. There is no doubt that recombination may influence calculation of age of strains based on molecular clocks, but in both calculations controls were included that confirmed the assumptions of the molecular clock, and in neither case is there evidence that such recombination actually occurred early in the epidemics. Moreover, regions of the genome were examined that do not lend themselves to recombination. Schierup and Forsberg [30] call attention to the impact of recombination on molecular evolution, but their assumptions rely on either multiple introductions of chimpanzee SIV or frequent co-infection in humans at a time when HIV-1 prevalence was low- 0.2% or less in the late 1950s [31-33].

On page 216, Hooper argues that cases of polio that occurred in four villages vaccinated in early 1958 were caused by reversion to virulence of the CHAT strain. However, wild polio was occurring in the villages before vaccination [4, 19], and considering the low efficacy of CHAT in the tropics as later determined in Léopoldville [20], the more likely explanation is that the vaccine failed to completely stop the circulation of wild virus. No suggestion of vaccine-caused polio was ever associated with CHAT vaccination in the United States, Poland or Croatia.

Also, we are told that not only was vaccine made in chimpanzee cells, but that it was probably further passaged in the HeLa cell line. The «explanation» of this comes in 18 pages (99-116). However, after digging through the florid prose, all that one finds is speculation built on speculation, plus innuendos that people know more than they are saying. For example, the acknowledged fact that Dr. Stefan Pattyn used HeLa and human amnion cells for virus isolation in Elisabethville is converted by Hooper into the supposition that they were used for polio vaccine manufacture, despite Dr. Pattyn's denial [4, 6, 34]. No one would question the fact that HeLa cells were used for virus isolation in laboratories throughout the world in the late 1950s, but to propose that they were used as the substrate of vaccine callously intended for Africans is both vile and unsubstantiated.

The article is replete with other examples of literary acrobatics, an excellent example of which is found on page 90 (*italics ours*). «He [Jervis] *could* have obtained chimp kidneys and sera from Osterrieth in Stanleyville, or he *could* have used chimpanzees or other primates from Bukavu (or *possibly* from Usumbura or Kabunambo). It is my *belief* that *if* Jervis used local primates to produce primary tissue culture to amplify the vaccine, he *most likely* would have used chimpanzees, for by that stage this was the African primate species of which was best known and characterized for the Koprowski collaborations».

Q.E.D.?

In any case, the supposed presence of chimpanzees at Bujumbura or Kabunambo has already been refuted [6]. Hooper (pp. 89-90) attempts to blur the issue by referring to the presence of «primates» when the issue is the presence of chimpanzees.

At the end of his 203 page tome, Mr. Hooper, having exhausted both us and himself with speculation, resorts to the literary device of putting his accusations in the

mouth of Emile Zola. They are indeed quite a mouthful, as aside from the three of us, the accusations are leveled against Robin Weiss, Simon Wain-Hobson, John Moore, Paul Osterrieth, Beatrice Hahn, Paul Sharp, Bette Korber, Kevin De Cock, Stefan Patyn and Henry Gelfand. But perhaps it is indicative that these accusations should be attributed to Emile Zola, who was after all a writer of fiction as well as of journalism.

But even worse than personal attacks, Mr. Hooper's speculations are causing serious harm to the efforts to eradicate polio. Recently (October 28, 2003 - New York Times) journalists reported that three northern states in Nigeria suspended a polio immunization program led by the World Health Organization because they suspect that the vaccine spreads AIDS and causes infertility. Nigeria, one of only seven countries where polio cases are still prevalent, has the highest number of cases in the world, and cases of polio are spreading from Nigeria. This indicates that Edward Hooper in his obsessive struggle to link AIDS and polio has affected the global effort to eliminate polio from the world. On the contrary – perhaps unwittingly – he has contributed to the spread of polio in Nigeria. If he has the courage, instead of chasing ghosts in the Stanleyville laboratory, he should go to Northern Nigeria now and convince the people that there is no harm whatsoever in continuing the campaign to eradicate polio.

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Pervenuta il 24 dicembre 2003,
in forma definitiva il 14 maggio 2004.

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