BOOKS: HISTORY OF MEDICINE

Is AIDS Man-Made?

Robin A. Weiss

Thanks to immunization, polio like smallpox may soon be eradicated. But did the trials of early polio vaccines trigger AIDS? The central thesis of Edward Hooper's new book, *The River*, is that they did. Hooper argues that both AIDS viruses, HIV-1 and HIV-2, first infected humans via contaminated oral poliovirus vaccines (OPV). He claims these vaccines were grown in kidney cell cultures derived in the 1950s from chimpanzees and sooty mangabeys, respectively, that were infected with simian immunodeficiency viruses (SIVs). Although this notion has been explored before, no one previously has researched the history of polio vaccine trials and early AIDS cases so exhaustively. Hooper builds up layer upon layer of circumstantial evidence and plausible conjecture, until he declares: "The reader must make up his mind or her mind. I have made up mine." Yet after having read his 858 pages of text and 175 pages of notes and references, I remain undecided on the origins of HIV.

The River
A Journey to the Source of HIV and AIDS
by Edward Hooper
Little, Brown, New York, 1999. 1104 pp. $35. ISBN 0-316-37261-7. Penguin, London, 1999. 1104 pp. £25. ISBN 0-7139-9335-9.

The River is a towering achievement; right or wrong in its main conclusion, there is much to learn from Hooper's exposition. The book, a strange fusion of personal quest and scientific treatise, is a thriller in which the main culprit is revealed early. Hooper's dry observations on the players, big and small, in OPV and AIDS are worthy of Raymond Chandler. Indeed, "the big sleep" well describes our complacency over 44 years' use of primary monkey kidney cells as a substrate for live viral vaccines.

In his previous book (*1*), Hooper tellingly described how AIDS spread into southwest Uganda in the early 1980s. In *The River*, he traces the first evidence of AIDS and argues convincingly that it is a new human disease. He then extols the proposed link to polio vaccine trials in former Belgian colonies in central Africa (the Congo, Rwanda, and Burundi). Massive field trials of prelicense Koprowski and Sabin oral vaccines were conducted on hundreds of thousands of Africans, and millions of Poles and Russians. The Sabin vaccine, which won the race for World Health Organization approval, was first propagated in kidney cultures of rhesus and cynomolgus macaques, and later in African green monkeys. For the Congo and Polish trials pioneered by Hilary Koprowski (of the Wistar Institute, Philadelphia), although it seems astonishing, there are no precise data on the passage histories of the vaccine pools and batches nor any records of the simian species used in cultures.

Camp chimp. Djamba was a pet that wandered freely about the Lindi camp, where a chimpanzee colony was established for Koprowski's polio experiments.

Were chimpanzee kidneys used in the production of oral polio vaccines? This is the nub of Hooper's case. He points to the Wistar Institute or to Belgian laboratories using Wistar strains. Numerous chimps and bonobos (pygmy chimps) were kept at Camp Lindi, outside Stanleyville (Belgian Congo). Some were used there for testing the safety of vaccines, but what happened to the majority of the animals? Although Hooper reveals that some chimp kidneys were sent to Philadelphia for tissue culture, there is no record of vaccine production in them. If chimpanzee kidneys were used, however, it seems odd that the one pool of OPV (CHAT 10A-11) that, according to Hooper, might have been contaminated found its way back to the Congo—and not to Sweden, Poland, or the United States, where other Koprowski trials took place. Hooper wonders if Ghislain Courtois, the director at Lindi, might have amplified the pools of CHAT vaccine in Stanleyville. The author reveals that the veterinarian Alexandre Jezierski independently grew attenuated poliovirus in chimpanzee kidney cultures in the Congo. Because the Pasteur Institute's Pierre Lépine used local baboon kidneys, could the French also have used chimp cells? In addition, Hooper suspects that French and Portuguese activities led to the West African origin of HIV-2 from sooty mangabeys. To me, the possible use of small batches of experimental OPV made locally seems a more plausible source of contamination than the Wistar preparations. As one of the investigators of that time, Abel Prinzie, told Hooper: "We were acting in full innocence, not understanding what sort of Pandora's box we were opening."

Can the OPV-HIV link withstand scrutiny? Hooper calls for the probing of archived vaccine samples for HIV contamination, though one vial of Wistar's CHAT OPV stored in Stockholm has already tested negative. He and I agree that it might be more telling to search stored samples for mitochondrial DNA that could reveal the species of kidney cells used. After Tom Curtis' notorious 1992 *Rolling Stone* article on OPV (*2*) and Koprowski's litigious response, John Garrett and colleagues in England experimentally examined the survival of human and simian immunodeficiency viruses in OPV preparations. No live retrovirus came through the procedure, but Hooper critiques the general validity of these tests.

HIV-1 has apparently colonized humans three times, giving rise to the HIV-1 M, N, and O groups (*3*). Only group M has become pandemic. HIV phylogeneticists doubt that HIV-1 M could have diversified from an ancestral chimpanzee virus between the first African OPV trial (in 1957) and the first documented HIV sequence, found in a 1959 blood sample taken in Leopoldville (now Kinshasa).

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Hooper's suggestion that the diversification of HIV-1 M into HIV subgroups occurred before introduction to humans seems unlikely.

Hooper argues that OPV is the only thing special about the mid-20th century that could trigger such zoonoses. Yet, as he discusses, establishing AIDS as an infectious human disease required two steps: the cross-species jump of the virus and its onward transmission. The second step may be the modern one, given the colonial and post-colonial turmoil (*4*), the truck routes, and the all-too-ready use of syringe and needle for medical treatments in Africa. Hooper cites human T cell leukemia virus (HTLV-1) as an ancient infection because it traveled with African slaves to the New World. But he does not mention what are probably more recent HTLV-1 introductions, including transfer from chimpanzees (*5*). Although AIDS is clearly a new human condition, we do not know whether rare, sporadic infections of simian immunodeficiency viruses have occurred throughout history, as in the cases with HTLV-1 and rabies.

Neither am I persuaded by Hooper's attempts to correlate sites of the OPV trials to HIV's later appearance: For example, HIV-1 group M instead may have moved eastwards from Leopoldville, which is nearer to the habitat of the source subspecies of chimpanzee (*3*). Although the river Congo flows east to west, the boats navigate in both directions. But if one must seek an iatrogenic origin of HIV, there are the malaria-attenuation experiments conducted at the Institute of Tropical Medicine in Antwerp from the late 1930s to 1955 in which humans were inoculated with chimpanzee blood (*6*). Antwerp is far from Africa, but Belgians were constantly traveling between the home country and its colonies.

Nonetheless, there are important lessons to be learned from Hooper's analysis. In the polio epidemics of the 1950s, the pressure to test vaccines was overwhelming. Similarly, today "something must be done" about AIDS. Thus commerce and the combined will of the National Institutes of Health and the World Health Organization have led to trials in the slums of Bangkok of an HIV vaccine that is unlikely to be protective. Once again, the follow-up studies seem inadequate; let us hope that the vaccine is not harmful. Another worrisome development is the suppression of scientific debate through lawsuits claiming defamation (*7*), even though those lobbying against vaccines are just as quick to resort to the courts.

For 45 years, regulatory authorities have been worried silly that using permanent cell lines as vaccine substrates may somehow transfer cancer-causing properties. Ironically, it was primary, macaque kidney cells that yielded oncogenic SV40 as an OPV contaminant. Well-tested non-oncogenic cellular substrates such as MRC-5 and VERO now exist, so it is timely that a September workshop sponsored by the U.S. Food and Drug Administration (*8*) reopened the debate on the use of primary cells versus cell lines for live attenuated vaccines.

The River does not prove the claim that testing oral poliovirus vaccines created AIDS, but even if Hooper is wrong we have had a close call. African green monkey kidneys are still used as the main cell-substrate for OPV. Millions of doses must have been made from SIV-positive monkeys before screening was introduced, so we are lucky that African green monkey SIV and D-type macaque retroviruses have not spread to humans.

References

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BROWSINGS

Small Worlds. The Dynamics of Networks Between Order and Randomness. *Duncan J. Watts.* Princeton University Press, Princeton, NJ, 1999. 207 pp. $39.50, £24.95. ISBN 0-691-00541-9. Princeton Studies in Complexity.

Watts presents an engaging and informative introduction to small worlds, networks in which every node (or everyone) is separated by only a short chain of intermediaries. He develops a crash course in the theory of graphs to explain network structure and how small worlds might arise. To demonstrate the importance of such networks, Watts explores the relationships between local and global dynamics in simple models of the spread of infectious diseases, computation in cellular automata, cooperation in game theory, and coupled phase oscillators.

Statistics on the Table. The History of Statistical Concepts and Methods. *Stephen M. Stigler.* Harvard University Press, Cambridge, MA, 1999. 500 pp. $45, £27.95. ISBN 0-674-83601-4.

In a 1911 dispute about the effect of parental alcoholism upon children, the statistician Karl Pearson challenged the Cambridge economists Marshall, Keynes, and Pigou by insisting that quantitative evidence requires statistical evaluation. This clash is the focus of the title (and the only completely new) essay in Stigler's collection. Other chapters take up topics ranging from the meter of Virgil's poetry to the cause of the Great Depression. Some of the pieces discuss subtle ideas such as the aggregation and regression paradoxes; others are nontechnical. But all examine ideas with an eye for their relevance to current disputes.

CREDIT: PEDRO A. SAURA RAMOS/COURTESY ABRAMS

The Cave of Altamira. *Antonio Beltrán, Ed.* Abrams, New York, 1999. 180 pp. $49.50, C$75. ISBN 0-8109-1989-3.

The paintings and engravings of animals that decorate Altamira cave in northern Spain form one of the finest and most important examples of Paleolithic art. The size, antiquity, and quality of the images, however, led to considerable skepticism when they were discovered in 1879. Essays in this book summarize current understanding of the artists and their art, including its creation, preservation, interpretation, and conservation. Photographs by Pedro A. Saura Ramos provide overviews and close details of the figures, such as the large male (above) that stands apart from the herd of painted bison on the roof of the Polychrome Chamber.