Did Africans get HIV from chimps?

Not likely, asserts biophysicist Eleni Papadopulos-Eleopulos in her latest paper rejected by Nature

The science journal Nature continues its de facto policy of rejecting all submissions that question the HIV-causes-AIDS model. Its editors recently rejected the following commentary composed by the AIDS research team headed by Australian biophysicist Eleni Papadopulos-Eleopulos.

The rejected article addresses a recently published letter by scientists who claimed to have discovered the original human source of HIV: a simian "immunodeficiency" virus (SIV) newly identified (by them) from a particular subspecies of African chimpanzees. The authors declared that the genetic sequencing of their new SIV closely resembles that of HIV. And since the chimpanzees live in the same region as some humans who test "HIV-positive," the authors concluded that the humans there somehow contracted HIV (or what became HIV) from those chimpanzees.

Not so fast, say the Australians. The published authors presented no evidence that they had isolated any virus, so there's no basis for claims of a new viral species or a viral genome. Nor did they demonstrate a close similarity between the purported SIV and HIV gene sequences. To the
contrary, the published sequences differed significantly. As for the possibility of trans-species transmission, the Australians note that none of the presumably infected chimpanzees had managed to transmit the purported virus to their own children or sex partners.

Most scientists consider Nature the world's leading research publication. Papadopoulos-Eleopulos's carefully argued letter typifies the high quality of dozens of AIDS reappraising submissions, including several of hers, that Nature has rejected over the years. and the sloppy, implausible letter she criticizes exemplifies the poor quality of the dozens of pro-HIV submissions Nature publishes each year. A comparison of the two suggests that when Nature's editors consider the topic of AIDS, they practice poor judgment and censorship. -- Editor

IN A LETTER to Nature (Feb. 4), Gao et al. claimed to have proven:

(i) the existence of a new simian immunodeficiency virus (SIVcpz), in a chimpanzee, by identifying the virus's genome;

(ii) that the chimpanzees in which his group found this SIV belong to a certain subspecies, P.t. troglodytes (their chimpanzee, Marilyn, as well as two of the other three chimpanzees in which to date a SIVcpz was reported, GAB1 and GAB2);

(iii) that these chimpanzees live in the same area of Africa with humans who are said to be infected with certain genetic groups of HIV ("the natural range of P.t. troglodytes coincides uniquely with areas of HIV-1 group M, N and O endemicity");

(iv) the humans there acquired their HIV from the chimpanzees ("HIV-1 infection of humans occurred as a result of cross-species transmission of SIVcpz from P.t. troglodytes"); and

(v) those chimpanzees are the original source for humans of HIV ("P.t. troglodytes is the primary reservoir for HIV-1").

A close analysis of the evidence on which Gao's group bases its claims raises several issues that contradict those claims:

(a) Marilyn was "wild-caught in Africa (country of origin unknown),
exported to the United States as an infant." [1]

Two of the chimpanzees, GAB1 and GAB2, originated in Gabon. GAB1, who was 4 years old when reported HIV-1 positive, was caught when she was "about 6 months" and was kept with another 49 wild-caught animals at the International Centre of Medical Research (CIRM) in Gabon. GAB2, who was also reported HIV-1 positive, was about 2 years old when she was shot in the wild, kept in a village for 2 days and then was brought to CIRM, "where it died of its wounds one week later." [2]

In the 1989 study, where the "HIV-1 seropositivity" of GAB1 and GAB2 was reported, the authors (which included one of Gao's co-authors, Peeters) concluded: "...on examination, none of the people caring for the animals and none of those living in the village showed antibodies to HIV/SIV. Furthermore, the region where the chimpanzee was captured is known to have a low seroprevalence rate.... It has been suggested that human AIDS retroviruses originated from monkeys in Africa. However, this study and other previous studies on SIV do not support this suggestion." In other words, by the time that "HIV infection" and AIDS had already reached their peaks in the US, Europe, and Australia, the number of individuals proven HIV seropositive in Gabon were few if any.

A 1990 study published in *Nature* by researchers from CIRM and the Pasteur Institute, including Wain-Hobson, where the authors described "the molecular cloning and sequencing" of SIVcpzGAB1, states: "In Gabon, only 2 out of 83 chimpanzees tested were seropositive, indicating that SIVCPZ is not widely dispersed in this region.... Of more than 250 chimpanzees caught over the last 15-20 years in West Africa, none was seropositive. This might explain the absence of naturally infected chimpanzees in captivity in the US as virtually all are of West African origin." [3]

How is it possible to espouse "prevalence in the natural host," "geographic coincidence," and "plausible routes of transmission" as evidence to substantiate the claims that HIV-1 originated in P.t. troglodytes and that this sub-species is the natural reservoir for HIV-1?

(b) The three P.t. troglodytes -- GAB1, GAB2 and Marilyn -- were said to be infected with HIV-1/SIVcpz on the basis of an antibody test. However, given that:
(i) as Philip Mortimer points out, "...it may be impossible to relate an antibody response specifically to HIV-1 infection." [4]

(ii) when the blood was collected none of the animals was perfectly healthy although none had AIDS.

(iii) the only way to prove the specificity of an antibody test is to use the virus isolation as a gold standard. Although no effort has been spared, no SIVcpz could be isolated either from GAB2 or Marilyn (see comments below for GAB1).

(c) How is it possible to claim proof for infection on the basis of an antibody test?

(i) If GAB1 and Marilyn were infected then, given that the animals were brought to the colony as infants where no other animals or humans working there were infected and, according to Weiss, "Chimpanzees in captivity are mostly taken from the wild before they become sexually active and so rarely harbor SIV," how did these two chimpanzees become infected? [5]

(ii) Since the three chimpanzees found positive were all female, and since HIV/SIV is acquired following sexual maturity, how did they become infected?

(iii) If the animals were infected with a virus SIVcpz and this was transmitted to humans, why was this not transmitted to any other of the 49 animals at CIRM where GAB1 was kept or to the 93 animals in the colony where Marilyn was kept, not even to her 6 living offspring or her mates? (By the age of 26 she had a total of 14 pregnancies). [6]

(d) The additional "lines of evidence" that Gao used to substantiate transmission are based on genomic studies. Gao claimed to have shown that "All HIV-1 strains known to infect man, including HIV-1 groups M, N, and O, are closely related to just one of these SIVcpz lineages, that found in P.t. troglodytes." Indeed, if all these HIV-1 and SIVcpz strains represented one and the same virus, then their genomes will have to be "closely related." In fact they should represent a unique molecular entity. Even in the genomes of RNA viruses, including influenza, which are considered to be most variable, a 1% sequence difference is considered to represent "extreme variability." [7] This is because small genetic
differences lead to significant phenotypic differences. For example the difference between the human and the chimpanzee genome is less than 2%.

In the 1989 study of SIVcpzGAB1 Peeters wrote: "Nucleic acid hybridization experiments appear to indicate that the virus is different from HIV-1 and HIV-2." A 1990 *Nature* paper by researchers from CIRM and the Pasteur Institute, including Wain-Hobson, states: "Several regions of the chimpanzee sequences were more than 50% divergent with respect to HIV-1BRU. Some parts of the gag gene were almost as varied as the hypervariable regions in env.... The vpu gene found only in the type 1 viruses was particularly different (64% divergent to HIV-1BRU).... It is also apparent that the SIVCPZ genome was not simply a more diverged HIV-1 isolate.... It is not possible to conclude that SIVCPZ was the precursor to HIV-1, if indeed infection ever passed in that direction. Even given this premise the vpu data indicates that SIVCPZ was not the immediate precursor." [3]

In a 1994 study of the SIVcpzGAB2, Peeters wrote: "The genetic distance between SIVcpz-gab [SIVcpz GAB1) and SIVcpz-gab2 is 14.1%. Genetic distances to the HIV-1 genotypes A, B and D strains are 13.7 to 16.3%, whereas distances to group O HIV-1 strains are 15.4 to 18.5%." Contrary to Gao, in 1994 Peeters concluded: "On the basis of their respective distances to each other and to the HIV-1 strains, SIVcpz-gab and SIVcpz-gab2 can be assigned as representative for two distinct genetic lineages of HIV-1-related chimpanzee lentiviruses." [8]

By 1993 it was reported that "in the A-G HIV-1 genotypes the intragenotypic gag distances averaged 7%, whereas the inter-genotypic distances averaged 14%.... The maximum level of variability in gag is still well below that observed for the envelope region of HIV-1." [9]

The HIV-1 group O has "65% similarity to HIV-1 and 56% similarity to HIV-2 consensus sequences. The env gene of MVP-5180 [HIV-1 group O] had similarities to HIV-1 and HIV-2 of 53 and 49% respectively.... Comparison of the MVP-5180 amino acid sequences with that of the Gabon chimpanzee virus showed similarities of 70, 78 and 53% in the gag, pol and env genes, respectively." [10]

As far as the genomic differences between HIV-1 group N, on the one hand, and group M and O on the other is concerned, it suffices to quote
from the 1998 study where its existence was first reported. "Proviral DNA amplification with several sets of HIV-1 group M and O primers was attempted on pelleted end-cultured cells. Amplification was negative with eight different group M env, gag or pol primers and five group O env or gag primers." [11] How is it possible to claim proof for the existence of a unique molecular entity which constitutes the genome of a unique retrovirus HIV-1/SIVcpz?

(e) The only way to prove that an RNA (and its cDNA) is the genome of a retrovirus is to demonstrate that it comes from a retrovirus particle and such RNA codes for its proteins. This can be done only by obtaining the particles separate from everything else, purifying, isolating them. [12]

In the 1989 study, where Peeters reported the isolation of SIVcpzGAB1, stimulated peripheral blood lymphocytes "from healthy human donors" were co-cultured with the same type of cells from the chimpanzees. Supernatant from the co-culture was centrifuged for 10 minutes at 400,000g. Detection in the pellet of reverse transcriptase activity, using An (dT) [12-18] as template primer, was considered proof for SIVcpzGAB1 isolation. Such a method for viral isolation is no different from claiming that elevations in serum liver enzymes proves the existence of gallstones and, moreover, that the gallstones have been isolated from the patient and are in the surgeon's hands separate from everything else. The SIVcpzGAB1 "genome" was obtained either by hybridizing the RNA present in the pellet (they presented no proof that the pellet contained even retrovirus-like particles), where one would expect to find ample cellular RNA, with probes "from HIV-1oyi, a Gabonese HIV-1 strain," or from "SIVCPZ-infected human lymphocytes," again using HIV-1oyi as a probe. The "genome" thus obtained was compared with the genome of HIV-1BRU.

We could find no details as to how the HIV-1oyi "genome" was obtained. HIV-1BRU is the "HIV-1" which, according to Weiss, was "discovered by Barre-Sinoussi and her colleagues in 1983." The senior author of the 1983 Barre-Sinoussi study, Luc Montagnier, in 1997 not only acknowledged that they did not isolate HIV-1BRU, but their "pure" virus from where they chose some RNA and called it HIV RNA, did not even contain particles with "morphology typical of retroviruses." [13] The only evidence ever presented as proving the existence of the SIVcpzGAB2 genome was reported by Peeters and his associates. They
write: "From this chimpanzee we have been unable this far to isolate a lentivirus, but some of the primary peripheral blood mononuclear cells (PBMCs) have remained available in a frozen state. To investigate the genetic relationship to the SIVcpz-gab isolate [SIVcpzGAB1], proviral DNA was extracted from these primary PBMCs [no mention is made how it was possible to extract the proviral DNA from the chimpanzee DNA], and a 280-base pair (bp) fragment of the pol gene was amplified by a nested polymerase chain reaction (PCR). Subsequently, PCR fragments were cloned and sequenced." [8] No mention is made as to how they obtained the PCR primer. Gao et al used "consensus sequences" as primers and the following method: "Here we used the polymerase chain reaction (PCR) to amplify HIV- or SIV-related DNA sequences directly from uncultured (frozen) spleen and lymph-node tissue obtained at autopsy in order to characterize the infection responsible for Marilyn's HIV-1 seropositivity. Amplification and sequence analysis of subgenomic gag (508 base pairs (bp)) and pol (766 bp) fragments revealed the presence of a virus related to, but distinct from, known SIVcpz and HIV-1 strains. Because virus isolation from the autopsy tissues was unsuccessful, we used PCR to amplify and sequence four overlapping subgenomic fragments that together comprised a complete proviral genome, which we termed SIVcpzUS."

However,

(i) The specificity of the PCR for HIV has never been proven. The only way to obtain such proof is to use virus isolation as a gold standard. Even if one accepts the claims for SIVcpzGAB1 isolation, it is agreed that, although no effort has been spared, SIVcpz could not be isolated from the other two animals. This means that the PCR results obtained for the genomes of SIVcpzGAB2 and SIVcpzUS are false.

(ii) Even if they were specific for retroviruses; given that:
(a) The genome of all humans and animals contain retroviral proviruses, i.e., genomes of the endogenous retroviruses. [14]
(b) There are homologies between the genomes of different retroviruses, especially in the gag and pol genes. In fact, according to Montagnier and Wain-Hobson, the gag and pol genes "are generally conserved among retroviruses." [15]
(c) In not one of the studies which claimed proof for the existence of the SIVcpz genomes did the authors use controls.
(iii) How is it possible to claim that the sequences detected in the DNA "of SIVcpz-infected human lymphocytes," the PBMCs of GAB2 and in Marilyn's "spleen and lymph-node tissue" were those of an exogenous retrovirus which is transmitted from one chimpanzee to another and from chimpanzee to humans and not those of an endogenous retrovirus?

(iv) Since there is no proof that the three chimpanzees ever came in contact with HIV-1-infected humans or animals or that they transmitted such a virus to other humans or animals, is it not more "plausible" to conclude that if these animals did harbor a retrovirus, the retrovirus was endogenous? In analyzing the "SIVcpz" molecular biology one cannot help reflecting upon the words of Sir John Maddox, "Is there a danger, in molecular biology, that the accumulation of data will get so far ahead of its assimilation into a conceptual framework that the data will eventually prove an encumbrance? Part of the trouble is that the excitement of the chase leaves little time for reflection. And there are grants for producing data, but hardly any for standing back in contemplation." [16]

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RETHINKING AIDS HOMEPAGE
www.rethinkingaids.com
HIV isolated?

NATURE ALSO rejected this letter from Papadopulos-Eleopulos's team, which examined an article that Nature did publish. In "News and Views" (Nature Feb. 4), Robin Weiss and Richard Wrangham stated "the retrovirus that is the main cause of AIDS has been a puzzle ever since it was discovered by Barre-Sinoussi and her colleagues in 1983."

Sirs:

To isolate HIV, the authors used the long-accepted method for retroviral isolation: banding (ultracentrifugation) in density gradients ("Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for AIDS," Science 220, 1983). They claimed to have shown that the density of 1.16g/ml -- the sucrose density at which retroviral particles band -- contained "purified, labeled virus"; that is, the 1.16g/ml band contained nothing but retrovirus particles isolated from everything else.

Last year the French journalist Djamel Tahi interviewed the senior, most quoted author of the Barre-Sinoussi paper, Luc Montagnier of the Pasteur Institute (Continuum 5, 1998; www.virusmyth.com/aids/data/dtinterviewlm.htm). Tahi asked Montagnier why his group did not publish electron micrographs proving that the 1.16g/ml band contained isolated HIV particles. Montagnier answered: they published no such proof because, even after a "Roman effort," at the density of 1.16g/ml they could see no particles with "morphology typical of retroviruses." He gave similar answers to repeated questions, including "I repeat, we did not purify," that is, isolate HIV.
Given the important and highly significant differences in the consequences of these contradictory claims, it is a matter of urgency for the other 11 authors of the 1983 study, and especially Barre-Sinoussi and her co-workers from the Pasteur Institute, to either confirm or refute Montagnier's statements.

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Recent publications by the Papadopulos-Eleopulos group

ELENI PAPADOPULOS-ELEOPULOS'S team recently published the
following articles, which -- like all their previous articles -- can be accessed at www.virusmyth.com/aids/perthgroup:


"Looking Back on the Oxidative Stress Theory of AIDS," (Continuum 5:5, midwinter 1998-99). This article provides an excellent synopsis of EPE's explanation for how all the risk factors (narcotics, anti-AIDS drugs, poverty, blood therapy, rectal semen) may cause both AIDS and "HIV."

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