AIDS AND THE PUBLIC DEBATE

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The NIH and Biomedical Research on AIDS

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During the three decades preceding the identification of acquired immunodeficiency syndrome (AIDS) as a new, deadly infectious and contagious disease, the United States federal government had expanded its activities in the areas of disease control, of medical research, and of regulation of drugs, biologicals, and devices. These efforts were embodied in three agencies of the United States Public Health Service (PHS): the Centers for Disease Control and Prevention (CDC); the National Institutes of Health (NIH); and the Food and Drug Administration (FDA). In this paper, I want to sketch an overview of the response to AIDS of the National Institutes of Health, the federal government's principal agency for support of biomedical research. I will place the NIH response in the context of its role among the PHS family of agencies and of its mission to uncover new knowledge in the biomedical sciences. Having examined how NIH responded to this new disease, I will then describe what unforeseen changes AIDS has brought to the NIH.

Since World War II, federal activity in health has been divided among the several agencies of the U.S. Public Health Service.[1] In 1980, just before AIDS was identified, there were six health agencies under the PHS umbrella. Of these, the FDA was the Service's principal regulatory agency.[2] The CDC, now called the Centers for Disease Control and Prevention but originally known as the Communicable Disease Center, assumed front-line responsibility for identifying the causes of epidemic outbreaks and assisting states with disease control.[3] The NIH was charged with conducting research to discover new knowledge in relation to health.[4] Before World War II, the CDC did not exist, and the NIH performed disease-monitoring functions in addition to the task of uncovering new knowledge. The current division of labor between the CDC and the NIH was crafted in 1946 in the context of the early antibiotic era, when these so-called miracle drugs held promise of utterly vanquishing bacterial diseases.[5] It was solidified in the ensuing decades as vaccines against polio and measles dramatically reduced the incidence of those diseases and a worldwide vaccination program against smallpox apparently eliminated that virus as a human pathogen.[6] By the 1970s, the CDC had demonstrated repeatedly its ability to handle outbreaks of diseases such as typhoid fever and also elucidated the causes of two previously undefined diseases—Legionnaires' disease and toxic shock syndrome.[7]

Initiation of PHS Response

In 1981, as isolated cases of unusual opportunistic infections and Kaposi's sarcoma were gradually perceived as comprising a larger pattern of immunosuppression, the CDC assumed principal responsibility for the Public Health Service's response to AIDS.[8] The CDC leader-

ship did not operate in a vacuum, however. William H. Foege, the CDC director, and the person named to oversee the CDC's AIDS effort, James W. Curran, Chief of the Operational Research Branch, Venereal Disease Control Division, Center for Preventive Services, were knowledgeable about experts in many medical fields who also worked for the PHS, and they called on them whenever it seemed appropriate. For example, in a 30 July 1981 memo to Vincent T. DeVita, Jr., director of the National Cancer Institute (NCI), Foege noted that Curran had already utilized the Kaposi's expertise of several NCI units and requested that DeVita designate a formal contact person for ongoing collaboration.[9] DeVita appointed William D. DeWys, Chief of the Clinical Investigations Branch, Cancer Therapy Evaluation Program, Division of Cancer Treatment, as NCI liaison on the new syndrome and further suggested that the NCI and the CDC sponsor a national conference on Kaposi's sarcoma.[10] This meeting was held in September 1981, with the goal of developing "a coordinated strategy regarding the etiology and treatment" of the disease.[11] Participants were unclear, however, about which came first, the wasting syndrome or the cancer and/or opportunistic infections.[12] What did emerge from this conference was the conviction that studies of this "new disease," as AIDS was then being called, should be conducted systematically, under a common protocol, with all patients enrolled in the CDC case-control study.[13]

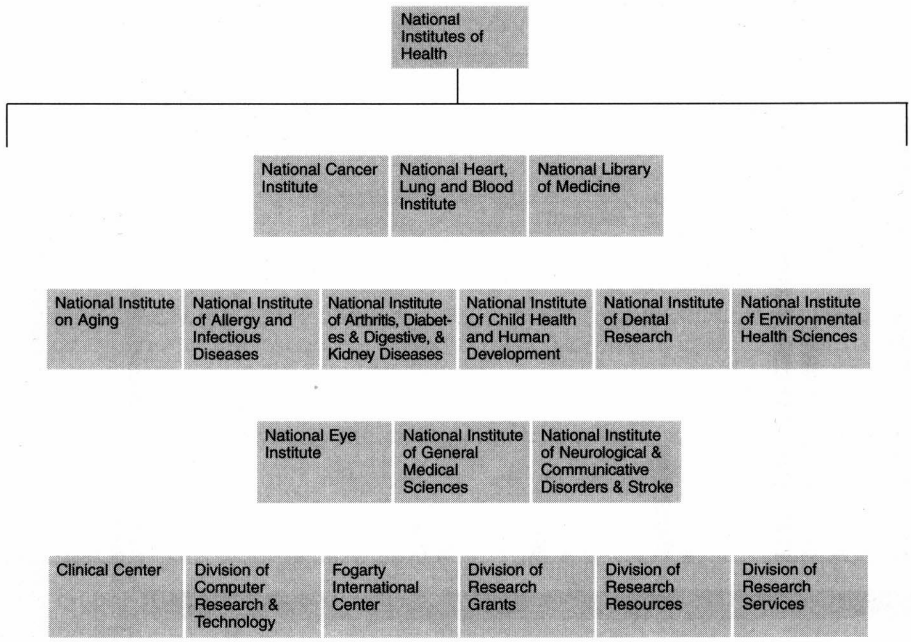
At a 30 June 1982 meeting held at the New York Department of Health, cases of AIDS were reported in intravenous drug abusers, heterosexual hemophiliacs, and Haitians as well as in gay men.[14] This midsummer 1982 meeting marks fairly specifically the point at which epidemiological data persuaded many investigators AIDS was caused by some sort of contagious agent. One NCI attendee returned to recommend that the NIH mount "a most urgent response," including the commitment of monies "in excess of our one million dollars."[15] Within two weeks, an NIH-wide Working Group on the "epidemic of acquired immunosuppression, opportunistic infections, and Kaposi's sarcoma" had been established to disseminate information among interested investigators at the NIH and to maintain liaison with the CDC.[16] At the higher administrative level of the Department of Health and Human Services, findings about AIDS were circulated through regular meetings of PHS agency heads with the Assistant Secretary for Health.[17]

Response of the NIH Extramural Programs

NIH funding for research is divided into the extramural programs of the institutes, centers, and divisions—which make grants, contracts, and other awards to investigators across the United States, and in some foreign countries—and the intramural programs of the various components, most of which are located in laboratories on a campus in Bethesda, Maryland.[18] Funds for grants and contracts in the extramural programs comprise about 89 percent of the NIH budget; funds for the intramural programs, about 11 percent.[19] Figure 1, the 1981 NIH organizational chart, reveals the emphasis on chronic diseases that characterized biomedical research funding in the early 1980s.[20] Only one institute, the National Institute of Allergy and Infectious Diseases (NIAID), was partially dedicated to the study of infectious diseases. The other seventeen semi-autonomous components emphasized cancer, heart disease, aging, arthritis, and other broadly defined, noninfectious problems. Between 1971 and 1975, moreover, Congress had directed the NIH to establish seventeen different targeted programs for research on specific chronic disease problems.[21]

This emphasis on chronic disease research meant that the problem of AIDS did not fit easily into the NIH as it existed in 1981. The underlying medical problem of AIDS patients—the immunodeficiency—was of interest to immunologists, who may have been

Figure 1. The National Institutes of Health, June 1981

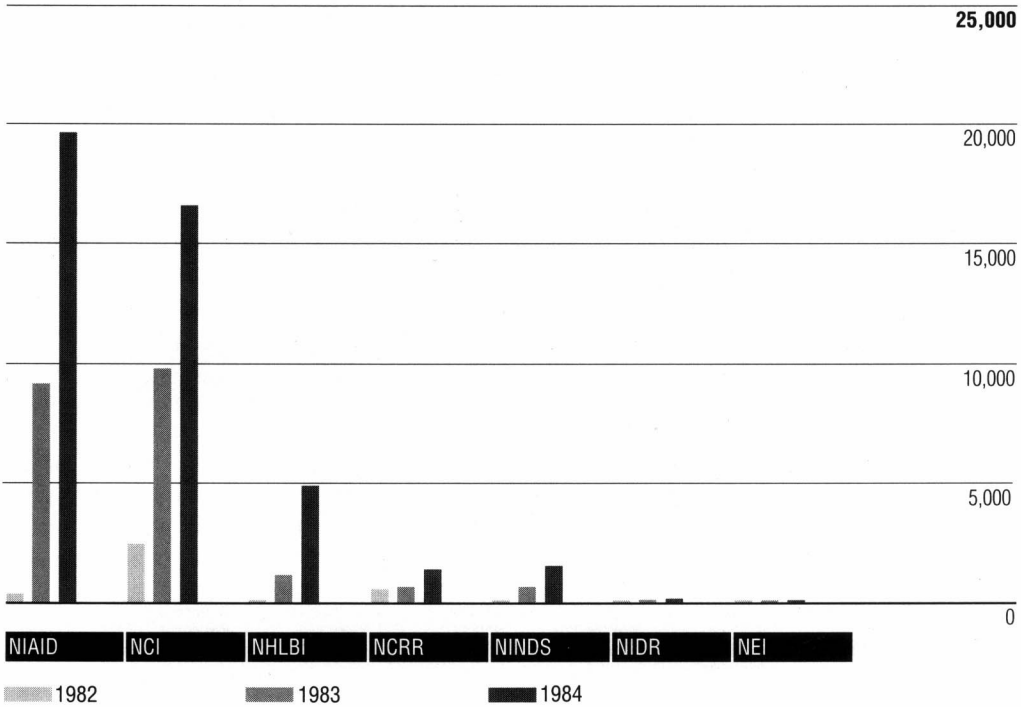


Source: NIH, Office of Program Planning and Evaluation and Division of Research Grants, *Basic Data Relating to the National Institutes of Health, 1981 (Washington, D.C.: NIH Publication No. 81-1261)*, p. *i.*

funded by any of several institutes, because in the early 1980s, molecular immunology was such a fruitful field.[22] Research on Kaposi's sarcoma, with which some patients presented, fell into the purview of the National Cancer Institute, and research on opportunistic infections fell under the mission of the NIAID. Before an etiological agent was discovered, therefore, there was some question as to which institute should take the lead in research on AIDS, because of the disease's multi-faceted nature.[23]

Furthermore, the administrative mechanism for distributing grants was also based on the presumption that NIH research would focus on acquisitions of long-term knowledge, not on public health crises such as AIDS. The process went like this: University-based investigators submitted research proposals, which were separated by the NIH according to subject area and referred to groups of nonfederal scientists who were experts in each area—i.e., the peers of the proposers. These review panels gathered three times each year, usually on the NIH campus in Bethesda, to evaluate the proposals for scientific merit. After receiving ratings from the review panels, the applications were reviewed a second time by the advisory councils for each institute, which considered the proposals from the perspective of each institute's mission, placing them in the context of nation-wide policy concerns about diseases and of the need to further research in selected areas. From the time an investigator submitted a proposal until the time funds were received, about eight or nine months elapsed, under normal circumstances.[24] Since 1946, when this program was established, some twenty-two studies of the system had attempted to balance the elitism inherent in any pursuit of

Figure 2. NIH AIDS Funding Profiles, FY 1982-84

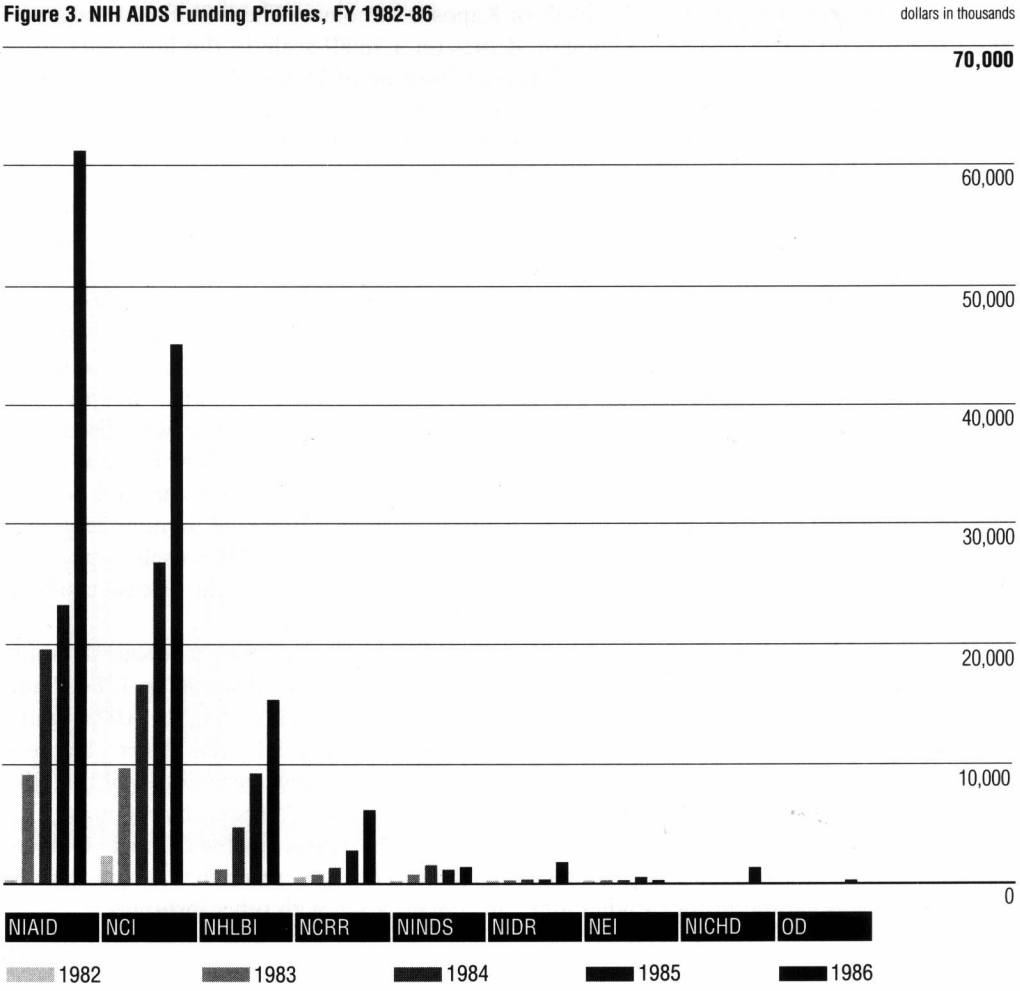


Source: NIH Data Book, 1992 (NIH Publication No. 92-1261)

excellence with the democratic imperative to ensure access of all groups to funding and to ensure accountability for expenditures of appropriated funds.[25] Major issues addressed included conflict of interest, inability to provide adequate review in highly specialized areas, concern that the review groups were not representative of the current trends in science, fear of missing the unrecognized genius by funding only "safe science," the volume of grants assigned to study section members, and the burden for both applicants and reviewers imposed by new laws and regulations.[26] None of these studies, it is worthy of note, considered the speed at which awards were made to be of great concern.[27] The NIH was thus surprised when AIDS activist groups and other critics decried the length of time it took for funding new grant proposals to study AIDS. As has been described elsewhere, it was as if the biomedical research community had spent four decades carefully crafting a great ocean liner, only to be asked why the ship would not fly.[28]

In the early 1980s, the extramural program utilized several different types of awards to fund research on AIDS.[29] In August 1982, the NCI issued its first request for investigators to submit grant applications relating specifically to AIDS.[30] This formal request was designed to bring into AIDS work those institutions that did not already participate in an NCI cooperative agreement, a funding mechanism similar to a grant, but one in which the awarding institute retained substantial programmatic involvement. Institutions already involved in cooperative agreements were eligible to apply for supplemental funds to inaugurate research on AIDS.[31] The NIAID had also begun to add AIDS monies to existing grants and to fund new awards. Before 1 October 1983, a program project grant on sexually transmitted diseases at the University of Washington was allocated just over $100,000

Figure 3. NIH AIDS Funding Profiles, FY 1982-86



Source: NIH Data Book

to expand its work to cover AIDS; a Georgetown University interdisciplinary research program on immunologic diseases was completely converted to study the AIDS problem; and new grants of varying sizes were made for a variety of studies, from laboratory and epidemiological research to assessing the psychosocial needs of AIDS patients.[32] Both the NCI and the NIAID also utilized the contract mechanism for some studies. The first NIAID contract, for example, was awarded to the New York Blood Center in fiscal year 1983 for the collection of specimens for detection of etiologic agents.[33]

NIH budget information, depicted graphically in Figures 2-4, reveals clearly how funding for AIDS has been divided among the NIH components.[34] These data encompass both extramural and intramural funding and cover fiscal years, which do not conform to calendar years but run from 1 October of the previous year to 30 September of the year given. Money designated for fiscal year 1990 may thus be released in October 1989. Figure 2, which includes appropriations for fiscal years 1982, 1983, and 1984, shows that in fiscal years 1982 and 1983, the National Cancer Institute led in AIDS funding, in large part

because of its keen interest in the problem of Kaposi's sarcoma. The NIAID also began to fund research on AIDS in 1982, although at first on a small scale in the intramural program.[35] The early AIDS funding in the National Institute of Dental Research (NIDR), the National Eye Institute (NEI), and the National Institute of Neurological Disorders and Stroke (NINDS—then called the National Institute of Neurological and Communicative Disorders and Stroke) also reflects intramural research and will be discussed below. In March 1983, the National Heart, Lung, and Blood Institute (NHLBI) was named the lead NIH institute to evaluate blood donor screening tests to reduce the risk of transmission of AIDS.[36] After the discovery of the AIDS virus in 1984, the NHLBI continued to collaborate with the Food and Drug Administration on tests to identify AIDS in the blood supply.

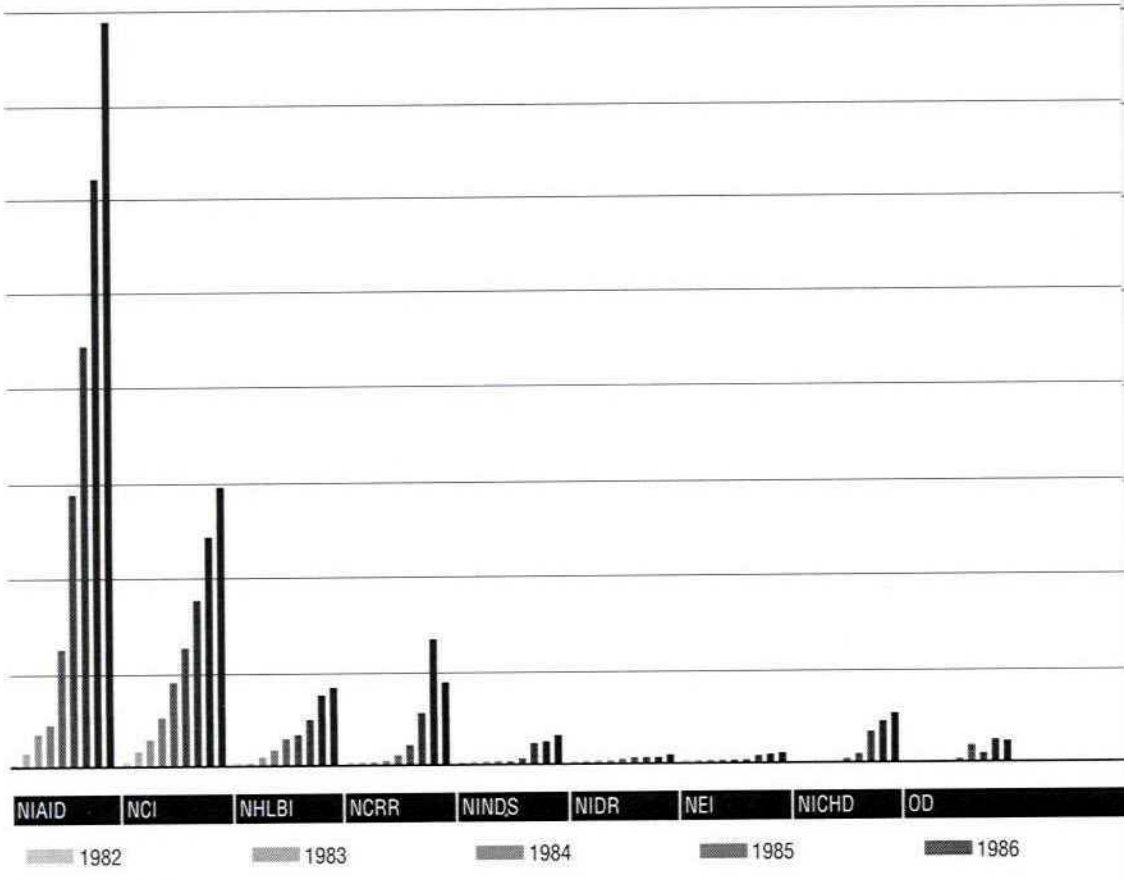
The final NIH component to become involved in this early period was the National Center for Research Resources (NCRR)—then called the Division of Research Resources—which funds, among other projects, the seven U.S. Regional Primate Centers.[37] In 1981, not long after AIDS was recognized in humans, a similar wasting syndrome was discovered among monkeys in three of the primate centers, California, Oregon, and New England. This disease was quickly named Simian Acquired Immunodeficiency Syndrome and usually referred to as Simian AIDS. Studies of Simian AIDS provided a model of immunodeficiency in primates. In addition, NCRR investigators attempted to transmit AIDS itself to primates at the Regional Centers in order to develop an animal model in which the disease could be studied and in which putative therapies and vaccines could be tested.[38]

Figure 3 adds fiscal years 1985 and 1986 to the AIDS funding profile. It reveals the spurt of work in the NIAID and in the NCI just after the AIDS virus was identified in 1984,[39] and the point in time—fiscal year 1986—when Congress expanded NIH funding for AIDS significantly. This is also when the NIAID assumed leadership of the NIH AIDS effort. Figure 4 updates the funding profile through fiscal year 1990 and shows how virtually all of the NIH institutes, including the Office of the Director (OD), established AIDS research programs. This figure also shows spikes in funding in 1989 and 1990 for the NCRR and the National Institute of Child Health and Human Development (NICHD). These represent the inauguration of large clinical and natural history studies, often in collaboration with other institutes.[40]

Response of the NIH Intramural Programs

Because the extramural program had been structured to move deliberately, it was the NIH intramural programs that in 1981 and 1982 were able to redirect resources most rapidly to investigate AIDS. Intramural AIDS efforts arose from individual initiative rather than in response to any top-down administrative directive and therein reflected traditional NIH reliance on investigator-initiated research. The first AIDS patient arrived at the NIH Clinical Center on 16 June 1981, eleven days after the initial report about the new syndrome was published in the *Morbidity and Mortality Weekly Report* from the CDC.[41] Thomas Waldmann, a distinguished NCI immunologist, admitted the referred patient under his Omnibus Metabolism Branch protocol. Waldmann and his associates attempted unsuccessfully to save the patient, who was beset by severe opportunistic infections and had essentially no immune response.[42] Almost exactly six months later, on 15 January 1982, a second AIDS patient arrived at the Clinical Center and was taken into the protocol on Human Immune Problems investigated by Anthony S. Fauci, then chief of the NIAID Laboratory of Immunoregulation.[43] For this and later patients, Fauci, his postdoctoral fellow H. Clifford Lane, and Henry Masur, Chief of Critical Care Medicine in the Clinical Center, formed a core team to study the pathogenesis of AIDS while they attempted the reconstitution of the

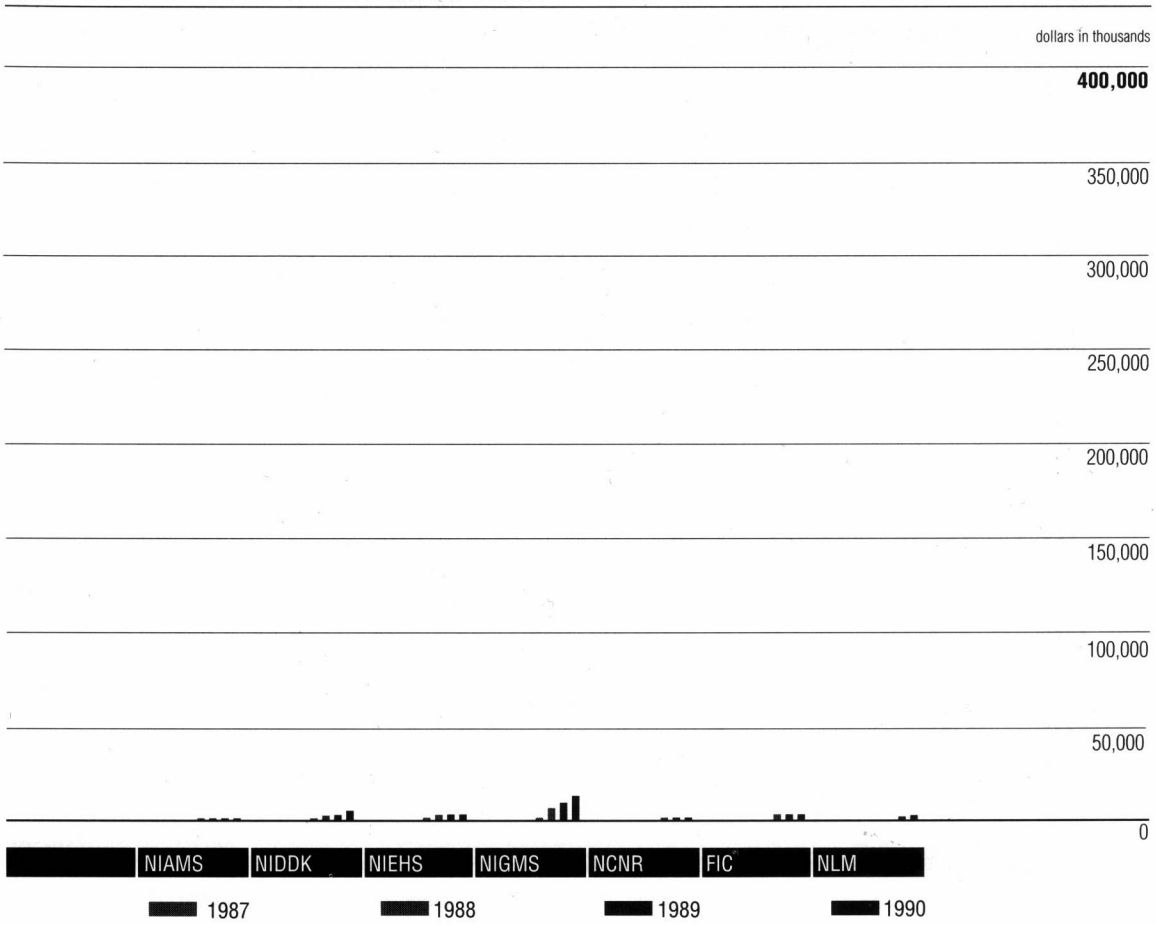
Figure 4. NIH AIDS Funding Profiles, FY 1982-90



Source: NIH Data Book

immune systems of AIDS patients, at first utilizing interferon and interleukin-2. They also took advantage of the fact that one AIDS patient had a healthy identical twin to transplant bone marrow from the healthy twin to the immunocompromised twin. Data showed definite improvement in the patient's immune system after the procedure, but the benefit soon disappeared and the patient died, suggesting that the causative factor in AIDS was not corrected but rather remained to infect and destroy the transplanted cells.[44] After the discovery of the AIDS virus, Fauci and the members of his laboratory modified their strategy to a two-pronged approach, adding antiviral therapies to immune reconstitution efforts.[45]

This group also established collaborations with other intramural experts in order to deal with the rare diseases suffered by AIDS patients. A group of investigators met weekly to review the information learned and to formulate new strategies.[46] Cytomegalovirus retinitis, which caused blindness and also attacked the gastrointestinal system, was one major concern. Robert B. Nussenblatt, Alan Palestine, and their NEI colleagues were thus enlisted to search for a drug that would control this opportunistic virus. The first drug tried was then known as DHPG, now called ganciclovir. It was chemically similar to acyclovir, which had recently been found effective against herpes virus infections.[47] Ganciclovir and foscar-



net, a later therapy studied by NEI, are the drugs of choice against cytomegalovirus infections in AIDS.[48]

NINDS investigators, including Nobel laureate D. Carleton Gajdusek, also joined the intramural clinical consultation to study neurological complications of AIDS, especially the so-called AIDS dementia.[49] NIDR scientists addressed the problems of AIDS patients who suffered oral candidiasis and oral Kaposi's sarcoma lesions.[50] Phillip Smith and Sharon Wahl of NIDR also demonstrated that macrophages and their precursors, monocytes, immune system scavengers that normally engulfed and destroyed foreign bacteria, were not able to migrate toward inflammatory stimulants in people infected with AIDS.[51]

As noted above, the National Cancer Institute took the lead in studying AIDS patients with Kaposi's sarcoma. The earliest intramural NCI activity in this area came out of a cancer epidemiology program that studied unusual clusters of cancer cases and traced family cancer connections. In the spring of 1981, one member of this group, James Goedert, was asked to consult on a diagnosis of Kaposi's sarcoma in a young man who was a friend of his family. After pronouncing that this would be impossible because Kaposi's "just didn't occur in young people," Goedert learned of other cases and, with others in his group, launched the first prospective epidemiological study of people at risk for AIDS. Since that time, this pro-

gram has expanded to include studies of how AIDS is transmitted from infected mothers to their babies.[52]

In 1982 and 1983 several other programs of note were initiated within the intramural program to facilitate research on AIDS. Michael Roberts of the NIDR issued recommendations to practicing dentists of precautionary procedures they should take in managing their patients with AIDS, and David K. Henderson, the hospital epidemiologist in the NIH Clinical Center issued precautions for health care workers that helped to minimize fear in the years before the cause of the disease had been determined.[53] The National Library of Medicine began to compile and publish an AIDS bibliography that is now also available as the computer database AIDSLINE, and Ruth Guyer, an immunologist on the staff of the NIAID intramural director, began editing and circulating and a newsletter called the *AIDS Memorandum*, which provided scientists a venue in which to share AIDS research findings rapidly and informally, without compromising their chances to publish in a mainstream journal. When the major professional journals began to publish articles on AIDS more quickly, this newsletter was discontinued.[54] In 1987, moreover, the Office of the Director instituted a targeted antiviral program aimed at utilizing the particular intramural expertise in structural biology and structural chemistry to a better understanding of the AIDS virus.[55] Intramural investigators submitted competitive applications like their extramural associates to be peer reviewed for funding under the OD targeted antiviral program. With these funds, X-ray crystallography, nuclear magnetic resonance, electron microscopy, and computer imaging processing studies were conducted to analyze the three-dimensional structure and organization of HIV proteins and to determine the shape of protein-bound drugs.[56]

Because of controversy surrounding it, the best known NIH research on AIDS may be that of Robert C. Gallo and his colleagues on etiology.[57] In his book, *Virus Hunting*, Gallo attributed his interest in research to find the AIDS agent to a 1982 seminar presented by James W. Curran, in which Curran cited epidemiological evidence indicating that AIDS was caused by a communicable pathogen with an affinity for helper T cells, which it then destroyed.[58] This intrigued Gallo, who had recently identified the first pathogenic human retrovirus, which also affected these cells. That retrovirus, however, caused helper T cells to proliferate uncontrollably rather than to die. Nonetheless, the affinity of the unknown pathogen for such a specific component of the immune system already known to be affected by one retrovirus suggested that a similar agent might cause AIDS. Gallo, Luc Montagnier at the Pasteur Institute in Paris and Jay Levy at the University of California, San Francisco, School of Medicine, all searched for, isolated, and characterized a retrovirus that has since come to be known as the Human Immunodeficiency Virus, or HIV.[59] By 1985 Gallo's laboratory also developed a test for AIDS called ELISA, or enzyme-linked immunosorbent assay.[60] It can be argued that this test, which is the initial assay used to safeguard the blood supply in the United States and in many other countries, has been to date the single most effective medical intervention in preventing new HIV infections.

With the discovery of an etiological agent, worldwide research on AIDS entered a short, intense period that lasted about two years during which the AIDS virus was characterized and evaluated to see whether therapies and/or vaccines could be quickly found to halt the epidemic. Intramural NIAID and NCI molecular biologists determined the genetic structure of HIV and discovered two of the virus's nine genes.[61] They also revealed the virus's propensity for genetic drift, which was much greater than that of the influenza virus. This meant that vaccine development might prove extremely difficult.[62] Even so, both the NIAID and the NCI launched vaccine development initiatives.[63]

Therapies for people with AIDS have focused on antiviral drugs, on efforts to reconsti-

tute the immune system, and on drugs to treat opportunistic infections and cancers. Virtually every antiviral AIDS drug was initially screened using the rapid in vitro assay developed by Samuel Broder and his intramural colleagues in the NCI.[64] Drugs that looked promising after this screening were then tested in animals and, if they appeared sufficiently nontoxic, became candidates for clinical trials. Many Phase I studies of AIDS drugs were conducted intramurally in the NIH Clinical Center.

Consequences of AIDS for the NIH

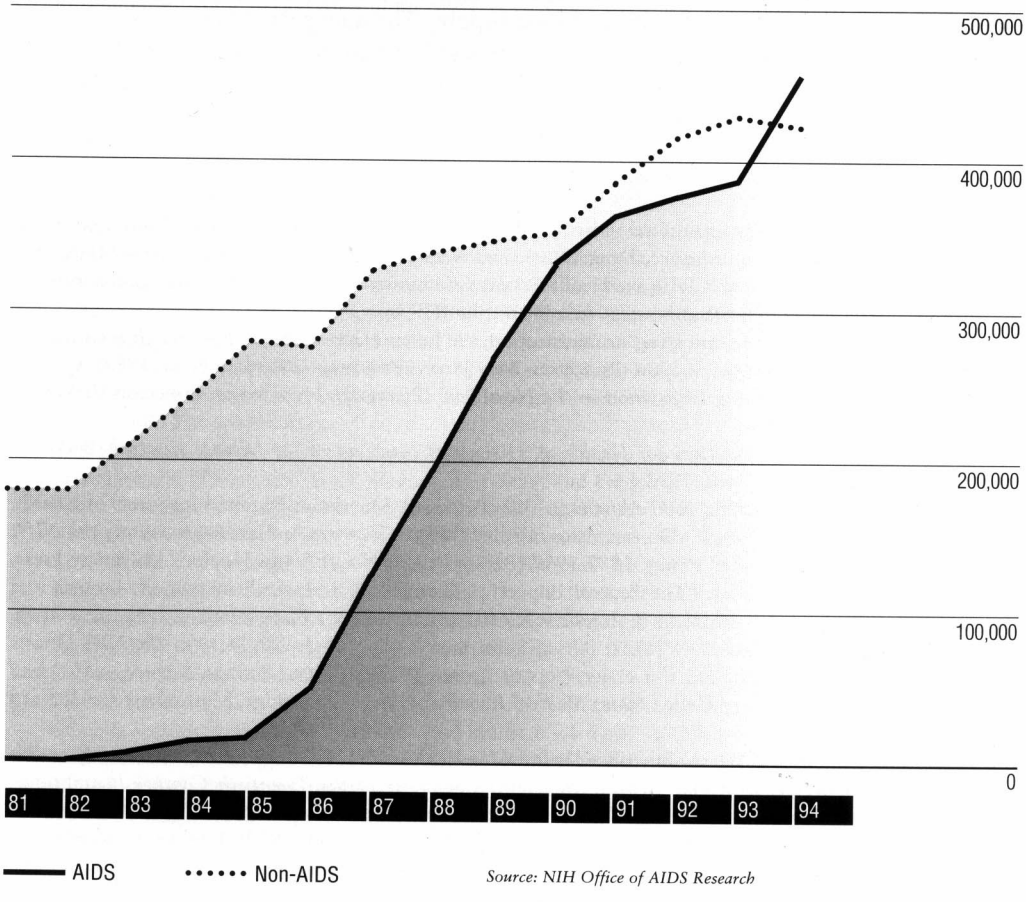
As the AIDS epidemic was unforeseen, so were its consequences for biomedical research at the NIH. One major consequence of AIDS has been the changes wrought by AIDS activists in the construction of clinical trials. People dying with AIDS believed that their immediate predicament warranted speedy access to putative therapies and discounted the importance of concerns over long-term side-effects.[65] Because the NIAID designed and ran clinical trials of AIDS drugs, AIDS groups brought pressure on the institute to change the way clinical trials were conducted. By October 1991 NIAID sponsored trials focused on three different approaches to treating the underlying immune deficiency in AIDS and the opportunistic infections and cancers. These included the standard clinical trial protocols known as the AIDS Clinical Trials Group; the Terry Beirn Community Programs for Clinical Research on AIDS, community-based studies that complement the ACTG; and the Division of AIDS Treatment Research Initiative, whose hallmark is speed in conducting "clinical trials and related research that evaluate new therapies and novel treatment approaches for those with HIV disease."[66]

A second consequence of AIDS was that traditional disease-related lobbying for increased research funds was transformed. AIDS activist groups were much more vocal and visible in demanding, not requesting, funding for AIDS than had been their earlier counterparts seeking funds for other diseases. Their efforts proved so successful that other groups, notably women with breast cancer and their families, have recently decided to base their crusade for funds on the AIDS model. "Since we are a crisis-oriented society," argued Sarah Fox, a professor of family medicine at the University of California, Los Angeles, "the people who make the most noise get the most publicity. Interest groups do count as opposed to data and rationality."[67]

A third consequence of AIDS has been to raise anew the debate over the best way to achieve medical breakthroughs: by developing a targeted approach and centralized direction or by the more traditional reliance on basic research and serendipitous observations of the individual investigator. For AIDS, calls for more emphasis on applied research have been couched as advocacy for an "AIDS research czar" or a "Manhattan Project" for AIDS.[68] In contrast, Barbara R. Jasny, a senior editor at *Science* magazine, emphasized in a recent issue the importance of continuing to investigate fundamental questions. She stated: "A cure may well come from an approach that has not been considered yet. Finding such an approach will require open-mindedness, a willingness to challenge accepted dogma, and a high degree of trust and collaboration among researchers from many disciplines, HIV-infected individuals, government, and industry."[69] With the enactment of the 1993 NIH Reauthorization Act, those advocating centralization have succeeded in requiring all new funds for AIDS to be funneled not to individual institutes but to the NIH Office of AIDS Research.

AIDS has also skewed research priorities significantly, especially within the NIAID. As funding for AIDS expanded in the early 1980s, many NIH grant applicants added AIDS as

Figure 5. NIAID Extramural Funding, AIDS versus Non-AIDS FY 1981-94



Source: NIH Office of AIDS Research

a project descriptor if any tenuous connection could be justified in order to increase, if only marginally, their chances for funding. As Figure 5 reveals, however, AIDS has grown to become an ever-larger portion of the NIAID budget. The 1994 estimate shows funding for AIDS as equaling or even surpassing funding for all other NIAID research combined.[70]

Conclusion

In a 1986 essay, historian Charles E. Rosenberg noted that "the great majority of Americans . . . look to the National Institutes of Health, not to the Bible, for ultimate deliverance from AIDS."[71] This observation reflects the key position that this federal agency has held since early in the AIDS epidemic and likewise demonstrates society's faith in "the authority of medicine and the truth of its agreed-upon knowledge," as Rosenberg stated.

This paper has sketched in broad strokes the NIH response to AIDS in its context as one of the agencies of the Public Health Service, each of which is charged with specific public health responsibilities, and within the NIH mission to discover new knowledge relating to health. NIH research—whether funded through the extramural programs or conducted within the intramural laboratories—has elucidated the etiology of AIDS, made headway in

describing the pathogenesis of the disease, informed efforts to develop therapies and vaccines, and produced a test to protect the blood supply. The unexpected budgetary and organizational consequences of responding to this disease have altered some aspects of the NIH response to AIDS but not its central role in funding and coordinating efforts to discover the information that will ultimately prevent or cure AIDS.

Notes

1. See Figure 1 for an organizational chart. The PHS health agencies were the Food and Drug Administration (FDA); the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA); the Centers for Disease Control (CDC); the Health Services Administration (HSA); the National Institutes of Health (NIH); and the Health Resources Administration (HRA).
2. On the history of the Food and Drug Administration, see James Harvey Young, *Pure Food: Securing the Federal Food and Drugs Act of 1906* (Princeton, New Jersey: Princeton University Press, 1989); Charles O. Jackson, *Food and Drug Legislation in the New Deal* (Princeton, New Jersey: Princeton University Press, 1970).
3. Elizabeth W. Etheridge, *Sentinel for Health: A History of the Centers for Disease Control* (Berkeley: University of California Press, 1992).
4. National Institutes of Health, *NIH Almanac*, 1992 (Bethesda, Maryland: National Institutes of Health, NIH Publication No. 92-5), 1. On the history of the NIH see Victoria A. Harden, *Inventing the NIH: Federal Biomedical Research Policy, 1887-1937* (Baltimore, Maryland: Johns Hopkins University Press, 1986); G. Burroughs Mider, "The Federal Impact on Biomedical Research," in John Z. Bowers and Elizabeth F. Purcell, eds., *Advances in American Medicine: Essays at the Bicentennial*, 2 vols. (New York: Josiah Macy, Jr., Foundation, 1976), 2: 806-871; Stephen P. Strickland, *The Story of the NIH Grants Program* (Lanham, Maryland.: University Press of America, 1989); idem, *Politics, Science, and Dread Disease: A Short History of United States Medical Research Policy* (Cambridge, Massachusetts: Harvard University Press, 1972).
5. On the creation of the CDC, see Etheridge, *Sentinel for Health*, 16-17. On the history of the early antibiotic era, see Harry F. Dowling, *Fighting Infection: Conquests of the Twentieth Century* (Cambridge, Massachusetts: Harvard University Press, 1977); idem, *Medicines for Man: The Development, Regulation, and Use of Prescription Drugs* (New York: Alfred A. Knopf, 1970); John Parascandola, ed., *The History of Antibiotics: A Symposium* (Madison: University of Wisconsin Press, 1980); *Antibiotics Annual, 1958-1959* (New York: Medical Encyclopedia, 1959).
6. Etheridge, *Sentinel for Health*, 140-49, 168-177, 188-210; John R. Paul, *A History of Poliomyelitis* (New Haven, Connecticut: Yale University Press, 1971); Horace G. Ogden, *CDC and the Smallpox Crusade* (Washington, D.C.: Centers for Disease Control, 1987).
7. Etheridge, *Sentinel for Health*, 257-267, 305-307. After the organism that causes Legionnaires' disease was identified, the NIH became briefly involved in research on Legionnaires'. Research sponsored by the NIH fell into four categories: clarification of the etiology, elucidation of the mode of transmission, delineation of the pathology through the development of animal models, and characterization of different stains and surface antigens in order to develop diagnostic tests and possible vaccines. See Victoria A. Harden and Dennis Rodrigues, "Context for a new disease: aspects of biomedical research policy in the United States before AIDS," in Virginia Berridge and Philip Strong, eds., *AIDS and Contemporary History* (Cambridge: Cambridge University Press, 1993), 182-202, esp. Table 1, 188 and Figure I, 192.
8. Etheridge, *Sentinel for Health*, ch. 24, "The discovery of the AIDS epidemic," 321-340.
9. Memorandum, William H. Foege to Vincent T. DeVita, Jr., Re: Kaposi's sarcoma and opportunistic infections, 30 July 1981, file "Kaposi's sarcoma, 1981-1982," Division of Cancer Treatment files, National Cancer Institute, Bethesda, Maryland. Hereafter cited as DCT files, NCI.
10. Memorandum, Bruce Chabner, Acting Director, DCT, NCI to Director, Centers for Disease Control, Through Director, NCI, and Acting Director, NIH, Re: Kaposi's sarcoma conference, 6 August 1981, file "Kaposi's sarcoma, 1981-1982," DCT files, NCI.
11. Memorandum, Bruce Chabner to Director, Centers for Disease Control, Re: Kaposi's conference, 6 August 1981, file "Kaposi's sarcoma, 1981-1982," DCT files, NCI.
12. Summary of the workshop on Kaposi's sarcoma, sponsored by the Division of Cancer Treatment and the Division of Cancer Cause and Prevention, National Cancer Institute, and the Centers for Disease Control,

held 15 September 1981 at the National Institutes of Health, file "Kaposi's Sarcoma 1981-1982," Intramural Research 5-15, Office of the Director Central Files, NIH. Hereafter cited as OD files, NIH.

13. Memorandum, William A. Blattner to Acting Director, Division of Cancer Treatment, NCI, 13 October 1981, file "Kaposi's sarcoma, 1981-1982," DCT files, NCI.
14. Administrative Confidential Memorandum, Arthur S. Levine, Special Assistant for Scientific Coordination, DCT, NCI, to Director, NCI, through Acting Director, NCI, Re: Update on the epidemic of acquired immunodeficiency—Kaposi [sic] sarcoma—opportunistic infection, 2 July 1982, file "Kaposi's sarcoma 1981-1982," Intramural Research 5-15, OD files, NIH.
15. Ibid.
16. Memorandum, James B. Wyngaarden, Director, NIH, to Bureau/Institute/Division (BID) Directors, 13 July 1982, Re: Working Group on epidemic of acquired immunosuppression, opportunistic infections, and Kaposi's sarcoma; summary minutes of NIH Kaposi Sarcoma Working Group (KSWG), 20 July 1982, both in file "Kaposi's sarcoma, 1981-1982," Intramural Research 5-15, OD files, NIH. This group became known colloquially as the "Gordon committee," after its chairman, Robert S. Gordon, Jr.
17. Special Assistant to the Director, NIH, to "The Record," 25 May 1984, Re: First meeting of the PHS AIDS Executive Task Force, in Robert S. Gordon, Jr., Notebook, "PHS Executive Task Force on AIDS, 1984," NIH Historical Office.
18. NIH *Almanac*, 1992, 121-35. Intramural laboratories are also located in Hamilton, Montana; Research Triangle Park, North Carolina; Baltimore, Maryland; and Frederick, Maryland.
19. NIH *Almanac*, 1992, 111. The NIH extramural program provides nearly half the total federal basic research funding of universities and colleges in the United States. See National Institutes of Health, *NIH Data Book, 1992: Basic Data Relating to the National Institutes of Health* (Bethesda, Maryland: National Institutes of Health, NIH Publication No. 92-1261, 1992), 6.
20. National Institutes of Health, Office of Program Planning & Evaluation and the Division of Research Grants, *Basic Data Relating to the National Institutes of Health, 1981* (Bethesda, Maryland: National Institutes of Health, NIH Publication No. 81-1261, 1981), i.
21. These included cancer, heart disease, stroke, sickle-cell anemia, Cooley's anemia, arthritis, diabetes, epilepsy, sudden infant death syndrome, and multiple sclerosis. All initiatives and associated appropriations are listed in "Congressional Initiatives in Biomedical and Behavioral Research," in Appendix D, 36-38, 40, of U.S. President's Biomedical Research Panel, *Report of the President's Biomedical Research Panel*, 30 April 1976, 4 appendixes, 4 suppl. (Washington, D.C.: Government Printing Office, DHEW Publication Nos. (OS) 76-500 through 76-509, 1976).
22. Debra Jan Bibel, ed., *Milestones in Immunology: A Historical Exploration* (Madison, Wisconsin: Science Tech Publishers, 1988); Arthur M. Silverstein, *A History of Immunology* (San Diego, California: Academic Press, 1989); Pauline M. H. Mazumdar, ed., *Immunology, 1930-1980: Essays on the History of Immunology* (Toronto, Canada: Wall & Thompson, 1989).
23. In the intramural programs, there was also some duplication of epidemiological research and questions about cooperation between particular laboratories in the NIAID and in the NCI. See David G. Ostrow to Ginny Apuzzo, 24 April 1984, in Robert S. Gordon, Jr., Notebook, "Executive Task Force on AIDS, 1984," NIH Historical Office.
24. Catherine Henley, "Peer review of research grant applications at the National Institutes of Health, 1: The assignment and referral processes," *Federation Proceedings* 36(1977): 2066-2068; Henley, "Peer review of research grant applications at the National Institutes of Health, 2: Review by an initial review group," ibid., 2186-2190; Henley, "Peer review of research grant applications at the National Institutes of Health, 3: Review by an Advisory Board/Council," ibid., 2335-2338. On political questions relating to the peer review system, see Don K. Price, "Endless frontier or bureaucratic morass?" *Daedalus* 107(Spring 1978): 75-92.
25. Major studies of the NIH peer review system are summarized in "Selected Studies, Investigations, and Recommendations Related to the National Institutes of Health: An Annotated Bibliography," in Appendix D, "Selected Staff Papers," of U.S. President's Biomedical Research Panel, *Report of the President's Biomedical Research Panel*, 30 April 1976; 4 appendices, 4 suppl. (Washington, D.C.: Government Printing Office, DHEW Publication Nos. (OS) 76-500 through 76-509, 1976), 1-32.
26. For one example of discussions about peer review in the 1970s, see United States Congress, House, Committee on Appropriations, *Departments of Labor and Health, Education, and Welfare Appropriations for 1978: Hearings before a Subcommittee of the Committee on Appropriations*, part 3,

"National Institutes of Health," (Washington, D.C.: Government Printing Office, 1977), 56-57.

27. The only report in which I have found concern about the speed of the process was a General Accounting Office (GAO) study of grants made by the National Cancer Institute, which complained about "significant delays" in the funding process. See U.S. General Accounting Office, Comptroller General of the United States, *Administration of Contracts and Grants for Cancer Research, National Institutes of Health, Department of Health, Education, and Welfare B-164031(2)* (Washington, D.C.: General Accounting Office, 1971), 2-3. The National Cancer Act of 1971 (and later the National Heart, Blood Vessel, Lung, and Blood Act of 1972) authorized the NCI and the National Heart and Lung Institute to award grants up to $35,000 without review by the institute advisory councils. These small grants, however, were not exempted, as the GAO report had recommended, from peer review by scientific panels.
28. Harden and Rodrigues, "Context for a new disease," 190. See also Dennis Altman, *AIDS in the Mind of America* (Garden City, New York: Anchor Press/Doubleday, 1986), 48. For examples of criticism, see Sandra Panem, *The AIDS Bureaucracy* (Cambridge, Massachusetts: Harvard University Press, 1988), 5, 91-94; Randy Shilts, *And the Band Played On: Politics, People, and the AIDS Epidemic* (New York: St. Martin's Press, 1987), 93-95, 119-120.
29. Chronology of NIH activities in response to AIDS, prepared by the NIH Division of Legislative Activities, February 1984, in file "Kaposi's sarcoma, February 1984," Intramural Research 5-15, OD files, NIH.
30. National Cancer Institute, "Request for Cooperative Agreement Applications: RFA NIH-NCI-DCT-CTRP-82-13. Studies of AIDS (Kaposi's Sarcoma and Opportunistic Infections)," *NIH Guide for Grants and Contracts*, vol. 11, no. 9 (13 August 1982), 3-7.
31. William D. DeWys to Michael A. Friedman, 18 November 1981, file "Kaposi's sarcoma, 1981-1982" DCT files, NCI.
32. Grant awards information attached to Memorandum, Rosalind Gran, Division of Legislative Analysis, to James B. Wyngaarden, 24 February 1984, Re: NIH AIDS Activities—Information, file "Kaposi's sarcoma, February 1984," Intramural Research 5-15, OD files, NIH. A list of awards for fiscal years 1983 and 1984 by NIH institutes is in *Review of the Public Health Service's Response to AIDS: A Technical Memorandum* (Washington, D.C.: U.S. Congress, Office of Technology Assessment, OTA-TM-H-24, February 1985), 109-131.
33. Victoria A. Harden and Dennis Rodrigues, interview with Richard G. Wyatt, 28 March 1990, National Institutes of Health, Bethesda, Maryland, copy in NIH Historical Office; Moyer Material, Public Health Service Supplementary Budget Data, Justification of Appropriation Estimates for Committee on Appropriations, Fiscal Year 1985, 15, hereafter cited as Moyer Material for specific fiscal years.
34. Data on which these figures were prepared are from the NIH Office of AIDS Research and published in *NIH Data Book, 1992*, 20.
35. See below the discussion of Anthony S. Fauci's clinical work with AIDS patients in the intramural program during fiscal year 1982.
36. Memorandum, James B. Wyngaarden to Director, NHLBI, Re: Evaluation of blood donor screening tests to reduce risk of transmission of acquired immunodeficiency syndrome (AIDS), 14 March 1983, OD files, NIH; copy in Notebook on AIDS prepared by Amoz I. Chernoff, former chief, Division of Blood Resources, NHLBI, copy available in NIH Historical Office. See also Victoria A. Harden and Dennis Rodrigues, interview with Amoz I. Chernoff, 28 January 1993, Potomac, Maryland, copy in NIH Historical Office.
37. Leo A. Whitehair and William I. Gay, "The seven NIH Primate Research Centers," *Lab Animal* 10(1981): 26-34.
38. Moyer Material, FY 1985, 11; FY 1986, 16-17, 19; FY 1987, 18-19; William I. Gay, Notebook on AIDS activities of the National Center for Research Resources, copy in NIH Historical Office; Victoria A. Harden, interview with William I. Gay, 15 July 1992, National Institutes of Health, Bethesda, Maryland, copy in NIH Historical Office; C. J. Gibbs, Jr., D. C. Gajdusek, L. G. Epstein, D. M. Asher, Jaap Goudsmit, "Animal models of human disease: induction of persistent human T lymphotropic retrovirus infections in nonhuman primates and equines inoculated with tissues from AIDS patients or purified virus grown in vitro," in L. A. Salzman, ed., *Animal Models of Retrovirus Infection and Their Relationship to AIDS* (Orlando, Florida: Academic Press, 1986), 457-462.
39. Work on etiology is discussed in greater detail below.
40. Moyer Material, FY 1989, 35, 38.
41. "*Pneumocystis* pneumonia—Los Angeles," *Morbidity and Mortality Weekly Report* 30(5 June 1981):

250-252. Date of admission of the first NIH AIDS patient is noted in "NIH Response to AIDS," chronology prepared by the NIH Division of Legislative Analysis, 6 February 1984, attached to Note, Bel [Ceja] to Dr. Wyngaarden, Re: Response to Weiss ltr *(sic)* addressed to Dr. Brandt, 24 February 1984, file "Kaposi's sarcoma, February 1984," Intramural Research 5-15, OD files, NIH.

42. Victoria A. Harden and Dennis Rodrigues, interview with Thomas Waldmann, 14 March 1990, National Institutes of Health, Bethesda, Maryland, copy in the NIH Historical Office. Dr. Waldmann pointed out that, unfortunately, the medical record on the first AIDS patient disappeared after the patient's death, thus making it impossible to confirm certain specifics of his treatment. Comments on the multiple infections suffered by this patient as defined at autopsy are in Harden and Rodrigues, interview with Abe Macher, 29 April 1993, Rockville, Maryland, copy in the NIH Historical Office.
43. Victoria A. Harden and Dennis Rodrigues, interview with Anthony S. Fauci, 29 June 1993, National Institutes of Health, Bethesda, Maryland, copy in the NIH Historical Office. The date of admission is in Richard M. Krause to Edward N. Brandt, Jr., 15 January 1982, file "Kaposi's Sarcoma 1981-1982," Intramural Research 5-15, OD files, NIH.
44. The study also demonstrated the adoptive transfer of delayed-type hypersensitivity and an increase in the total number of peripheral blood helper T lymphocytes in the AIDS patient. See Fauci interview (n. 43); Victoria A. Harden and Dennis Rodrigues, interview with H. Clifford Lane, 12 March 1990, National Institutes of Health, Bethesda, Maryland, copy in the NIH Historical Office; Moyer Material, FY 1986, 18-19; A. H. Rook, Henry Masur, H. C. Lane, Winston Frederick, Tadashi Kasahara, A. M. Macher, J. Y. Djeu, J. F. Manischewitz, Lozannie Jackson, A. S. Fauci, and G. V. Quinnan, Jr., "Interleukin-2 enhances the depressed natural killer and cytomegalovirus-specific cytotoxic activities of lymphocytes from patients with the Acquired Immune Deficiency Syndrome," *Journal of Clinical Investigation* 72(1983): 398-403; H. C. Lane, Henry Masur, Alan Rook, L. C. Edgar, Gail Whalen, and A. S. Fauci, "Abnormalities of B cell activation and immunoregulation in patients with the Acquired Immunodeficiency Syndrome," *New England Journal of Medicine* 309(1983): 453-458.
45. A. S. Fauci and H. C. Lane, "Therapy of the Acquired Immunodeficiency Syndrome," in T. M. Baylers, M. C. Brain, and R. M. Cherniack, eds., *Current Therapy in Internal Medicine* (Philadelphia, Pennsylvania: B. C. Decker, 1983), 129-136. For an overview of current AIDS therapy, see A. S. Fauci, "Multifactorial nature of Human Immunodeficiency Virus disease: implications for therapy," *Science* 262(1993): 1011-1018.
46. The clinical collaborations are described in Lane interview (n. 44) and in Victoria A. Harden and Dennis Rodrigues, interview with Henry Masur, 22 November 1989, National Institutes of Health, Bethesda, Maryland, copy in the NIH Historical Office.
47. Victoria A. Harden and Dennis Rodrigues, interview with Robert B. Nussenblatt, 25 April 1990, National Institutes of Health, Bethesda, Maryland, copy in the NIH Historical Office; Moyer Material, FY 1986, 19, 22; FY 1987, 21-22; FY 1988, 9. See also the more general discussion of NEI contributions in Moyer Material, FY 1985, 17.
48. Nussenblatt interview; Moyer Material, FY 1990, 66; M. R. Rodrigues, Alan Palestine, R. B. Nussenblatt, Henry Masur, and Abe Macher, "Unilateral cytomegalovirus retinochorioditis and bilateral cystoid bodies in a bisexual male with the Acquired Immunodeficiency Syndrome," *Ophthalmology* 90(1983): 1577-1582; A. G. Palestine, Garth Stevens, Jr., H. C. Lane, Henry Masur, L. S. Fujikawa, R. B. Nussenblatt, A. H. Rook, and A. S. Mainschewitz, Barbara Baird, Margaret Megill, Gerald Quinnan, Edward Gelmann, A. S. Fauci, "Treatment of cytomegalovirus retinitis with dihydroxy propoxymethyl guanine," *American Journal of Ophthalmology* 101(1986): 95-101; Henry Masur, H. C. Lane, Alan Palestine, P. D. Smith, Jody Manischewitz, Garth Stevens, Jr., Leslie Fumikawa, A. M. Macher, Robert Nussenblatt, Barbara Baird, Margaret Megill, Alec Wittek, G. V. Quinnan, J. E. Parrillo, A. H. Rook, L. J. Eron, D. M. Poretz, R. I. Goldenberg, A. S. Fauci, and E. P. Gelmann, "Effect of 9-(1,3-dihydroxy-2-propoxymethyl) guanine on serious cytomegalovirus disease in eight immunosuppressed homosexual men," *Annals of Internal Medicine* 104(1986): 41-44; M. A. Polis, M. D. deSmet, B. F. Baird, Susan Mellow, Judith Falloon, R. T. Davey, Jr., J. A. Kovacs, A. G. Palestine, R. B. Nussenblatt, Henry Masur, H. C. Lane, "Increased survival of a cohort of patients with Acquired Immunodeficiency Syndrome and cytomegalovirus retinitis who received sodium phosphonoformate (Foscarnet)," *American Journal of Medicine* 94(1993): 175-180.
49. Moyer Material, FY 1985, 11; FY 1986, 16; G. M. Shaw, M. E. Harper, B. H. Hahn, L. G. Epstein, D. C. Gajdusek, R. W. Price, B. A. Navia, C. K. Petito, C. J. O'Hara, J. E. Groopman, E-S. Cho, J. M.

Oleske, Flossie Wong-Staal, R. C. Gallo, "HTLV-III infection in brains of children and adults with AIDS encephalopathy," *Science* 227(1985): 177-182.

50. NIDR investigators also studied the gastrointestinal manifestations of cytomegalovirus infection. See Moyer Material, FY 1985, 10; FY 1986, 14; FY 1987, 17.
51. Moyer Material, FY 1985, 10; FY 1986, 14; FY 1987, 17; P. D. Smith, Kiyoshi Ohura, Henry Masur, H. C. Lane, A. S. Fauci, S. M. Wahl, "Monocyte function in the Acquired Immune Deficiency Syndrome: defective chemotaxis," *Journal of Clinical Investigation* 74(1984): 2121-2128.
52. Victoria A. Harden and Dennis Rodrigues, interview with James J. Goedert, 10 March 1993; interview with William A. Blattner, 2 March 1990; interview with Robert Biggar, 6 November 1989, National Institutes of Health, Bethesda, Maryland, copies of all in NIH Historical Office. For a review of epidemiological studies, see J. J. Goedert and W. A. Blattner, "The epidemiology and natural history of Human Immunodeficiency Virus," in V. T. DeVita, Jr., S. Hellman, and A. A. Rosenberg, eds., *AIDS: Etiology, Diagnosis, Treatment, and Prevention*, 2nd ed. (Philadelphia, Pennsylvania: J. B. Lippincott, 1988), 33-60.
53. Moyer Material, FY 1985, 10; FY 1986, 15; Minutes of the Medical Board of the NIH Clinical Center, 6 July 1982, 4, manuscript collection, National Library of Medicine.
54. Moyer Material, FY 1985, 16. NLM's AIDS bibliography was initiated in June 1982. By May 1983, 179 citations to AIDS published between January 1980 and April 1983 had been compiled. See NIH Historical Office AIDS Chronology File; National Library of Medicine, "Acquired Immunodeficiency Syndrome (AIDS)," January 1980 through April 1982, 179 citations, including addendum, prepared by Charlotte Kenton, *Literature Search*, no. 83-1. Copies of the *AIDS Memorandum* are in the manuscript collection, National Library of Medicine.
55. Moyer Material, FY 1990, 79; Associate Director for Extramural Affairs to Director, NIH, 20 November 1986, Re: NIH AIDS Targeted Antivirals Plan, Notebook, "AIDS Planning Session with the Director, NIH, February 1987," copy in NIH Historical Office.
56. Moyer Material, FY 1990, 55, 71.
57. There are many accounts, from various points of view, of the discovery of the AIDS virus. Some of the major ones include Robert C. Gallo and Luc Montagnier, "The chronology of AIDS research," *Nature* 326(1987): 435-436; idem, "AIDS in 1988," *Scientific American* 259(October 1988): 41-48; R. C. Gallo, *Virus Hunting: AIDS, Cancer, and the Human Retrovirus: A Story of Scientific Discovery* (New York: Basic Books, 1991), 127-204; John Crewdson, "The Great AIDS Quest," Special Report, *Chicago Tribune*, 19 November 1989, section 5. A recent perspective on the scientific community and controversy surrounding Gallo is in Freeman J. Dyson, "Science in trouble," *American Scholar* 62(1993): 513-525.
58. Gallo, *Virus Hunting*. In this book, Gallo did not provide a date for the seminar presented by Curran that inspired his research on the etiology of AIDS. In a private communication to the author, however, Curran stated that it was his presentation of AIDS epidemiological data to the National Cancer Advisory Board (NCAB) on 1 December 1982. Gallo, who had just won the Lasker award for his discovery of the first human retrovirus, was scheduled on the NCAB agenda to describe his award-winning work, but this presentation was preempted by Curran's talk on AIDS. Curran stated that as he talked with Gallo before the meeting, he encouraged Gallo to look for a viral agent that destroyed T cells. See "Presentations at the NCAB meeting 1 December 1982," file "Kaposi's sarcoma, 1981-1982," DCT files, NCI.
59. In May 1986, a multinational committee suggested in nearly simultaneous letters to *Science* and *Nature*, two international scientific journals of record, that the name Human Immunodeficiency Virus was a more descriptive and less cumbersome designation for the AIDS virus that either Gallo's or Montagnier's first designations. See John Coffin, Ashley Haase, J. A. Levy, Luc Montagnier, Steven Oroszlan, Natalie Teich, Howard Temin, Kumao Toyoshima, Harold Varmus, Peter Vogt, and Robin Weiss, "Human Immunodeficiency Viruses," *Science* 232(1986): 697; idem, "What to call the AIDS virus?" *Nature* 321(1986): 10.
60. Moyer Material, FY 1986, 5-6, 25; S. H. Weiss, J. J. Goedert, M. G. Sarngadharan, A. J. Bodner, R. C. Gallo, and W. A. Blattner, "Screening test for HTLV-III (AIDS agent) antibodies: specificity, sensitivity, and applications," *Journal of the American Medical Association* 253(1985): 221-225.
61. Moyer Material, FY 1989, 23; FY 1990, 12. The structural genes are called *gag*, *pol*, and *env*. The five accessory genes are *tat*, *art/trs*, *3'orf*, *R*, and *U*. Flossie Wong-Staal of the NCI discovered the virus's "R", or *vpr*, gene, and Malcolm Martin of the NIAID identified the the "U" or *vpu* gene. See William A. Haseltine and Flossie Wong-Staal, "The molecular biology of the AIDS virus," *Scientific American*

259(October 1988): 52-62; M. E. Klotman and Flossie Wong-Staal, "Human Immunodeficiency Virus (HIV): gene structure and genetic diversity," in R. C. Gallo and G. Jay, eds., *The Human Retroviruses* (San Diego, California: Academic Press, 1991), 35-67.

62. Moyer Material, FY 1987, 8-9, 22; Ing-Ming Chiu, A. Yaniv, J. E. Dahlberg, A. Gazit, S. F. Skuntz, S. R. Tronick, and S. A. Aaronson, "Nucleotide sequence evidence for relationship of AIDS retrovirus to lentiviruses," *Nature* 317(1985): 366-8.
63. Moyer Material, FY 1988, 10.
64. Moyer Material, FY 1986, 10; Hiroaki Mitsuya, Makoto Matsukura, and Samuel Broder, "Rapid in vitro systems for assessing activity of agents against HTLV-III/LAV," in Samuel Broder, ed., *AIDS: Modern Concepts and Therapeutic Challenges* (New York: Marcel Dekker, 1987), 303-333.
65. Peter S. Arno and Karynh L. Feiden, *Against the Odds: The Story of AIDS Drug Development, Politics, and Profits* (New York: HarperCollins, 1992).
66. "Clinical trials for AIDS therapies," National Institute of Allergy and Infectious Diseases *Backgrounder*, June 1993.
67. Gina Kolata, "Rethinking the statistics of 'epidemic' breast cancer," *New York Times*, 28 February 1993, E4.
68. David Brown, "Bill seeks to coordinate NIH research on AIDS: skeptics fear proposal could slow progress," *Washington Post*, 22 February 1993, A4.
69. Barbara R. Jasny, "AIDS 1993: unanswered questions," *Science* 260(1993): 1219.
70. Figures were supplied by the budget office of the National Institute of Allergy and Infectious Diseases.
71. Charles E. Rosenberg, "Disease and social order in America: perceptions and expectations," *Milbank Quarterly* 64, supplement 1(1986): 34-55; reprinted in idem, *Explaining Epidemics and Other Studies in the History of Medicine* (Cambridge and New York: Cambridge University Press, 1992), quotation from p. 275.