

The early days of the HIV-AIDS epidemic in the USA

Harold W Jaffe

The work of epidemiologists before the isolation of human immunodeficiency virus 25 years ago demonstrates the power of the epidemiological method to gain an understanding of disease pathogenesis.

This year marks the 25th anniversary of the discovery of the AIDS virus. On 20 May 1983, Barre-Sinoussi *et al.* reported the isolation of a T lymphotropic retrovirus from the lymph node of a homosexual man with unexplained lymphadenopathy¹. Although the French team wrote that “the role of this virus in the etiology of AIDS remains to be determined,” subsequent work at the Pasteur Institute and the US National Cancer Institute established that the virus, called ‘lymphadenopathy-associated virus’ by the French and ‘human T lymphotropic virus III’ by the Americans and now known as ‘human immunodeficiency virus’, was the causative agent.

Although the importance of this discovery cannot be underestimated, it is also important to understand the epidemiological work that preceded the discovery. It was this work that established AIDS as being most likely caused by a transmissible agent, defined the transmission routes of the agent, suggested its natural history and also provided the basis for initial prevention guidelines. As a participant in this early work, I am pleased to have the opportunity to describe some of it as both history and an illustration of the power of the epidemiological method to gain understanding of a new disease in the absence of an identified cause.

My own involvement in the early investigations was almost by chance. I was a young medical officer working in the Venereal Disease Control Division at what was then called the Center for Disease Control (CDC) in Atlanta,

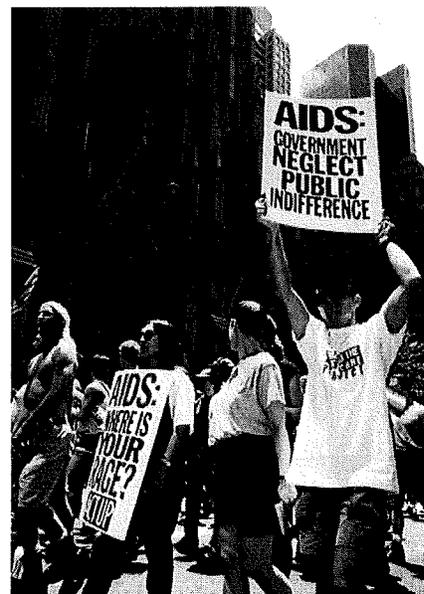
Georgia. At the time, we were concerned about increasing rates of sexually transmitted diseases in men who have sex with men (MSM), and we were more than a little interested when we saw the first report of a strange illness occurring in MSM.

The beginning

The report had come from Wayne Shandera, a CDC medical officer assigned to the Los Angeles County Health Department. Michael Gottlieb, an immunologist at the University of California at Los Angeles Hospital, had told Shandera about several young MSM who had been diagnosed with *Pneumocystis carinii* pneumonia (PCP). The five reported cases were highly unusual because at the time, PCP typically occurred in adults with underlying causes of immune suppression, such as the receipt of cancer chemotherapy or drugs to prevent rejection of a transplanted organ. Yet none of these men had those predisposing risk factors. Furthermore, the three patients tested had profoundly low T lymphocyte counts.

The publication of the report on 5 June 1981 (ref. 2) raised a series of questions. First, was this really a new disease, or had similar cases occurred in the past without being reported? Second, were cases being seen elsewhere? Third, why were the cases occurring in MSM? And fourth, were other unusual diseases also occurring in MSM?

Because this disease did not fit neatly into any of the CDC’s organizational units, a task force of perhaps a dozen people with a wide range of expertise was created to examine the problem. To answer the first question, we turned to the CDC’s Parasitic Disease Drug Service, which supplied US physicians with



A crowd of ACT UP activists march in front of St. Patrick’s Cathedral, New York.

medications to treat unusual parasitic infections. The only drug available to treat PCP in 1981 was pentamidine isethionate. A record review showed that almost all previous pentamidine requests had been for people with an obvious cause of immune suppression. Beginning in the second half of 1980, however, a few requests had been received for people fitting the profile of the Los Angeles cases³. Thus, the disease might have begun a bit earlier than 1981 but not much earlier.

The answers to questions two and four came only a month after the Los Angeles report: MSM in San Francisco and New York City were also being diagnosed as having PCP⁴.

Department of Public Health, University of Oxford, Oxford OX3 7LF, UK.

e-mail: harold.jaffe@dphpc.ox.ac.uk



this period was the 10 December 1982 publication of report of a possible case of transfusion-associated AIDS⁸. A 20-month-old child who had received multiple transfusions after birth developed unexplained immunodeficiency. Although AIDS had not been previously described in children, the features of this child's illness more closely resembled AIDS than other forms of pediatric immunodeficiency. One of the 19 blood donors was a man who developed AIDS 9 months after donation.

Only a week later, four other infants with unexplained immunodeficiency were reported⁹. These infants had not received transfusions; two had Haitian mothers whose health status was unknown. The mothers of the other two infants reported intravenous drug use; one of these mothers died of AIDS, whereas the other had early signs of the disease.

Finally, in early January 1983, the CDC published a report from New York City of two women who had developed immunodeficiency after repeated sexual contact with men who had AIDS¹⁰. One of these men was an intravenous drug user, whereas the other was bisexual. Neither woman had any other known risk factor for the disease.

Together, these three reports plus the 'Patient 0' investigation strongly suggested an infectious cause of AIDS. The putative agent could be transmitted through sexual contact, either homosexual or heterosexual; from mother to child; and through blood and blood products. Furthermore, the source of transmission could be a person who had not yet developed the disease, which indicated that the agent could be carried asymptotically.

AIDS and the blood supply

The growing concern about the safety of the blood supply gave rise to an important meeting held at the CDC in January 1983. From the perspective of the CDC, the purpose of the meeting with the US Food and Drug Administration, the National Hemophilia

Foundation, blood-banking organizations and groups representing MSM was to describe the occurrence of AIDS in transfusion recipients and people with hemophilia and then discuss potential prevention measures. However, the meeting quickly became a contentious debate rather than a constructive discussion. Although we presented a series of cases that we believed to be AIDS that resulted from the receipt of blood or blood products, the representatives from the blood banks and hemophilia-treatment community were not convinced that the disease was AIDS and were unwilling to accept our evidence that an 'AIDS agent' was contaminating the blood supply. Blood bankers also rejected the concept of using a surrogate (albeit nonspecific) test, such as the hepatitis B antibody test, to exclude potential donors. In part, this may have represented a legitimate concern about creating a blood shortage. In my view, however, much of the discussion simply reflected the unwillingness of the blood-banking and hemophilia-treatment communities to believe that blood and blood products, seen by them as lifesaving, could be transmitting a lethal infection.

Fortunately, private discussions held over the next few months were more productive and in March 1983, the US Public Health Service published the first comprehensive set of recommendations for the prevention of AIDS¹¹. The recommendations noted that "available data suggest that the severe disorder of immune regulation underlying AIDS is caused by a transmissible agent." Although no test existed to detect this agent, those at highest risk were noted to be those with symptoms or signs suggestive of AIDS, the sexual partners of AIDS patients, sexually active MSM with multiple partners, Haitian entrants to the United States, past or present intravenous drug users, people with hemophilia, and sexual partners of people at greater risk of contracting AIDS. The publication also recommended avoiding having sexual contact with people known or suspected to have AIDS and noted that having multiple sexual partners increased the risk of

AIDS. Further, as a 'temporary measure', members of these risk groups were advised not to donate plasma or blood. Although some of these recommendations were controversial, I think they were essentially correct at the time, even though the cause of AIDS was yet to be found.

Unfortunately, the AIDS epidemic did not stop with the identification of the causative agent. A million Americans have been reported with AIDS since 1981, and about 33 million people are now living with human immunodeficiency virus-AIDS worldwide.

Conclusions

I have often been asked what it was like to be one of the early AIDS investigators. To me, it all began as a medical mystery. I was caught up in being a 'medical detective' without much thought of the broader implications of what we were investigating. As time went on, however, I gradually began to see that what we were studying was much bigger than I had first imagined. Once it was clear that the disease was sexually transmitted, we knew that the disease would not be limited to MSM. And once we knew that the agent was in the blood supply, we knew many more people were at risk. The medical mystery would soon become the global pandemic.

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