Roundtable

Peer review and the origin of AIDS—a case study in rejected ideas

by Brian Martin

The purpose of peer review has been widely misconceived, David Horrobin (1990) argues. Whereas most scientists see quality control as the central purpose of peer review, Horrobin says that for biomedical science that purpose should be improvement of the care given to patients. Quality control is important, to be sure, but it must be balanced by openness to innovative ideas (Chubin and Hackett 1990).

Some of the problems faced by unconventional ideas can be illustrated by the following case study of the hypothesis that AIDS originated from contaminated polio vaccine. The aim of presenting this story is not to argue that this particular theory is correct. Nor is it to blame any particular individuals. What is at issue is the normal processes of peer review and publication within the scientific community and whether these processes are the most appropriate to benefit society as a whole.

An unconventional theory of the origin of AIDS

Today's standard theory of the origin of AIDS is that a simian immunodeficiency virus (SIV) carried by an African monkey was transmitted to and survived in a human to become human immunodeficiency virus (HIV). This transmission could have happened in any of a number of ways: blood from a butchered monkey entering a human's blood through a cut, monkey blood being injected into humans as part of sexual customs, a human eating undercooked African monkey meat, or a monkey biting a human (Grmek 1990, Hrdy 1987, Karpas 1990). However, there is a large number of other theories, such as the manufacture of HIV by biological warfare laboratories (Lederer 1987, 1988).

The focus of this article is one particular nonstandard theory: that HIV was introduced into humans via a contaminated polio vaccine. I present this theory not because it is the most likely to be correct but because it illustrates well some of the problems of peer review in dealing with unorthodox ideas.

In 1987, an independent scholar named Louis Pascal, based in New York City, developed the idea that AIDS originated from contaminated polio vaccines used in Africa in the late 1950s. After reflection and study of the medical literature, he developed some strong arguments and unearthed considerable evidence for this hypothesis. Here, in outline, is the argument:

There are two main types of HIV, called HIV-1 and HIV-2. Current variants of HIV-1 (linked with AIDS in most parts of the world) appear to have diverged from a common ancestor from central Africa a little before 1960, whereas current variants of HIV-2 appear to have diverged from a common ancestor from western Africa. The closest known relatives to HIV are SIVs found in monkeys and chimpanzees. An SIV similar to HIV-2 is known, but no SIV has been conclusively shown to be highly similar to HIV-1; however, further SIVs continue to be discovered.

Pascal noted that polio vaccines are cultured on monkey kidneys, and therefore SIV from an infected monkey could have contaminated a batch of vaccine. An infected monkey could have been used, because monkeys with SIVs may show no sign of disease. Polio vaccines could not be screened for SIV contamination before 1985, the year SIVs were discovered.

There is a precedent for contamination of polio vaccines. Since the early 1960s, it has been known that the monkey virus SV40 was probably transmitted to tens of millions of people through polio vaccination campaigns in the west (Shah and Nathanson 1976). (A number of findings suggest increased risks to human health from SV40, but there have been no major studies of populations exposed to the virus; Elswood and Stricker in press.) Pascal postulated a similar process for SIVs.

Pascal identified a live polio vaccine developed by Hilary Koprowski, of the Wistar Institute in Philadelphia, as the one most likely to have led to AIDS, and he even named the batch most likely to be responsible. This vaccine was given to 325,000 people in central and west Africa in the years 1957–1960. Pascal (1991) says that it is no coincidence that the rate of HIV infection is extremely high in central Africa and in Kinshasa, Zaire.

A point in immunology aids the argument. Pascal (1991) points out that for a virus to infect a different species, it is helpful to reduce the resistance of the new host's immune system. Koprowski's polio vaccine was given to many children less than one month old, before their immune systems were fully developed. Furthermore, these infants were given 15 times the adult dosage because they produce antibodies less easily.

Although HIV is transmitted most readily through exchange of blood or semen, it can be transmitted orally, especially via breast-feeding or when mucosal immunity is impaired. Koprowski's vaccine was administered orally. The virus could have entered the blood through mouth ulcers or lesions.

Much more could be said about this hypothesis, including a whole series of rebuttals and replies. Like any moderately complex theory, there is latitude for elaboration and modification in the face of challenges. For the purposes of this article, it is only nec-

essary to argue that this hypothesis is worthy of further study.

Response of the scientific community

Pascal wrote up his findings to publish as a short article. From 1987 to 1988, he sent his manuscript to 13 biologists and AIDS researchers, and a few other individuals, inviting comment. From this correspondence he received only one brief acknowledgment. In 1988, he submitted his manuscript to *Lancet*, *Nature*, and *New Scientist*. *Lancet* rejected it with no reason given. *Nature* rejected it with the rather cryptic comment that although the theory "cannot be ruled out, it does not seem readily to fit the epidemiology of AIDS" (Pascal 1991, p. 11). *New Scientist* replied two years later, saying that the manuscript was being sent out for refereeing, but it did not communicate thereafter.

Pascal had a better response from several philosophers to whom he wrote in 1987 and 1988. He received advice and encouragement, including the suggestion to write an article for the *Journal of Medical Ethics*. Pascal wrote a new article for this journal, but it was rejected for being much longer than the standard maximal length. Finally, he wrote an article for *African Commentary*; it was accepted but the magazine ceased publication before Pascal's work appeared.

Why was Pascal so unsuccessful in getting his ideas considered? There are at least three plausible reasons. First, Pascal is not a professional scientist. He has no advanced degree and no institutional affiliation, and he studied the origin of AIDS out of personal interest and social concern. It is commonplace to note that individuals without relevant degrees and prime institutional locations stand little chance of being taken seriously by the scientific community (Caplow and McGee 1958, Wallis 1979). It mattered little that Pascal's articles and correspondence show—by my own assessment—an incisive intellect, a comprehensive grasp of the literature, and scrupulous attention to detail. It seems that Pascal was not considered a peer, so his submissions were not given a fair trial by peer review.

A second reason is that Pascal's articles are not written entirely in the dry, concise, and passionless style demanded by scientific journals. His early articles display somewhat more emotion and concern than is typically allowed.

It might be said that Pascal should have tried other journals; after all, it is difficult for anyone to be published in *Lancet*, *Nature*, or *New Scientist*. He should have done his utmost to put his articles in the standard style. But Pascal, working outside scientific institutions, believed (Pascal 1991) that scientists and editors had a duty, given the importance of what he had to say, to either refute or accept his arguments. Without an apprenticeship in formal scientific training, he lacked practice in the skills to play the publication game.

Even without these handicaps, there is a third reason why Pascal would have had enormous difficulty gaining a hearing. Quite simply, his ideas are highly threatening to the medical research community. To acknowledge that the highly touted and highly successful campaigns to wipe out polio may have inadvertently triggered the deadly disease AIDS would be incredibly damaging to the image of medicine and medical research. At a minimum, many people would be much more reluctant to be immunized. Much tighter controls over medical research could be another consequence. As Horrobin (1990) notes, new ideas are threatening to the status of the guardians of the establishment. As a consequence, it is a regular experience for new ideas to be rejected under the pretext of quality control; Horrobin (1990) gives numerous examples.

That this factor might have been sufficient by itself to block consideration of Pascal's work is suggested by a response to Gerasimos Lecatsas (a virologist at the Medical University of Southern Africa, Pretoria) and Jennifer Alexander (a microbiologist at the University of Witwatersrand, Johannesburg), who suggested independently in a letter to the *South African Medical Journal* that polio vaccine should be considered as a possible source of AIDS (Lecatsas and Alexander 1989). Schoub et al. (1990) attacked Lecatsas and Alexander's letter as "reprehensibly irresponsible misinformation" and "recklessly wild and unscientific speculation."

Pascal's difficulties were brought to my attention in 1990 by philosopher Richard Sylvan of the Australian National University in Canberra, who knew my long-standing interest in the suppression of intellectual dissent (Martin et al. 1986). My subsequent correspondence with Pascal demonstrated to me the seriousness of his concerns and the high quality of his work. After his article for the *Journal of Medical Ethics* was rejected, I arranged for its publication in a working paper series at my university (Pascal 1991).

Circulation of Pascal's paper generated considerable interest. It stimulated replies from eminent biologists (supportive comments from W. D. Hamilton, a zoologist at Oxford University in Oxford, England, and critical comments from his colleague, Robert M. May); it led to stories in magazines and newspapers (Cribb 1992), an offer for publication in book form (not proceeded with), and correspondence from around the world. Ironically, this piece of writing, which is much more passionate than Pascal's earlier efforts circulated to scientific journals, has produced a much greater response from scientists. Many of them complain about the style, but they pay attention to the arguments.

The *Journal of Medical Ethics*, which had rejected Pascal's submission, subsequently published an editorial on the subject. It points out the availability of the article, discussing the journal's reasons for rejecting it, and commenting that Pascal's thesis "is an important and thoroughly argued one and ought to be taken seriously by workers in the AIDS field" (Gillon 1992).

The publication of Pascal's article might have served as a neat case study in how an idea spreads from a single point of publication, but the process was perturbed and indeed overwhelmed by a separate development. In 1991, independent of Pascal, AIDS activist Blaine Elswood of San Francisco developed and pursued the idea that AIDS developed from contaminated polio vaccine. Elswood, who is employed as an administrative assistant at the University of California at San Francisco, does not have a prestigious position or eminent research record. But Elswood, in collaboration with medical researcher Raphael Stricker of the California Pacific Medi-

cal Center, San Francisco, wrote a scientific article. It was rejected promptly, with a referee's report, by the *British Medical Journal*. They then submitted it to *Research in Virology*. Luc Montagnier wrote to Stricker in February 1992 that he would recommend publication. But months later the board of the journal decided that it would only accept a much shorter contribution as a letter to the editor, specifically requesting removal of a section on SV40.

Elswood and Stricker prepared a letter to the editor as requested, but many more months passed before its formal acceptance and publication. The letter (Elswood and Stricker 1993) was followed, in an unusual procedure, by a rebuttal from the journal's editorial board. Elswood and Stricker's original article was later accepted for publication in *Medical Hypotheses* (Elswood and Stricker in press).

Meanwhile, Elswood had provided information to and exchanged ideas with journalist Tom Curtis of Houston, Texas, who further investigated the topic, interviewed key figures in the polio vaccination field (notably Albert Sabin, Jonas Salk, and Koprowski), and wrote an impressive story for *Rolling Stone* (Curtis 1992). This story, with its wide circulation, immediately generated stories in newspapers, magazines, television, and radio, including in *Science* and *New Scientist*, with assessments ranging from sympathy to antipathy. Again, there is an irony: a popular story produced more willingness by scientists to acknowledge the theory than did repeated approaches to biologists and submissions to journals.

The theory that AIDS originated from live polio vaccination campaigns in Africa in the late 1950s has now been widely circulated. So, although it might have been prematurely rejected before, it might be thought that it will receive fair assessment from now on. But will it?

All the factors that weighed against the theory before it was widely known continue to operate. First, it has been developed and publicized primarily by people outside the scientific mainstream. Second, the theory has been presented in a style quite different from the usual staid scientific journal article. Finally, the theory continues to be threatening to the medical research establishment. I predict that the theory will be ignored as much as possible and, when it cannot be ignored, be attacked.

One obvious test of the theory is to check whether stocks of polio vaccines used in the early campaigns are contaminated with SIV. Medical researcher Robert Bohannon of Houston, Texas, publicly offered to do this test. His early requests to obtain samples from the Wistar Institute in Philadelphia were not answered. Administrators at the institute have not said whether or not they will do the testing. Many months have passed. At the least, there seems to be a certain lack of urgency to test the theory.

The Wistar Institute did set up a committee to examine the theory. The committee's brief report (Basilico et al. 1992) said that the chance that AIDS developed from 1957–1960 polio vaccination campaigns in Africa was "extremely low"—but it did not make the obvious comparison with the chance of other proposed origins of AIDS. Even so, the committee recommended that polio vaccines no longer be cultured on monkey kidneys, because they conceivably may be contaminated by as yet undiscovered monkey viruses.

Another response has been Koprowski's threats of legal action against some news media that publish stories on the link between his polio vaccines and AIDS (Holden 1993). Since the threats, some media seem to have been quiet on the topic. Koprowski launched a legal action against Curtis and *Rolling Stone* in December 1992 (Holden 1993). Since then, neither Curtis nor any other journalist has published a major story on the case.

Pascal, Lecatsas, Stricker, and a few others continue to pursue theories implicating various polio vaccines in the origin of AIDS (Goldberg 1992, Kyle 1992). These theories seem to be supported by recent evidence concerning humans contracting SIV from monkeys (Khabbaz et al. 1992) and by the discovery of a monkey that tests positive for an HIV-1-like virus (Lecatsas and Alexander 1992).

Does it matter?

One response to claims about polio vaccine and AIDS has been to say that the origin of AIDS does not really matter, because it does not help the fight against AIDS today. This response suggests a reluctance to confront an unwelcome possibility. In the case of nearly every other disease, an understanding of the cause or origin of the disease is considered to be valuable in prevention or cure.

Pascal believes that if his hypothesis is correct, it has implications of the greatest significance. There are quite a number of different SIVs, and new ones continue to be discovered. Since the Wistar committee report (Basilico et al. 1992), there has been no announcement of any change in the practice of using monkey kidneys to culture polio vaccines. Pascal (1991) argues that new varieties of HIV, due to different SIVs, may have been entering the human species every few years through this route. So far, two HIVs dominate in cases of AIDS. But Pascal suggests that a million or more people eventually may die from each SIV that enters the human species and that other, completely different, simian viruses also pose a great risk. Although vaccine preparation procedures are much stricter today than in the 1950s, unanticipated contamination is all too possible.

On an issue such as AIDS, where the stakes in human lives are high and there continue to be large unknowns, it makes sense for the scientific community to be open to a wide range of theories, including ones that are quite unorthodox and indeed outrageous. There could be a high cost to pay if one of the theories, ignored because it seemed too unlikely, turns out to be correct. Such an approach of tolerance for a diversity of competing ideas makes a lot of sense whenever the social costs of being wrong are substantial (Feyerabend 1978).

Unfortunately, the scientific reception system is ill suited to dealing with unorthodox and challenging views, especially when they come from outsiders (Savan 1988, Wallis 1979). It requires courageous scientists to openly consider unorthodox ideas, and courageous editors to publish that work. Without such courage, it can be predicted that those with challenging ideas occasionally will find a popular audience. When, as sometimes occurs, those ideas end up being considered correct, it is the scientific community that loses credibility.

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