causes of primary hypercholesterolaemia.[8] The identification of more patients with FDB should enable further studies to define the influence of diet and hypolipidaemic drugs on circulating LDL particles in these patients. Meanwhile our results indicate that lovastatin appears to reduce total and LDL cholesterol as effectively in patients with FDB as in those with other forms of primary hypercholesterolaemia.[8-11]

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VIEWPOINT

Simian retroviruses, poliovaccine, and origin of AIDS

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Scientists recognised the problems of undetectable simian viruses in poliovaccines in the 1950s when live SV-40, discovered in all Salk inactivated vaccine, appeared in Sabin's original seed strains. As an attorney I was prompted to seek out documents from US government and vaccine manufacturers by a medicolegal case of paralysis in a contact of a vaccinee. When that case was settled my background as a graduate electrical and mechanical engineer prompted my continued scientific inquiries. These have led to a hypothesis on the origin of AIDS.

In 1976 tests on of some monopools of live poliovaccine detected type C RNA viruses. After an almost two year study by the US Bureau of Biologics one such monopool was released in 1977, under an amendment to the manufacturer's licence, held by Lederle, permitting up to "100 organisms"/ml in the final vaccine. Such virions were associated with reverse transcriptase activity in the vaccine and when passed into other cell lines, but no retrovirus recognised at that time was detected and they were assumed to be harmless in small quantities. Poliovaccine has a sterling safety record but that very safety led to non-approved uses of the vaccine for treatment of herpetic lesions. What I propose is a link between HIV-related retroviruses from the African green monkey in poliovaccine lots, the use of this vaccine by homosexuals in a manner unanticipated when the vaccine was licensed, and the onset of the AIDS epidemic in the United States.

Some ten years ago simultaneous outbreaks of Kaposi sarcoma and serious opportunistic infections began to be reported among homosexual men, especially in New York City, San Francisco, and Los Angeles. In 1982 the US Centers for Disease Control concluded that the coincidence of Kaposi sarcoma and *Pneumocystis carinii* pneumonia "strongly suggests the occurrence of a single epidemic of underlying immunosuppression in homosexual men".[1] In the following year the cause of this acquired immunodeficiency syndrome (AIDS) was found to be a novel retrovirus which we now know as HIV. The cause of AIDS might have been identified but the source had not. Subsequently Essex and colleagues reported that the African green monkey, the species used in the production of most live poliovaccine in the US, was a reservoir of simian immunodeficiency virus (SIV).[2] 30–70% of these monkeys in the wild carry this virus and it does them no harm; however, SIV does cause "simian AIDS" in the African macaque. The harmlessness of SIV in green monkeys indicates that monkeys carrying such a virus would not be excluded from vaccine production because they would show no obvious signs of illness. SIV has some virological and biological properties in common with HIV. However, HIV (or HTLV-III or LAV) was novel in that it was not thought to be endogenous in man and could be distinguished from the then known animal retroviruses by techniques such as nucleic acid hybridisation. Similarly the US government's tests in 1976–77 on virions from poliovaccine lot 3-444 established them as unlike any of the known type-C viruses (retroviruses), and the vaccine was released for use provided it contained fewer than 100 organisms per dose and did not contain viruses "known to be harmful to man".

Presumably the regulatory authorities concluded that the presence of any such monkey virus would not affect man because there would be no transfer from the digestive tract to the lymph and blood systems and because there was no reason to suspect inter-species transfer. At that time this

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must have seemed correct, otherwise there would surely have been an outbreak in the child recipients of the vaccine. We need to remember that HIV is not thought to be transmitted via tears or urine, for example—indeed it is not perceived to be as infectious as hepatitis B virus, and a few (50–100) organisms per dose of vaccine would not be expected to affect the children taking it. This implies that if the "single epidemic of immunosuppression" began around 1977–78 and stemmed from the African green monkey, it impacted on heterosexuals and male homosexuals differently, because of differences in the type of sexual contact or in the rate of exposure to the virus or its progenitor.

I suggest that the key lies in the use of poliovaccine, contaminated with small numbers of type-C retroviruses, for the treatment of herpetic lesions, a sexually transmitted condition the prevalence of which in homosexual men is indicated in the early case-reports of those who died from AIDS. In 1974 Adolph Tager proposed[3] live oral poliovaccine for the treatment of recurrent herpes, and multiple poliovaccine doses given monthly were suggested by clinicians in New York and California.[4] The doses used for this purpose would have exceeded the "100 particle per dose" safety limit and could have provided a point source for infection that spread to sexual contacts. Other adults would also have been exposed to the putative progenitor HIV at that time, hence the need to speculate that this virus either survived passage through the gastrointestinal system because of the rate of exposure and/or bypassed it because of the nature of the sexual activity.

Was there, therefore, no concern about extraneous viruses in live poliovaccine? A series of memoranda from 30 years ago shows that there certainly was. Indeed some manufacturers who were invited to make the live vaccine declined for this reason, Merck & Co being an example.[5] Regulations brought out in the 1950s[6] referred to the exclusion of "viable" microbial agents, but a simian virus might not be considered viable in man. These regulations apparently differed from the National Institutes of Health proposed restriction on the inclusion of simian viruses unless they had been proved not to be harmful to man. In 1972, after discovery of 80–110 nm viruses in its production fluids, Lederle implemented a "cytomegalovirus contingency plan" in a response to regulations requiring additional testing for extraneous viruses. The discovery of unknown type-C particles in poliovaccines would not therefore necessarily have led to their elimination from released vaccine lots. Interpretation of the regulations allowed for a wide discretion, and even though the neurovirulence regulations were not strictly followed it did seem that a very safe product was being produced and used without significant reactions in the United States. A 1980 statement from the commissioner of the FDA implied that the only microbial agent that could be released within poliovaccine lots would be type C retroviruses.[8] Since (at least up to 1985) the regulations did not insist on tests for such viruses, their presence is highly likely.

What was the viral agent? In 1976, Phillip McGrath, director of electronmicroscopy at the US Bureau of Biologics (BOB), recorded that three samples of Lederle poliovaccine lot 3–444 contained, besides large numbers of 18–28 nm polioviruses, spherical particles 80–100 nm in diameter resembling oncornaviruses. A rough estimate put their number at between 1000 and 100 000 per ml vaccine. By 1977 some oncornaviruses had been shown to cause leukaemia and tumours in laboratory animals. An important characteristic was their possession of RNA-directed polymerase or reverse transcriptase. This large subfamily of the retroviruses consists of four types, A-D, and most of them are C-type viruses 80–110 nm wide with a central core inside the envelope. In 1975 Dr John Petricianni and Dr J. B. Milstein of BOB described a simple, rapid screening test for type-C RNA tumour viruses, based on a sensitive reverse transcriptase assay.[8] In 1976, Milstein reported such activity in lots 3–444, 1–212 and others. Importantly, reverse transcription exhibited by one vaccine monopool was also exhibited by the particle within it when grown into other cell lines. The discovery of suspect particles, specifically C-type RNA retrovirus, in 3-444 and in other lots prompted extensive testing of lot 3-444 by the Food and Drug Administration. Indeed the length of time this vaccine lot was held (20 months) was unprecedented. The US government set up a special committee to test and consult on the vaccine and the agent within it but eventually BOB permitted its release. An agent capable of genetically transmitting RNase-sensitive RNA copying ability would not be released today—or permitted for use in multiple doses by males with a homosexual lifestyle. The manufacturer's position, one that was accepted by the government of the day, seems to have been that any such organisms would stay within the intestinal system of the child since this was an oral vaccine; there was no known harmful effect for man and the microbe would not remain viable. Some companies developed alternative methods of poliovaccine manufacture (eg, in human diploid cell lines) but at that time Lederle released press statements extolling the safety of poliovaccine made in the African green money substrate. It seems the years of safety in vaccine production led both manufacturers and government to overconfidence—yet they had recognised one extraneous agent (cytomegalovirus) some years earlier and had done nothing further to test for them (see above).

My hypothesis that the virus particles found in those vaccine lots were HIV (or some variant) can be tested by analysing stored samples by the polymerase chain reaction. Reverse transcriptase analyses of released vaccine have shown up positive for such simian viruses up to 1985, and a critical look should now be taken at all such vaccines. If US government laboratories have already done PCR tests on stored samples of the incriminated lots of poliovaccine which remain, the results should be made public.

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