

Analysis of polio vaccine could end dispute over how AIDS originated

Could an effort to rid Africa of polio have caused the AIDS pandemic? While labs prepare to test the vaccine, researchers are at war over the theory.

Paris

Since 1992, some of the last remaining samples of an oral polio vaccine (OPV) given to millions of Africans have been locked in a fridge — itself locked in another fridge — at the Wistar Institute in Philadelphia. Only director Clayton Buck has the keys. The samples, dating from the 1950s, are suspected by some of being the origin of AIDS.

The 'OPV-HIV' hypothesis — that HIV-1 jumped to humans from contaminated polio vaccines distributed in central Africa during the 1950s — has come to prominence via *The River: A Journey Back to the Source of HIV and AIDS* (Allen Lane), a book by journalist Edward Hooper (see *Nature* 401, 325; 1999).

It is known that HIV-1 came from chimps and HIV-2 from sooty mangabeys, but researchers disagree on how the original viruses crossed the species barrier. Although Hooper's book fails to reveal a smoking gun, it offers circumstantial evidence that kidneys from these animals might have been used to produce a vaccine called CHAT (records no longer exist). In a bid to settle the matter, Buck will soon open the fridge and send samples to three laboratories to find out whether they contain any trace of infection with a precursor of HIV.

The names of the laboratories are being kept secret, says Buck, to "avoid media pressure, and to ensure that the studies are blind; so that other labs don't know who is doing what". At the same time, he says, one of the world's leading mitochondrial DNA analysis laboratories will seek to identify the primate species used to prepare the samples.

Chances of detection are slight

Buck admits, however, that the studies may not settle the matter. Only six to nine samples will be tested, which means that, even if the vaccines had been contaminated, the probability of detecting the virus is slight. He also points out that the samples are over 40 years old, and in unknown condition.

"If the results are negative, then we can say: 'Mr Hooper had an interesting idea, he did a lot of very nice documentation, but perhaps his assumptions were not valid, and we need to look elsewhere,'" says Buck, who maintains that chimps were used only to test the toxicity, not in vaccine preparation.

Results should be revealed in May, at a meeting organized by Britain's Royal Society.



In the dock: were captured African chimps used to make polio vaccine, not just to test it?

"The meeting will make the debate a little less wild than it has been in the past," says Pat Bateson, the society's biological secretary, who says opposing AIDS researchers are currently in deadlock. "The OPV-HIV hypothesis is an interesting argument, and it ought to be thrashed out." He hopes the meeting will "get agreement on what new evidence might settle the argument".

Accidents can happen. Millions of people were accidentally contaminated with simian virus 40 in the 1950s through contaminated polio and adenovirus vaccines made in monkey kidney cells; luckily it seems to have done little lasting harm. But Maurice Hilleman, director of the Merck Institute for Therapeutic Research in West Point, Pennsylvania, who carried out some of these trials, is sceptical of the OPV-HIV hypothesis. He says that chimpanzees were never used to make vaccines, as they were expensive and unsuitable for the large amounts of tissue needed.

But Simon Wain Hobson, an AIDS researcher at the Institut Pasteur in Paris, and Robin Weiss of University College, London, say Hooper's hypothesis needs to be examined. Hobson admits that the book produces no direct evidence, but says he was unable to demolish its arguments. In particular, he found Hooper's correlation in space and time between the emergence of AIDS and the vaccination campaigns "compelling".

"Why did all these strains of HIV suddenly appear at same time?" Hobson asks. He has played Sherlock Homes in the past, showing that the AIDS virus that Robert Gallo, of the US National Cancer Institute, claimed to have discovered was identical to one earlier discovered at the Institut Pasteur, a sample of

which had been lent to Gallo. Hobson argues that the possibility that AIDS is man-made should give grounds for caution in allowing xenotransplants to proceed.

But other scientists criticize him for lending credence to what they claim is little more than a conspiracy theory. John Moore, of the Aaron Diamond AIDS Research Center in New York, fears the publicity is hampering vaccination efforts in developing countries.

Beatrice Hahn, a scientist at the Howard Hughes Medical Institute, argues that the weight of evidence suggests AIDS probably arose much earlier (see *Science* 287, 5453, 607; 2000). She believes that AIDS was transmitted to humans "via cutaneous or mucous membrane exposure to infected animal blood" through hunting, butchering or eating uncooked contaminated meat. Dirty needles could also have caused "rapid serial passage of viruses in humans, thereby facilitating viral adaptation to the new host".

Distraction from a bigger issue

Hooper, says Hahn, has "come up with a hypothesis, but failed to demonstrate that chimpanzee or sooty mangabey kidneys were even used". She argues that it is a distraction from a bigger issue, namely that there are dozens of HIV-like viruses in wild monkey populations, and that if natural transfer of AIDS viruses from chimpanzees to monkeys has already occurred, there is no reason why it should not happen again.

Hahn also points to recent mathematical models of the evolution of HIV by Bette Korber, of the Los Alamos National Laboratory in New Mexico, which calculate that the AIDS viruses jumped to humans between 1910 and 1930. Hobson argues that Korber's model relies on many assumptions, which, when combined with the margins of error, fail to kill the HIV-OPV hypothesis.

For his part, Hilary Koprowski, who developed the vaccine at the Wistar Institute, says it is ironic that he is being "demonized" in the year that the World Health Organization is making a final push to eradicate polio. "Hooper's book is based on preconceptions, not facts," says Koprowski.

He has "very mixed feelings" about the Royal Society meeting, and has yet to decide whether to attend. "This is not a response to Hooper," he says. "Hooper must come up with the proof."

Declan Butler