Search for the Origin of HIV and AIDS

Although the Research Article from B. Korber *et al.* ["Timing the ancestor of the HIV-1 pandemic strains," (9 June, p. 1789)] and the excellent commentary thereon by D. M. Hillis (p. 1757) both acknowledge the possibility that AIDS began through an iatrogenic event involving an oral polio vaccine (OPV) administered in Central Africa in the late 1950s, they deem the hypothesis "unlikely." I would like to question the evidence proffered to support that conclusion.

On the basis of information supplied by the former deputy director of the Wistar Institute, Stanley Plotkin, Korber *et al.* claim that the chimps at Camp Lindi (where the OPV experiments were conducted) were infants or juveniles, with ages up to 10 years. Not so. The laboratory databook that Plotkin sources (currently in my possession) details 54 survivors of the 416 chimps involved in the polio experiments conducted between June 1956 and February 1958. One male chimp is clearly identified as "adult," which, according to primatologist Jonathan Kingdon, indicates an age of 15 years or more. It may be that other adults were among the approximately 360 chimps that died, or were sacrificed, during this research.

A single adult chimp, SIV-infected from birth, would by the late 1950s have been carrying a divergent range of SIV quasi-species, sufficient to "spark" the various HIV-1 Group M subtypes if its cells were involved in vaccine production. This scenario complies with Korber's dating parameters, as does that of multiple SIV-infected chimps.

The low (1%) SIV prevalence in chimps quoted by Korber is predominantly based on data from young juvenile *Pan troglodytes troglodytes*. Nobody has yet documented SIV prevalence in wild adult or sexually active chimps. Neither has anyone systematically studied SIV prevalence in Congolese *Pan troglodytes schweinfurthii* and *Pan paniscus* (the species held at Lindi). There may even have been some *Pan troglodytes troglodytes*, for two apes came from a zoo and one from Mbandaka, close to the troglodytes' range. Furthermore, different species were caged together at Lindi, which may have allowed onward SIV spread and cross-species transmission.

Korber claims, sourcing my book *The River*, that "a small number of primate kidneys were needed for OPV cultures." The pages cited actually reveal that up to 80 pairs of chimp kidneys may have been required to make the 1 million vaccine doses fed in the Congo. During this early stage of vaccine development, many experimental batches and lots were prepared.

Dr. Korber's work is painstaking and useful—but it dates an abstraction. It does not tell us if the 1931 "last common ancestor" of HIV-1(M) was a chimp virus or a human virus. It does not tell us how—or where—AIDS began.

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Responses

Hooper questions the accuracy of a communication concerning the ages of the chimpanzees kept at Camp Lindi, a footnote in (*1*) that stated, "A record of the ages of chimpanzees from Camp Lindi used for research noted a range from <1 to 10 years, with more than 80% less than 4 years old, personal communication, Stanley Plotkin, data taken from the laboratory notes of Fritz Deinhardt." Hooper's letter supports what Plotkin established: Most chimpanzees at Camp Lindi were young, and in this way typical of those tested for SIVcpz in recent years.

> "[O]ur model [for the origin of HIV]...is difficult to reconcile with the OPV hypothesis."

Our model indicates that there was significant diversity in the M group lineages by the time the OPV trials were conducted (*1*). Two scenarios could reconcile such apparent diversity with the OPV hypothesis: (i) multiple SIVcpz-infected kidneys were used for OPV production or (ii) the diversity arose from a single chimpanzee kidney.

Given the scarcity of SIVcpz in captive chimpanzees, the first scenario is highly unlikely. Hundreds of captive chimpanzees in primate centers, sanctuaries, and zoos have been tested for SIVcpz, and only seven infections have been identified to date (*2, 3*). The majority of captive chimpanzees are acquired as infants or juveniles. Field studies of African green monkeys and sooty mangabies show that SIV prevalence in these species correlates with sexual maturity (*4*), thus a selection bias may account for the low SIVcpz prevalence in captive chimpanzees, and so the age of the animals at Camp Lindi is germane.

SIVcpz prevalence also appears to have a geographic gradient that disfavors the OPV hypothesis: SIVcpz-infected chimpanzees with known geographic origin are all from west-central Africa. For example, while an infection rate of 7% (2/28) was reported for chimpanzees from Cameroon (*2*), no evidence of SIVcpz infection was found in adult chimpanzees from two wild communities in the Tai Forest, Cote D'Ivoire, and one in Kibale National Park, Uganda (*3*). Therefore, an HIV introduction through multiple infected kidneys is improbable, even if we accept Hooper's estimate that up to 80 pairs of chimpanzee kidneys were used for OPV production. This number in itself is highly questionable, as those directly involved with the production of OPV firmly state that chimpanzee kidneys were never used (*1*).

The second scenario is also problematic. Animals infected long enough to have a diverse population of SIV genetic variants would have been rare, if present at all, given the age and geographic data discussed above. There is no evidence that OPV culture conditions would have maintained diversity, and many lineages would have needed to survive the cross-species jump and emerge as distinct epidemic strains in humans. Finally, and importantly, recombination in vivo (*5*) makes it implausible that a single animal's quasi-species could have established the many distinct M-group clades that are monophyletic throughout the genome.

As emphasized in our paper, we have not dated a cross-species transmission event, but estimated the timing of the beginning of M group diversification. Considered in isolation, our model does not formally refute the OPV hypothesis. It does, however, suggest significant diversification predating the OPV trials, which is difficult to reconcile with the OPV hypothesis. By contrast, there was ample opportunity for exposure to infected chimpanzee blood though hunting, and for subsequent HIV expansion in human populations (*6*). Our analyses are consistent with such a scenario. Natural transfer is not unusual—many viruses have crossed from animals to man (*7*), although many are constrained, self-limited events without epidemic potential.

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Hooper asserts, with no confirmatory evidence, that we used chimpanzee cell cultures to make oral polio vaccine tested in the then–Belgian Congo between 1957 and 1960.

The suggestion that 80 pairs of chimpanzee kidneys would have been needed to make the few lots used in the Congo is untrue. In fact, no chimpanzee cultures were ever used for polio vaccine preparation. Moreover, as attested by witnesses, nearly all the animals captured for the camp were young: the only extant records show that 80% were 4 years of age or less, and 100% were less than 10 years old. The male "adult" mentioned by Hooper, presumably so labeled because it was significantly older than the other chimps, weighed 26 kg. This weight corresponds to an age of approximately 7 years, 10 years at the outside, but certainly not 15 years (*1*).

The paper by Korber *et al.* (*2*) is further evidence that the events postulated by Mr. Hooper never took place.

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Nuclear Power and Climate without Proliferation

The analysis in the Policy Forum "A nuclear solution to climate change?" by W. C. Sailor, D. Bodansky, C. Braun, S. Fetter, and B. van der Zwaan (*Science*'s Compass, 19 May, p. 1177) is diminished by inclusion of the myth—popular in the United States—that efficient use of nuclear resources is a proliferation threat. Quite the contrary, destruction of weapons materials in spent nuclear fuel by their use for production of electricity in fast, so-called breeder reactors is an essential component of good nonproliferation practice. Depleted uranium at U.S. enrichment plants, which was used by the United States Department of Energy (DOE) to produce plutonium for weapons, would also be destroyed in fast reactors. The electricity produced from existing nuclear by-products would be equivalent to that needed by the United States, at present use rates, for hundreds of years.

The nuclear solution presented by Sailor *et al.* would recover less than 1% of the energy from uranium. Spent fuel would be disposed of in a geologic repository. Depleted uranium—millions of tons of weapons source material—would accumulate indefinitely.

International Atomic Energy Agency (IAEA) safeguards are required for plutonium-239 in spent fuel deposited in a geologic repository. However, virtually no one accepts the IAEA contention that planned satellite surveillance can be reasonably assured for 10,000 years. Moreover, the time required for significant decay of plutonium-239 is not 10,000 but 240,000 years.

Since safeguards for these periods of time are not credible, spent fuel must be reprocessed to permit permanent disposal of unwanted fission products, i.e., high-level radioactive waste. Disposal of this waste is essential for viability of nuclear power and is a requirement of virtually all nations. Reprocessing only in well-designed, well-managed, and safeguarded facilities operated by nations with large nuclear power programs, and immediate fabrication of weapons materials into fuel assemblies for their destruction through production of electricity, provide the greatest assurance against a proliferation threat from nuclear power.

The du Pont company completed designs for such facilities in 1978, based on its experience in reprocessing at the DOE Savannah River Plant and on the experience of others. Among many important features of these designs was the elimination of accumulations of separated plutonium. Unfortunately, these designs were rejected by leaders of the DOE in order to support national laboratory reprocessing concepts that had led to earlier problems (failures and proliferation) and poorly focused research on "proliferation-resistant" fuel cycles. During this same time period, political decisions were made that led ultimately to cancellation of U.S. fast reactor development.

U.S. nuclear policies based on best science and best applications of science will result in nuclear power being used as the solution for climate change and other energy and environmental problems.

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Retraction

In the course of carrying out experiments that were a direct extension of our recent *Science* paper "Stable RNA/DNA hybrids in the mammalian genome: inducible intermediates in immunoglobulin class switch recombination" (*1*), we discovered differences from those in the paper. The first author (R. B. Tracy) has admitted to data alteration such that the primary conclusions of the paper are in question. Because of this, the authors are retracting the entire paper on class switch recombination (*1*). We are deeply regretful for any scientific misconceptions that have resulted from these studies. [Note that the following related paper is also being retracted for the same reason: R. B. Tracy and M. R. Lieber, "Transcription-dependent R-loop formation at mammalian class switch sequences," *EMBO J.* **19**, 1055 (2000).]

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CORRECTIONS AND CLARIFICTIONS

NetWatch : "Bioweapon worries" (23 June, p. 2091). It was incorrectly stated that the 1972 Biological Weapons Convention has not been ratified. The last sentence should have read, "You can also read the 1972 Biological Weapons Convention, in force since 1975 but currently subject to debate as countries wrangle over ways to strengthen it."

News Focus: "Stress: The invisible hand in Eastern Europe's death rates" by Richard Stone (9 June, p. 1732). The two graphs on p.1733 should have been credited to V. Shkolnikov, F. Mesle, and D. Leon. In addition, in the graph labeled "Mortality of Russian men," the ratio was based on Russian mortality figures for 1998 and western mortality figures for the period 1992–1995.

Perspective: "An infrared look behind stars" by C. J. Hogan (14 Apr., p. 281). In five instances in the text, the unit micrometers "μm" should have been millimeters "mm": in column 2 on p. 281 (0.8 to 3 mm), in column 3 on p. 281 (0.8 to 3 mm, 0.8 mm, and 0.4 mm), and in column 1 on p. 283 (0.8 mm).