Regional Oral History Office
The Bancroft Library

University of California
Berkeley, California

The San Francisco AIDS Oral History Series

THE AIDS EPIDEMIC IN SAN FRANCISCO: THE MEDICAL RESPONSE, 1981-1984

Volume III

Arthur J. Ammann, M.D.	PEDIATRIC AIDS IMMUNOLOGIST: ADVOCATE FOR THE CHILDREN
Paul A. Volberding, M.D.	ONCOLOGIST AND DEVELOPER OF THE AIDS CLINIC, SAN FRANCISCO GENERAL HOSPITAL
Constance B. Wofsy, M.D.	INFECTIOUS DISEASE PHYSICIAN, AIDS EDUCATOR, AND WOMEN'S AIDS ADVOCATE

Introduction by James Chin, M.D., M.P.H.

Interviews Conducted by
Sally Smith Hughes, Ph.D.
in 1992, 1993, 1994, 1995

Since 1954 the Regional Oral History Office has been interviewing leading participants in or well-placed witnesses to major events in the development of Northern California, the West, and the Nation. Oral history is a method of collecting historical information through tape-recorded interviews between a narrator with firsthand knowledge of historically significant events and a well-informed interviewer, with the goal of preserving substantive additions to the historical record. The tape recording is transcribed, lightly edited for continuity and clarity, and reviewed by the interviewee. The corrected manuscript is indexed, bound with photographs and illustrative materials, and placed in The Bancroft Library at the University of California, Berkeley, and in other research collections for scholarly use. Because it is primary material, oral history is not intended to present the final, verified, or complete narrative of events. It is a spoken account, offered by the interviewee in response to questioning, and as such it is reflective, partisan, deeply involved, and irreplaceable.

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Arthur J. Ammann (b. 1936), pediatric immunologist: education and early career; early research in pediatric immunology and hypogammaglobulinemia; observing puzzling cases of immune deficiency in three infant sisters, searching for a cause, and recognizing AIDS; defining AIDS; issues of pediatric AIDS: struggling for recognition of the disease, treatment, surveillance, drug approval; immunologic studies of AIDS patients, including an infant at UCSF [University of California, San Francisco] in fall, 1982; transfusion AIDS; the search for an AIDS vaccine; service on AIDS committees; the Pediatric AIDS Foundation.
Paul A. Volberding (b. 1949), AIDS oncologist: education and early career; attraction to oncology; Kaposi's Sarcoma at SFGH [San Francisco General Hospital]; establishing SFGH's AIDS Clinic; working with the San Francisco community; the bathhouse controversy, 1983-1984; continued discussion of the AIDS Clinic, SFGH; the AIDS inpatient ward at SFGH; San Francisco community physicians; oncology and AIDS.
Constance B. Wofsy (1942-1996), infectious disease physician: education and early career; joining Paul Volberding and the AIDS Clinic at SFGH; Kaposi's Sarcoma Clinic and Study Group, UCSF; the Division of AIDS Activities, SFGH; infection control guidelines; makeup of the AIDS Clinic, SFGH; clinical trials; the AIDS inpatient ward at SFGH; AIDS Provider Education and Experience [APEX]; *Pneumocystis carinii* pneumonia research; the bathhouse controversy, 1983-1984; women with AIDS; the San Francisco model of comprehensive AIDS care.

Introduction by James Chin, M.D., M.P.H., Clinical Professor of Epidemiology, School of Public Health, University of California, Berkeley.

Interviewed 1992, 1993, 1994 by Sally Smith Hughes, Ph.D., for the San Francisco AIDS Oral History Series. Regional Oral History Office, The Bancroft Library, University of California, Berkeley.

ACKNOWLEDGEMENTS

The Regional Oral History Office wishes to express deep gratitude to Evelyne and David Lennette of Virolab, Inc., for their financial support of this project, incisive conceptual contributions, and sustaining interest and enthusiasm.

This volume is dedicated to the
memory of Constance Wofsy (1942-1996).

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PREFACE--by David A. Lennette, Ph.D., and Evelyne T. Lennette, Ph.D.

As two young medical virologists working in Pennsylvania, we experienced first hand some of the excitement of medical detective work. We had our first glimpse of how personalities can shape the course and outcome of events during the swine influenza and Legionnaires' disease outbreaks.

On our return to California, we were soon embroiled in another much more frightening epidemic. In 1981, our laboratory began receiving samples for virologic testing from many of the early San Francisco AIDS patients--whose names are now recorded in Randy Shilts' book *And the Band Played On*. Our previous experience with the legionellosis outbreak had primed us for this new mystery disease. While the medical and scientific communities were hotly debating and coping with various issues during the following three years, we were already subconsciously framing the developments in an historical point of view. In San Francisco, dedicated junior physicians and researchers banded together to pool resources and knowledge out of necessity, and in doing so, organized part of the local medical community in a very unusual way. Once again, we were struck by how the personalities of each of these individuals shaped the course of events. Even before HIV was discovered, we knew we were witnessing a new page in the history of science and medicine.

The swine flu and legionellosis outbreaks were both very local and short lived. We now speak of them in the past tense. The AIDS epidemic, sadly, is still spreading unimpeded in much of the world. We know that it will be with us for a long time and that it is very unlikely that either of us will live long enough to read the closing chapter on AIDS.

Future generations will some day want to know how it all got started. The existing scientific reports and publications provide depersonalized records of some of the events, while newspaper articles and books give glimpses as summarized by observers. What are missing are the participants' own accounts and perspectives.

It is now more than a dozen years after the recognition of the AIDS epidemic in the United States. So much has happened and changed--already, some of the participants in early events have retired, records are being discarded and destroyed, and memories of those days are beginning to fade. We felt their oral histories had to be recorded without delay.

We had previously sponsored oral histories on virology with Dr. Edwin H. Lennette, David's father, and Dr. Harald N. Johnson, and were familiar with the methods and work of the Regional Oral History Office. We met to talk over the recording of the AIDS epidemic with Willa Baum, head of the office, and Dr. Sally Smith Hughes, medical history interviewer. After

some discussion, we agreed that the events from 1981-1984 needed to be documented and we would fund it. This was a time when many crucial decisions on the clinical, public health, social, and political issues pertaining to AIDS were made with little scientific information and no precedents to rely on. The consequences of many of these decisions are still being felt today. With the discovery of HIV, however, the framework for decision making shifted to different ground, and a pioneering phase was over. Once we decided on the scope of the project, it was a simple task to identify prospective interviewees, for we worked with many of these individuals during those years.

Dr. Sally Hughes has shared our enthusiasm from the beginning. We are pleased that her efforts are now coming to fruition.

David A. Lennette, Ph.D.
Evelyne T. Lennette, Ph.D.

November 1994
Virolab, Inc.
Berkeley, California

SERIES INTRODUCTION--by James Chin, M.D., M.P.H.

As the California state epidemiologist responsible for communicable disease control from the early 1970s to the late 1980s, I had the privilege and opportunity to work with all of the participants who were interviewed for the San Francisco AIDS Oral History Project. I consider it an honor to have been asked to provide a brief introduction to the role that these individuals played in the history of AIDS in San Francisco during the early years. Before I begin, the following quote from Dr. James Curran, in a December 1984 issue of the *San Francisco Chronicle* sums up what has happened to all of the participants in this oral history project:

> I'd like to sound more upbeat about this, but there are some unavoidable facts we need to face. AIDS is not going away. Gay men don't want to hear that. Politicians don't want to hear that. I don't like to hear that. But for many of us, AIDS could well end up being a lifelong commitment.

The first recognized cases of AIDS were reported in the *Morbidity and Mortality Weekly Report (MMWR)* on June 5, 1981. I recall this report vividly. A few months earlier, the Centers for Disease Control (CDC) had begun sending an advance copy of the *MMWR* text to state health departments. The advance text of the June 5 *MMWR* had a lead article on the sudden and unexplained finding of five apparently unrelated cases of *Pneumocystis carinii* pneumonia in five young gay men from Los Angeles. The *MMWR* text was received in my office just before our weekly Tuesday afternoon staff meeting was to start. I handed the text to Tom Ault, who was responsible for the state's venereal disease field unit and asked him to have some of our federal- or state-assigned staff in Los Angeles assist in the investigation of these cases. I remember saying to him that it may not turn out to be much of anything, but it may be the start of something. I never imagined that that something would eventually develop into a worldwide epidemic of disease and death.

In the ensuing weeks and months, it became apparent that the mysterious illness reported from Los Angeles was also present among gay men in San Francisco. From 1981 to 1984, the numbers of AIDS cases reported from San Francisco rose almost exponentially--from a handful in mid-1981 to well over 800 towards the end of 1984. The impact that AIDS has had in San Francisco is unequaled on a per capita basis anywhere in the developed world. If the AIDS prevalence rate of about one AIDS case per 1,000 population that was present in San Francisco at the end of 1984 was applied nationally, then there would have been about a quarter of a million AIDS cases nationwide instead of the 7,000 that were actually reported. During the first few years of what was initially referred to as GRID (gay-related immune deficiency), there was general denial of the severity of this newly

recognized mystery disease even in San Francisco. The enormity of the AIDS problem was first fully accepted by the gay community in San Francisco, and physicians and researchers in the city rapidly became the leading experts in the country on the medical management, prevention, and control of AIDS. In contrast to Los Angeles and New York, which also have had large concentrations of AIDS cases, the gay community in San Francisco has been more unified and organized in developing political and community support for the treatment and care of AIDS patients.

The epidemiology of AIDS, namely, that it is caused primarily by a sexually transmitted agent, was fairly well established by 1983, well before HIV was eventually isolated and etiologically linked to AIDS in 1984. Public health investigations in San Francisco, spearheaded by Selma Dritz in 1981 and 1982, provided much of the key epidemiologic data needed to understand the transmission and natural history of HIV infection. The more formal epidemiological studies of AIDS among gay men in San Francisco were carried out by Andrew Moss at San Francisco General Hospital (SFGH) and Warren Winkelstein at the University of California at Berkeley. All of these studies were helpful to Mervyn Silverman (who during this period was director of the San Francisco Department of Public Health) to support his decision in October 1984 to close the San Francisco bathhouses. Selma Dritz retired from her position with the health department in 1984, and Mervyn Silverman has moved on to become the premier HIV/AIDS frequent flier in his current position as president of the American Foundation for AIDS Research, which is now supporting studies internationally.

Jay Levy was an established virologist when AIDS was first detected and reported in 1981. His laboratory isolated and characterized a virus which he initially called ARV--AIDS Related Virus. He continues to play a prominent role in the quest to better understand the pathogenesis of HIV. Herbert Perkins was the scientific director of the Irwin Memorial Blood Bank in San Francisco during the critical period around 1982-1985 when data began accumulating to indicate that the cause of AIDS might be an infectious agent which could be transmitted via blood. Under his direction, the Irwin Memorial Blood Bank in May 1984 was the first blood bank in the country to begin routine surrogate testing of blood units for the AIDS agent using a hepatitis B core antibody test. He retired as director of Irwin Memorial in April 1993, but remains very much involved in defending the blood bank from legal suits arising from transmission of HIV via blood transfusions during the early years. Don Francis did not work in California during the early 1980s, but directed epidemiologic and laboratory studies on AIDS as the first head of the AIDS laboratory at CDC in Atlanta during this time period. Following his request to become more directly involved with field work and HIV/AIDS program and policy development, he was assigned to work in my office in Berkeley in 1985. Don took an early retirement from CDC in 1992 and continues to actively work in the San Francisco Bay Area as well as nationally and internationally on the development of an AIDS vaccine.

The clinical staffs of San Francisco General Hospital and the University of California at San Francisco established the two earliest AIDS clinics in the country, and in 1983, Ward 5B at SFGH was set up exclusively for AIDS patients. In the early 1980s, Don Abrams and Paul Volberding were two young physicians who found themselves suddenly thrust into full-time care of AIDS patients, a responsibility which both are still fully involved with. As a result of their positions, experience, and dedication, both are acknowledged national and international experts on the drug treatment of HIV and AIDS patients. Merle Sande, John Ziegler, Arthur Ammann, and Marcus Conant were already well established and respected clinicians, researchers, and teachers when AIDS was first detected in San Francisco. Their subsequent work with HIV/AIDS patients and research has earned them international recognition. The Greenspans, Deborah and John, have established themselves as the foremost experts on the oral manifestations of HIV/AIDS, and Constance Wofsy is one of the leading experts on women with HIV/AIDS. There is rarely a national or international meeting or conference on AIDS where most, if not all, of these San Francisco clinical AIDS experts are not present and speaking on the program. The number of HIV/AIDS clinicians and research scientists from San Francisco invited to participate in these medical and scientific meetings usually far exceeds those from any other city in the world. All of these individuals have made tremendous contributions to the medical and dental management of HIV/AIDS patients in San Francisco and throughout the world.

As of late 1994, more than a decade since the advent of AIDS in San Francisco, Jim Curran's remark in 1984 that "...for many of us, AIDS could well end up being a lifelong commitment" has been remarkably accurate for virtually all the participants in this San Francisco AIDS Oral History Project.

James Chin, M.D., M.P.H.
Clinical Professor of Epidemiology
School of Public Health,
University of California at Berkeley

September 1994
Berkeley, California

SERIES HISTORY--by Sally Smith Hughes, Ph.D.

Historical Framework

In 1991, Evelyne and David Lennette, virologists and supporters of previous Regional Oral History Office (ROHO) projects in virology and horticulture, conceived the idea for an oral history series on AIDS. They then met with Willa Baum (ROHO director) and me to discuss their idea of focusing the series on the medical and scientific response in the early years (1981-1984) of the AIDS epidemic in San Francisco, believing that the city at this time played a particularly formative role in terms of AIDS medicine, organization, and policy. Indeed San Francisco was, with New York and Los Angeles, one of the three focal points of the epidemic in the United States, now sadly expanded worldwide.

The time frame of the oral history project is historically significant. Nineteen eighty-one was the year the epidemic--not until the summer of 1982 to be officially christened "AIDS"--was first recognized and reported. A retrovirus was isolated in 1983, and by early 1985, diagnostic tests were being marketed. These achievements signaled a turning point in the response to the epidemic. Its science shifted from a largely epidemiological approach to one with greater emphasis on the laboratory. As soon as the virus was determined, scientific teams in the United States and Europe raced to characterize it in molecular terms. Information about the molecular biology of the human immunodeficiency virus (HIV), as it was named, was in turn expected to transform AIDS medicine by providing a basis for treatment and prevention of the disease through new drugs and vaccines.

San Francisco continued to make important contributions to combating the epidemic, but by early 1985 it had lost its pioneering role. The AIDS test showed that the epidemic reached far beyond the three original geographic centers and involved large numbers of symptomless HIV-positive individuals, who were not identifiable prior to the test's advent. AIDS funding increased; the number and location of AIDS researchers expanded; research interest in the newly identified virus took center stage. San Francisco's salient position in the AIDS effort faced competition from new players, new research interests, and new institutions. The first phase of the epidemic was history.

Project Structure

Within the limits of funding and the years of the project (1981-1984), the Lennettes suggested eight potential interviewees whom they knew to have played important medical and scientific roles in the early years of the San Francisco epidemic. (Both Lennettes have close connections with the local AIDS research community, and Evelyne Lennette was a scientific collaborator of three interviewees in this series, Jay Levy and John and

Deborah Greenspan.) I then consulted Paul Volberding, an oncologist at San Francisco General Hospital with an international reputation as an AIDS clinician. He and others in the oral history series made several suggestions regarding additional interviewees, expanding my initial list to fourteen individuals.[1] My reading of primary and secondary sources and consultation with other authorities confirmed the historical merit of these choices.

The series consists of two- to ten-hour interviews with seventeen individuals in epidemiology, virology, public health, dentistry, and several medical specialties. By restricting phase one to San Francisco's early medical and scientific response to the epidemic, we aim to provide in-depth documentation of a major aspect, namely the medicine and science it generated in a given location, at a given time, under near-crisis conditions. Like any human endeavor, medicine and science are embedded in the currents of the time. As these oral histories so graphically illustrate, it is impossible to talk about science and medicine without relating them to the social, political, and institutional context in which they occur. One of the strengths of oral history methodology is precisely this.

This concentration on physicians and scientists is of course elitist and exclusive. There is a limit--practical and financial--to what the first phase of a project can hope to accomplish. It was clear that the series needed to be extended. Interviews for phases two and three of the oral history project, a series with AIDS nurses and a third with community physicians with AIDS practices, have been completed and serve to broaden the focus. The long-range plan is to interview representatives of all sectors of the San Francisco community which contributed to the medical and scientific response to AIDS, thereby providing balanced coverage of the city's biomedical response.

Primary and Secondary Sources

This oral history project both supports and is supported by the written documentary record. Primary and secondary source materials provide necessary information for conducting the interviews and also serve as essential resources for researchers using the oral histories. They also orient scholars unfamiliar with the San Francisco epidemic to key participants and local issues. Such guidance is particularly useful to a

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[1] A fifteenth was added in 1994, when the UCSF AIDS Clinical Research Center provided partial funding for interviews with Warren Winkelstein, M.D., M.P.H., the epidemiologist directing the San Francisco Men's Health Study. A sixteenth and seventeenth, with Lloyd "Holly" Smith, M.D., and Rudi Schmid, M.D., were recorded in 1995 when the UCSF Academic Senate allocated funds for transcription.

researcher faced with voluminous, scattered, and unorganized primary sources, characteristics which apply to much of the AIDS material. This two-way "dialogue" between the documents and the oral histories is essential for valid historical interpretation.

Throughout the course of this project, I have conducted extensive documentary research in both primary and secondary materials. I gratefully acknowledge the generosity of Drs. Arthur Ammann, Marcus Conant, John Greenspan, Herbert Perkins, Warren Winkelstein, and John Ziegler in opening to me their personal documents on the epidemic. Dr. Frances Taylor, director of the Bureau of Infectious Disease Control at the San Francisco Department of Public Health, let me examine documents in her office related to closure of city bathhouses in 1984. Sally Osaki, executive assistant to the director of the health department, gave me access to documents from former Mayor Dianne Feinstein's papers on her AIDS activities. I am grateful to both of them.

Dr. Victoria Harden and Dennis Rodrigues of the NIH Historical Office assisted by sending correspondence and transcripts of a short telephone interview with John Ziegler, which Rodrigues conducted.[1] I thank Dr. James Chin for his introduction to this series, which describes his first-hand experience of the epidemic as state epidemiologist at the California Department of Health Services where he was responsible for communicable disease control. I also thank Robin Chandler, head of Special Collections, UCSF Library, and Bill Walker, former archivist of UCSF's AIDS History Project and the San Francisco Gay and Lesbian Historical Society, for their assistance in accessing these rich archival collections.

The foregoing sources have been crucial in grounding the interviews in specifics and in opening new lines of questioning. A source to be noted, but untapped by this project, is the California AIDS Public Policy Archives, which is being coordinated by Michael Gorman, Ph.D., at San Francisco General Hospital.

Of the wealth of secondary historical sources on AIDS, the most pertinent to this project is Randy Shilts' *And the Band Played On*.[2] Although criticized for its political slant, it has been invaluable in providing the social, political, and ideological context of early AIDS efforts in San Francisco, particularly in regard to San Francisco's gay community.

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[1] Telephone interview by Dennis Rodrigues with John L. Ziegler, M.D., January 5, 1990. Tapes and transcripts of the interview are available in the NIH Historical Office, Bethesda, MD.

[2] Randy Shilts. *And the Band Played On: Politics, People, and the AIDS Epidemic*. New York: Penguin Books, 1988.

Oral History Process

The oral history methodology used in this project is that of the Regional Oral History Office, founded in 1954 and producer of over 1,400 archival oral histories. The method consists of background research in primary and secondary sources; systematic recorded interviews; transcription, editing by the interviewer, and review and approval by the interviewee; deposition in manuscript libraries of bound volumes of transcripts with table of contents, introduction, interview history, and index; cataloging in national on-line library networks (MELVYL, RLIN, and OCLC); and publicity through ROHO news releases and announcements in scientific, medical, and historical journals and newsletters and via the UCSF Library web page (http://www.library.ucsf.edu/).

Oral history as an historical technique has been faulted for its reliance on the vagaries of memory, its distance from the events discussed, and its subjectivity. All three criticisms are valid; hence the necessity for using oral history documents in conjunction with other sources in order to reach a reasonable historical interpretation.[1] Yet these acknowledged weaknesses of oral history, particularly its subjectivity, are also its strength. Often individual perspectives provide information unobtainable through more traditional sources. For example, oral history in skillful hands provides the context in which events occur--the social, political, economic, and institutional forces which shape the evolution of events. It also places a personal face on history which not only enlivens past events but also helps to explain how individuals affect historical developments.

The foregoing criticisms could be directed at the AIDS oral history series. Yet this series has several mitigating characteristics. First, it is on a given topic in a limited time frame with interviewees focused on a particular response, namely the medical and scientific. Thus although each interviewee presents a distinctive view of the epidemic, multiple perspectives on the same events provide an opportunity for cross-checking and verification, as well as rich informational content. Furthermore, most of the interviewees continue to be actively engaged in AIDS work. Hence, the memory lapses resulting from chronological and psychological distancing from events discussed are less likely to occur than when the interviewee is no longer involved.

An advantage of a series of oral histories on the same topic is that the information each contains is cumulative and interactive. Through individual accounts, a series can present the complexities and interconnections of the larger picture--in this case, the medical and scientific aspects of AIDS in San Francisco. Thus the whole (the series) is greater than the sum of its parts (the individual oral histories), and

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[1] The three criticisms leveled at oral history also apply in some cases to other types of documentary sources.

should be considered as a totality. To encourage this approach, we decided to bind several oral histories together in each volume.

Another feature of an oral history series is that later interviews tend to contain more detailed information because as the series unfolds the interviewer gains knowledge and insight from her informants and from continued research in primary and secondary sources. This was indeed the case in the AIDS series in which the later interviews benefited from my research in private document collections made available to me as the project progressed and by the knowledge I gained from the interviews and others connected with the AIDS scene.

A feature of this particular series is its immediacy, a characteristic less evident in oral histories conducted with those distanced from the topic of discussion. These are interviews with busy people who interrupted their tight schedules to look back, sometimes for the first time, at their experiences of a decade or so ago. Because many have not had the luxury of time to contemplate the full meaning of their pasts, the oral histories could be criticized for lacking "historical perspective." But one could also argue that documents intended as primary historical sources have more scholarly value if the information they contain is not filtered by the passage of years and evolving personal opinions.

The oral histories also have a quality of history-in-progress. With few exceptions, the interviewees are still professionally engaged in and preoccupied by an epidemic which unhappily shows no sign of ending. The narrators are living the continuation of the story they tell. Neither they nor we can say for sure how it will end.

Other Oral History Projects Related to AIDS

Oral history projects on other aspects of the San Francisco epidemic are essential for full historical documentation and also mutually enrich one another. Unfortunately, not enough is currently being done in this regard. Two local projects are Legacy, directed by Jeff Friedman, which focuses on the Bay Area dance community tragically decimated by AIDS, and Clarissa Montanaro's AIDS Oral History Project, which interviews people with AIDS. An installation, "Project Face to Face", directed by Jason Dilley and using excerpts from interviews with people with AIDS, was exhibited around the San Francisco Bay Area and in 1991 was part of the inaugural exhibit at the Smithsonian's Experimental Gallery.

AIDS oral history projects outside San Francisco include documentation by Victoria Harden, Ph.D., Caroline Hannaway, Ph.D., and Dennis Rodrigues of the NIH Historical Office of the contribution made by NIH scientists, physicians, and policymakers to the AIDS effort. Gerald Oppenheimer and Ronald Bayer at Columbia, with support from the National

Library of Medicine and the Royal Marx Foundation, are conducting interviews with AIDS physicians in several cities across the United States. The New Jersey AIDS Oral History Project, sponsored by the University of Medicine and Dentistry of New Jersey, interviews faculty and staff involved in the epidemic and representatives of organizations providing AIDS support services. Rosa Haritos, Ph.D., at Stanford relied substantially on oral history in her dissertation on the controversy between the Pasteur Institute and NIH over the discovery of the AIDS virus.[1] In England, Virginia Berridge, Ph.D., co-director of the AIDS Social History Programme at the London School of Hygiene and Tropical Medicine, employs oral history in her research on AIDS policy in the UK.[2] And Maryinez Lyons, Ph.D., at the University of London, uses interviews in her work on the political economy of AIDS in Uganda.[3] In France, Anne Marie Moulin, M.D., Ph.D., Director of Research at INSERM, Paris, has relied on oral history in some of her work on the epidemic in France. The anthropologist, Paul Farmer, used interviews heavily in his work on AIDS in Haiti.[4]

Emerging Themes

What themes can be extracted from these oral histories? What do they convey about the medical response to AIDS in San Francisco? Was it unique, or are there parallels with responses to other epidemics? What do these interviews tell us about the complex interweaving of factors--social, political, economic, and personal--which shaped reactions to this epidemic, in this city, in these years?

The short answer is that it is too soon to attempt definitive answers. This is the third volume in a lengthy series, and most of the oral histories are not completely processed nor has the information they contain been fully assessed.

Furthermore, there is an inherent danger in reaching definitive conclusions on the basis of oral histories with only seventeen individuals.

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[1] Rosa Haritos. Forging a Collective Truth: A Sociological Analysis of the Discovery of the AIDS Virus. Ph.D. dissertation, Columbia, 1993.

[2] See: Virginia Berridge and Paul Strong, eds. *AIDS and Contemporary History*. Cambridge: Cambridge University Press, 1993.

[3] Maryinez Lyons. AIDS and the Political Economy of Health in Uganda, paper presented at a conference, AIDS and the Public Debate: Epidemics and their Unforeseen Consequences, sponsored by the AIDS History Group of the American Association for the History of Medicine, Lister Hill Center, NIH, Bethesda, MD, October 28-29, 1993.

[4] Paul E. Farmer. *AIDS and Accusation: Haiti and the Geography of Blame*. Berkeley: University of California Press, 1992.

Obviously, this is not a statistical sampling. On the other hand, because these seventeen have been at the front line of the epidemic and in a city hit hard by the epidemic, their voices "count" more than their numbers might suggest. They also "count" because these individuals helped devise organizations and policies that have served as models for AIDS programs across the country and around the world. Thus, if used in conjunction with the traditional documentary sources, these oral histories "count" as rich historical sources on several levels.

Remembering these caveats, I will make some tentative suggestions about a few of the many themes which come to the fore as I put the first volume together. My thoughts will doubtless be modified and extended as I examine the oral history collection as a whole and assess it in the context of the existing literature on AIDS history.

--Professional and personal "preparation" for the epidemic:

Narrators invariably mentioned how their prior education and professional training and experience had prepared them for participation in the epidemic. Their training as oncologists or epidemiologists or infectious disease specialists "fitted them" in a deterministic sense to take notice when the epidemic was first recognized in San Francisco. Their interest piqued, they chose to become engaged because their professional knowledge, experience, and responsibility placed them in a position to contribute. How then to explain why others with similar backgrounds chose not to become involved? The interviews indicate that psychological makeup, humanitarian concerns, career ambition, sexual orientation, and simply being needed and on the scene also played a role.

--Organizing for the epidemic:

The oral histories describe at length, in detail, and on many levels how the academic medical profession in San Francisco organized to respond to the epidemic. The focus is on university physicians, but the oral histories show that it is impossible to talk about the medical response without at the same time mentioning its interconnections with the community physician, nursing, psychiatric, and social service professions, the gay community, and volunteer AIDS support organizations. Discussion of the coordinated medical system created in the early years of the epidemic, capsulized in the so-called San Francisco model of comprehensive AIDS care, permeates the oral histories. The complex process by which a community organizes to diagnose, investigate, and treat a newly recognized disease is detailed here, as are the spinoffs of these activities--the foundation of two AIDS clinics, an AIDS ward, and a specimen bank; funding efforts; education and prevention programs; epidemiological and laboratory studies; political action at the city, state, and national levels; and so on.

--The epidemic's impact on the professional and personal lives of physicians and scientists:

Surprisingly, despite the flood of AIDS literature and the centrality of the medical profession in the epidemic, there are few accounts by physicians of the epidemic's professional and personal impact.[1] The physicians' voices which speak--at times poignantly, but always with immediacy--through these oral histories are a small corrective to the impersonality of most of the literature on AIDS.

On a professional level, the narrators describe commitment, concern, cooperation, camaraderie, and conflict as attributes of their engagement in the epidemic. Clinicians and epidemiologists confronted by what they perceived as a medical emergency described the prevailing sense of urgency and dedication of the epidemic's early years--to stop the insidious spread of disease, to discover its cause, to devise effective treatments, to establish community care arrangements. Narrators talked of concern for an articulate, informed, and youthful patient population, with whom some identified and for whom most felt great sympathy. They also spoke of the camaraderie and cooperation of the physicians, nurses, social workers, and community volunteers assembled at UCSF and San Francisco General to run the AIDS clinics and ward. But they also mentioned conflict--personal and institutional rivalries, funding problems, and run-ins with the university administration, city politicians, and gay activists.

On a personal level, the interviews recount the epidemic's impact on individual lives--of fear of a devastating and lethal infection, of stigma and homophobia involved in dealing with socially marginal patient populations, of exhaustion and burnout, and of growth in human experience and insight.

--The epidemic as a social and cultural phenomenon:

These oral histories describe the complex interactions between disease and its social and cultural context. They indicate how the unique circumstances of San Francisco in the early 1980s--its large and vocal gay community, its generally cooperative medical and political establishments, the existence of a city budget surplus--shaped the response to the epidemic.

AIDS, like all disease, reflects social and cultural values. Implicit and explicit in the oral histories are evidence of stigma and homophobia, the politicization of the AIDS effort and those associated with it, and the tension between individual rights and social welfare.

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[1] A few personal accounts by physicians do exist. See, for example: G. H. Friedlander. Clinical care in the AIDS epidemic. *Daedalus* 1989, 118, 2:59-83. H. Aoun. When a house officer gets AIDS. *New England Journal of Medicine* 1989, 321:693-696. The Oppenheimer/Bayer oral history project, mentioned above, also seeks to document physicians' responses.

The foregoing themes are but a few of those inherent in these oral histories. I hope that scholars will be persuaded to explore these further and to discover and research those unmentioned. To serve as a rich, diverse, and unique source of information on multiple levels is after all a major purpose of this oral history series.

Locations of the Oral Histories

The oral history tapes and bound volumes are on deposit at The Bancroft Library. The volumes are also available at UCSF, UCLA, and other manuscript libraries.

Note Regarding Terminology

In this series, both interviewer and interviewee occasionally use the term "AIDS" to refer to the disease before it had been officially given this name in the summer of 1982. "AIDS" is also used to refer to the disease which in recent years has come to be known in scientific and medical circles as "HIV disease." In these oral histories, the term "AIDS" has been retained, even when its use is not historically accurate, because it is the term with which readers are most familiar.

Sally Smith Hughes, Ph.D.
Project Director

October 1996
Regional Oral History Office

LIST OF PARTICIPANTS IN THE SAN FRANCISCO AIDS ORAL HISTORY SERIES

VOLUME I

Selma K. Dritz, M.D., M.P.H, Epidemiologist, San Francisco Department of Public Health
Mervyn F. Silverman, M.D., M.P.H., Director, San Francisco Department of Public Health

VOLUME II

Donald I. Abrams, M.D., AIDS Internist at San Francisco General Hospital
Marcus A. Conant, M.D., AIDS Physician and Political Spokesman
Andrew A. Moss, Ph.D., Epidemiologist at San Francisco General Hospital

VOLUME III

Arthur J. Ammann, M.D., Pediatric AIDS Physician and Administrator, UCSF
Paul A. Volberding, M.D., AIDS Oncologist at San Francisco General Hospital
Constance B. Wofsy, M.D., Authority on *Pneumocystis carinii* Pneumonia and Women with AIDS, San Francisco General Hospital

IN PROCESS

Donald P. Francis, M.D., D.Sc., Epidemiology and Virology at the Centers for Disease Control
Deborah Greenspan, D.D.S., D.Sc., Oral Manifestations of AIDS
John S. Greenspan, D.D.S., Ph.D., AIDS Specimen Bank, UCSF
Jay A. Levy, M.D., Virologist, UCSF: Isolation of the AIDS Virus
Merle A. Sande, M.D., AIDS Activities at San Francisco General Hospital
Warren Winkelstein, Jr., M.D., M.P.H., The San Francisco Men's Health Study, UC Berkeley
John L. Ziegler, M.D., AIDS Oncologist at the Veterans Administration Medical Center, San Francisco

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Berkeley, California

The San Francisco AIDS Oral History Series

THE AIDS EPIDEMIC IN SAN FRANCISCO: THE MEDICAL RESPONSE, 1981-1984

Volume III

Arthur J. Ammann, M.D.

PEDIATRIC AIDS IMMUNOLOGIST: ADVOCATE FOR THE CHILDREN

Interviews Conducted by
Sally Smith Hughes
in 1992, 1993

Arthur J. Ammann, M.D., 1995

INTERVIEW HISTORY--by Sally Smith Hughes, Ph.D.

Art Ammann was interviewed because of his seminal role as professor of pediatrics and clinical immunologist at UCSF after a new immune deficiency disease, later christened "AIDS", was recognized in the summer of 1981. Fascinated by the scientific puzzle the epidemic presented, he began to attend the study group following the weekly meeting of UCSF's Kaposi's Sarcoma Clinic. As a member of this informal group, he offered invaluable experience in the clinical and laboratory aspects of immunodeficiency to the small group of investigators interested in the disease. Ammann was also director of the Pediatric Immunology/Rheumatology and Pediatric Clinical Research Center in the Department of Pediatrics at UCSF, and as such had access to the laboratory technology useful for defining the syndrome's immunological basis. He volunteered to run laboratory tests on the handful of adults presenting at the clinic with, among other conditions, acquired--ie, not inherited--anomalies of the immune system.

Early in the epidemic, Ammann cared for a woman with four children, all of whom, except for the oldest child, had a strange immune deficiency accompanied by increasingly serious opportunistic infections. Struggling to "fit" these cases into the more familiar model of a congenital anomalie, Ammann eventually came to the conclusion that the family had AIDS. The realization was devastating: not only did the mother and children have a fatal disease, but the cases suggested that AIDS was not confined to the four demographic groups--all composed of adults--which the Centers for Disease Control had described as at particular risk for AIDS. Ammann's cases and those of colleagues on the East Coast were startling indication that AIDS was not confined to adults; it could--and did--occur in children.

The realization launched Ammann on a path in pediatric AIDS which he continues to this day. His first hurdle, as he explains in the oral history, was to convince his medical colleagues that AIDS could occur in children. Not wanting to believe that an incurable disease could appear in the young and "innocent", many of his colleagues for years resisted the reality of pediatric AIDS which he and a few others were espousing.

In the fall of 1982, Ammann treated yet another child with unexplained immunodeficiency accompanied by rare opportunistic infections, a case which was to add another terrifying dimension to the epidemic. Because the child had received multiple blood transfusions at birth, Ammann consulted Herbert Perkins, the scientific director of the San Francisco blood bank, about the source of the transfused blood. Perkins, Ammann, and Selma Dritz, a health department epidemiologist, traced one of the blood donations to a man who had since died of AIDS. Although the evidence was circumstantial, the idea was electrifying that the AIDS "agent" was transmissible by blood and seemingly contaminating the blood supply. It also lent weight to the suspicion that a virus was at the root of AIDS. Ammann describes the effects of these findings on the biomedical, blood banking, and hemophiliac communities.

Prompted by disagreements with UCSF administration over the disbursement of AIDS funds--a topic he discusses in the oral history--he retired from UCSF in 1985 to join Genentech, a biotechnology firm located in South San Francisco. In 1992 he left Genentech to devote more time to his dual roles as chairman of the Health Advisory Board of the Pediatric AIDS Foundation and director of the Ariel Project for Prevention of HIV Transmission from Mother to Infant.

It is fair to say that pediatric AIDS has reclaimed Ammann's professional life. Aside from administrative and fund raising activities, he is frequently called upon to provide testimony before congressional and other governmental and scientific committees. His interviews tell of his campaigns for maternal antibody testing and AIDS vaccine development.

But who is the man behind the science and politics? The oral history provides glimpses of a humane and principled individual whose personal charm and dedication doubtless serve him well whether dealing with a sick child or a Senate subcommittee.

The Oral History Process

Three two-hour interviews were conducted between August, 1992 and January, 1993 in the headquarters of the Ariel project in Novato, California. We sat in Ammann's office overlooking a quiet estuary visited by egrets and a variety of other water birds. Ammann talked freely and informally of his diverse activities before and during the AIDS crisis. During the lapse between interviews 2 and 3, I looked through Ammann's office files and scrapbooks, which he brought from home, and generated more questions for the last session. The interviews were transcribed, edited, and sent to Ammann for review. He reviewed carefully, but without making substantial changes.

This oral history, as with others in this series, shows how the AIDS epidemic has transformed professional and personal lives. In this instance, Ammann's experience with the epidemic was a major force propelling him from a university position as physician and clinical immunologist to industry and finally to a position of political advocacy for pediatric AIDS.

Sally Smith Hughes, Ph.D.
Senior Interviewer

Regional Oral History Office
The Bancroft Library
October 1996

Regional Oral History Office
University of California
Berkeley, California

BIOGRAPHICAL INFORMATION

(Please write clearly, don't type. Use black ink.)

Your full name Arthur J. Ammann

Date of birth Aug 12, 1936 Birthplace Brooklyn

Father's full name Hans Ammann

Occupation Baker Birth & Death dates 6/8/1904 died March 1991

Mother's full name Marie

Occupation Housewife Birth & Death dates 3/30/1908 alive

Spouse's full name Marilyn

Children's full name Scott

Kimberly

Where did you grow up? Brooklyn

Present community San Rafael

Education Wheaton College New Jersey College of Medicine
(Undergraduate, Medical School, Internship, Residency)
Intern at Jersey City Medical Center Resident at U.C Med Center, S.F.

Occupation(s) Physician Immunology Pediatrics

Areas of expertise Pediatrics Immunology

Other interests or activities Photography Ethics

Active in which medical organizations? —

Other organizations —

I EDUCATION AND TRAINING

Medical Student, New Jersey College of Medicine, 1958-1962

Hughes: Please tell me where you went to medical school and how you got into pediatrics.

Ammann: I went to medical school at Seton Hall, which subsequently changed names to New Jersey College of Medicine when it became a state school. I had been interested in research as an undergraduate, but because it was difficult to do research in college, I didn't have an opportunity to do any until I got to medical school.

I had read some books in college about vestigial organs, which always struck me as a strange idea, why the human body would have an organ that wasn't needed. And one of those vestigial organs was the thymus gland. The medical texts in the fifties talked about the thymus gland being unnecessary and no one knowing what its function was. I had actually tried in college to do a small research project in mice, trying to take out the thymus glands. But I didn't have any mentor; I just got some mice, and I tried doing it and was not very successful. But it triggered my interest in doing research.

So when I got to medical school, I usually tried to get a summer job doing research. The first one I had was at the pharmacology department doing research on drug effects. It wasn't a very exciting project, but it at least taught me some of the basic research techniques.

As I went through medical school, some of the best teachers were in the department of pharmacology, where I was doing the research, and in pediatrics. So that got me going as to what my subspecialization would be, and I decided that pediatrics was going to be the most interesting area. There are still a lot of

unknown diseases in pediatrics. Some children with unidentified disease probably have genetic disorders of one type or the other which are yet to be discovered.

Resident Physician, Pediatrics, University of California, San Francisco, 1963-1966

Ammann: When I finished medical school, I applied for residency in pediatrics in several places, but mostly in California, and was accepted at the University of California at San Francisco.

Hughes: Because you wanted to come to California?

Ammann: Well, I wanted to leave the East Coast. The type of medicine in a big city hospital like the Jersey City Medical Center, which is where my medical internship was, had a lot of trauma cases. There were a lot of poisonings, accidents, and beatings, and I really felt that what I was studying there, in terms of medical care, was neglect and what harm people could do to one another.

I wanted to study the cause of diseases, rather than trauma, the cause of which seemed to me obvious. And I wanted to get away from East Coast influence, feeling that maybe West Coast medicine would be slightly different. That sounds strange nowadays, but I found out that there were differences in the way people approached medicine, how they thought about disease. My wife [Marilyn Mihm Ammann] and I had never been to California, so we thought that would be a good chance to go.

Hughes: What differences in medical approach did you find?

Ammann: The medicine that I was practicing on the East Coast in a big city hospital was: the patient came in, you tried to find out what he had, and then you treated that disease with an antibiotic or whatever was needed. The style of teaching on the West Coast placed more emphasis on pathogenesis: how did the patient get this disease? What caused the symptoms? And so it was good training. Patients were studied in much more detail. A patient was referred to a university hospital having already had an evaluation by a pediatrician who said, "I don't know what this patient has." It was a much more complex level of medicine in the West, and had a lot more teaching associated with it. And as I began to consider how the symptoms came about, that began to trigger my idea about research. There were lots of areas that were interesting for research.

Hughes: Were you determined on an academic career when you moved to California?

Ammann: Yes, I found that much more exciting than routine clinical medicine. My two years between my senior year in medical school and an internship in pediatrics were more like an internship in a city hospital. We had a lot of responsibility for patient care. But that was enough exposure to routine kinds of things, and I wanted the challenge of trying to figure out what was going on in diseases where there were no answers.

Hughes: But you still wanted to keep your hand in patient care?

Ammann: Yes, because my feeling was the questions came from the patients. You didn't manufacture the questions in your head; at least, I didn't. You would have a patient with a problem and say, "Why does this problem exist?" Research seemed to be to me to try to answer those questions.

I actually was very fortunate throughout my career, because every place that I was, there was always some mentor who was interested in teaching a student about research. I had that experience in medical school, and I had that experience during my residency program. At that time, it wasn't common for someone to do research during residency. But I was always interested in doing some sort of research project.

Hughes: Who was your mentor at UCSF?

Ammann: Well, the person who I still keep contact with is Richard Stiehm. He was a fellow in immunology with Dr. Hugh Fudenberg. Fudenberg at that time was one of the few immunologists in the world. There were very few people in the field of immunology. It was a young field. Dick Stiehm used to make rounds in pediatrics; he was a pediatrician. He started asking immunology questions, and I started getting very interested in immunology.

Research in Pediatric Immunology

Ammann: So I went to him one day and I said, "I'd like to do a research project in immunology that I could do while I'm still a resident." And we talked about one that was possible. This was interesting, because it really started me on an immunology career.

At that time, 1962, immunoglobulins could be measured for the first time. The technique had just become available. John Fahey, who is now at UCLA as head of microbiology, had devised a technique whereby you could put serum on plates, the serum would diffuse out, and then you'd have an antibody against the immunoglobulins. The antibody reaction formed a precipitation circle. You could quantitate the amount of IgG, IgM, and IgA antibodies by measuring the circle.

Dick Stiehm was aware of that technique and said it would be interesting to do a project in pediatrics to see whether or not breast milk was absorbed through the gastrointestinal tract in newborn babies. No one had ever answered that question. It's always been postulated that one of the effects of breastfeeding is that the baby might absorb human antibody from the mother's breast milk, and it would get into the serum and protect the baby against infection. But that had never been shown, and we decided to do a study looking at antibody levels in breast-fed babies and non-breast-fed babies. So we started collecting serums and then measuring antibodies. We were able to show that breast milk doesn't get absorbed.

In the process of doing that study, we noticed that there were a couple of babies whose antibody levels were sky-high. So I went back to find out what was wrong with those babies, if there was something different about them.

We found out that both babies had been infected with rubella virus. The mothers had gotten rubella during pregnancy, and they had congenital rubella syndrome. We had discovered, purely fortuitously, by having these babies in our study, that when babies get infected in utero, they make antibodies prematurely, and they have elevated antibodies at birth. That finding led to using IgM antibody testing, which is now fairly common, to detect congenital syphilis and congenital rubella and congenital toxoplasmosis. At that time, in 1962, it was a very novel discovery, and it resulted in a *New England Journal of Medicine* publication,[1] which was very exciting for me.

I learned many principles through that study. One is you could design a study for statistical analysis. Two, when you obtain unusual findings, you just don't dismiss them, but you pursue them and find out why. It really opened up a whole field of investigation--the detection of infection in utero and the

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[1] E. R. Stiehm, A. J. Ammann, J. D. Cherry. Elevated cord microglobulins in the diagnosis of intrauterine infections. *New England Journal of Medicine* 1966, 275:971-977.

ability to determine at birth whether an infant is infected with a virus or not.

Hughes: Yours was the first work in that area?

Ammann: That was the first work that was done in that area. And then others picked up on that. Now when people test to find out if the baby is infected with syphilis or toxoplasmosis, the question is, if you just do a routine antibody test, it can be positive from the antibody that comes from the mother--passive transfer. If you test for IgM antibody, and the baby has IgM, the baby has to make that because it doesn't come from the mother. So that means the baby was infected in utero, and that's the basis of tests that are now used routinely to detect infection.

So that got me interested in immunology, and at that time it was a wide-open field. Almost anything that you did was new.

Hughes: Was there actually a subspecialty called pediatric immunology?

Ammann: No, not at that time.

Clinical Immunology and Hypogammaglobulinemia

Ammann: The field of clinical immunology was started by Ogden Bruton, who was at Walter Reed Army Hospital. I forget the year that this happened, but Walter Reed had purchased a device that could measure proteins--albumen and globulin. Bruton had some pediatric patients who had repeated infections, and he didn't know what the cause was. But when this new machine came, he ran the blood through it. When he got back the results, he found out there was no gamma globulin. A specific portion of the globulin fraction was missing. And that's how hypogammaglobulinemia was discovered.

So clinical immunology really began with Colonel Ogden Bruton, who discovered hypogammaglobulinemia, and then opened up into the entire immune system, including human and animal immunity. For example, there were people like Robert Good doing thymectomies. Now, he did the first thymectomy studies and found out if you studied the animals carefully, that they became susceptible to infection and lost their lymphocytes and so on.

All of those observations were happening in the late fifties and the early sixties. As the techniques became available to look at antibody deficiency disorders, which were more common in children because most of these were genetic disorders and the

children became infected very early on, that whole area began to open up dramatically. At the time I got interested in pediatric immunology, it was really just beginning.

Captain, Travis Air Force Base, California, 1966-1968

Ammann: After I finished my residency, I was obligated to go into the air force for two years, 1966 to 1968. That was a bit traumatic, because that took me back to general pediatrics and routine illnesses. The experience helped me in terms of understanding general pediatrics, but frustrated me because I couldn't do any research during that time, and I was always looking for research projects to do. So I spent most of my time teaching, because nobody else wanted to teach. They had a residency program at Travis Air Force Base.

Hughes: You were teaching general pediatrics?

Ammann: Yes. I spent most of my time teaching, but I was free about half an afternoon a week to do something else. Where I went at that time was to attend a newborn follow-up clinic that Bill Tooley ran at UC Med Center in San Francisco. The reason I did that was because Bill was doing clinical research on patients. Because of some of my work on breastfeeding and evaluation of IgM in newborns, I wanted to keep in contact with the newborn area, although I definitely wanted to be in immunology.

Fellowships in Immunology, University of Minnesota Medical Center, 1968-1969, and University of Wisconsin Medical Center, 1969-1971

Ammann: During the time in the air force, I started looking for a fellowship in immunology. The person who was most well known in clinical immunology at that time was Robert Good at the University of Minnesota Medical Center. That's where I went when I left the air force in '68.

I was with Robert Good from '68 until '69, but during my fellowship I was actually working more closely with a professor by the name of Richard Hong. He made a career change and left Minnesota in 1969 to become the head of pediatric immunology at the University of Wisconsin. I decided to leave with him because I was doing more research with him, rather than with Robert Good who was traveling a lot.

I stayed in pediatric immunology research, and that's where I got interested in IgA deficiency, bone marrow transplantation and immunologic reconstitution. So I had a total of three years of immunology fellowship training, one at Minnesota with Bob Good, and then two years with Dick Hong at the University of Wisconsin.

Hughes: Did that training prove fundamental to your later research?

Ammann: Absolutely. I think fellowship training experience in the basics and the tools to continue research is necessary. And that's exactly what it did. It gave me the tools for diagnosing immunodeficiency, T-cell deficiency, and antibody deficiency. Because I spent all of my time doing research, it was probably the most productive time. Most of my work was published in 1971 and I am not sure now many articles and abstracts there actually were.

These were very basic reports in terms of diagnosis of immunodeficiency, which became very important for the recognition of new immunodeficiency disorders. That was the critical factor that eventually allowed my early diagnosis of AIDS, in terms of how AIDS was similar to or different from other genetic immunodeficiency disorders.

Robert A. Good and T-cell Deficiency

Hughes: When did T-cell deficiency achieve prominence in immunology?

Ammann: Well, that happened very quickly. Antibody deficiency was easy to detect, because you could obtain serum easily, you could freeze it, and you could take serum that had been frozen for ten years or more and run tests on it. We actually did that, and looked at the antibody levels of patients. Those studies were easy to do. But you couldn't freeze T cells. You had to look at them in real time.

The first hint of T-cell deficiency came from Bob Good's studies with thymectomy. That was the first time you could really say that the thymus was not a vestigial organ. The thymus was fundamental to preserving T-cell immunity.

Hughes: When were his studies done?

Ammann: Those were done in the fifties and early sixties. But the diagnosis of T-cell deficiency was crude. In most cases it was done just by looking at lymph node histopathology and saying,

"There are not as many lymphocytes," or, "there are not as many lymphocytes in the peripheral blood." Not very sophisticated.

Hughes: Was there the concept of a T cell?

Ammann: Yes. The concept began to evolve that a T cell came from the thymus gland, hence the name thymus or T cell. A lot of this work from Bob Good came in the sixties: that the B cells produced antibodies, and the T cells were thymus-derived.

When I was in Minnesota, Dr. Good would always say you could tell thymocytes in the peripheral blood from B lymphocytes or other lymphocytes by their size, because T cells are small. I had trouble understanding that; I didn't know how you could prove that. I remember looking at a microscope slide with Dr. Good and saying, "Now, tell me, is this a T cell or is this a B cell?" He was always dogmatic: "Very clearly, this is a T cell, because it is small." I said, "Well, it looks like the other cells to me."

But it turned out not to be true. It was only later when there were specific T-cell markers that you could tell that it didn't make any difference what the size of the cell was; it had to have a specific cell surface marker. Well, none of those were available then.

Hughes: So you could not distinguish T cells microscopically.

Ammann: No.

Pediatric Immunology, University of California, San Francisco

Studies of T-cell Rosetting

Ammann: And the first clue that there was a unique marker on a cell came from studies using sheep red blood cell rosettes. When I finished my fellowship and went to UC [in 1971 as an assistant professor of pediatrics], we were performing a technique for detecting T cells which was called T-cell rosetting. We would incubate lymphocytes from patients' blood with sheep red blood cells. The sheep red blood cells would adhere to thymic cells but not adhere to cells that didn't come from the thymus. So the term "T-cell rosette" began to evolve in the early seventies.

No one knew at that time why sheep red blood cells adhered to T cells. They tried mouse red cells, goat red cells, and horse

red cells, but only sheep red blood cells adhered. Well, now we know that there's a cross-reaction between a marker on sheep red blood cells and a receptor on T cells. We don't use that technique now. When monoclonal antibodies became available, it was found that there was one that recognized T cells. And not only were there T cells but there were subsets of T cells--helper cells and suppressor cells--which had been known about in the murine immunology field but had never been proven in the human.

We started working with monoclonal antibodies. In the late seventies, when the monoclonals became available, and into the early eighties, we were looking at the T4 and the T8 cells in the laboratory that we had set up at UC for immunology.

Hughes: That's the Pediatric Clinical Research Center?

Ammann: Yes.

To back up: When I finished my fellowship, I wanted an academic position and decided to look at several different places, one of which was UC San Francisco where I had been a resident. I had the opportunity to set up a pediatric immunology program so I decided to do that. That was in '71. All of my initial work was on congenital immunodeficiency disorders and autoimmune disorders, because I felt the two were related.

Hughes: You came with a promise from the administration that you would be allowed to set up a pediatric immunology center?

Ammann: Yes. Everything was easy, compared to nowadays. It just fell in place. You said, "I'm going to set up pediatric immunology as a subspecialty; I'm going to diagnose patients; I'm going to treat patients; I'm going to do research." You applied for a grant; you got the grant. It was just extraordinarily easy--because the field was new, it was exciting, and there was a lot of NIH [National Institutes of Health] money available in the seventies.

So we set up a pediatric immunology and rheumatology program for diagnosis and treatment, and then I also had the Pediatric Clinical Research Center, which I was in charge of. That gave me the opportunity to do clinical research on patients as well as laboratory research.

Technology in Immunology

Hughes: Talk about the impact of technology on immunology. I'm thinking of the cell sorter and instruments of that nature. What did they allow you to do that you couldn't have done before?

Ammann: Well, more precision was possible. Previously, if you had a patient with recurrent infection where you knew there was something wrong with the immune system, you could only diagnose hypogammaglobulinemia. If the patient had lymphopenia, low lymphocytes, you could say well, maybe there was a thymus defect or a T-cell defect. And then you'd immunize the patient; you'd see if he made antibodies. That was the fundamental workup.

What technology did was to separate out both quantitative and qualitative abnormalities. For example, we now know that in AIDS immunoglobulin levels can be elevated and they don't function. The patient has the equivalent of hypogammaglobulinemia. Or, you can have normal numbers of lymphocytes and the patient can have no T cells, because the lymphocytes are from other sources such as B cells. Or, there may be a very abnormal ratio of the T cells.

As the technology improved with monoclonal antibodies, functional assays, the ability to culture lymphocytes and to stimulate them with mitogens, it gave us an idea: if the cells or if the antibodies were there, were they functional? So we started asking those questions, and as answers came we began to define a number of diseases that would have been mysteries before technological advances occurred.

Enzyme Deficiency Diseases

Ammann: It also became apparent that there were certain markers of diseases. For example, there were enzyme deficiencies. Eloise Giblett, who was a blood bank researcher in Seattle and who ran enzymes for genetic analysis of blood donors, was asked to analyze some samples from a bone marrow transplant patient. Bone marrow transplantation was first successfully performed in 1968. That only became possible because there were techniques for matching blood. The whole area of histocompatibility typing began to appear at that same time. When you could match white blood cells, you could then do a bone marrow transplant from identical donors.

Sometimes, the donors were so identical that after a transplant, the question would come up, "Well, whose blood is surviving in this immunodeficient recipient?" Hilare Meuwissen in Albany, New York, who did a bone marrow transplant, sent a blood sample to Eloise Giblett who did these genetic markers. He said, "I'm having trouble determining who's the donor and who's the recipient. Can you figure it out for me?" When Eloise analyzed the pattern of enzymes in the blood for genetic markers, she found that the enzyme adenosine deaminase was completely absent in the patient. The lack of adenosine deaminase was then found to be the cause of a form of severe combined T- and B-cell immunodeficiency.

We had heard about this discovery and felt that there might be patients with enzyme defects. A patient who was referred to us had a very unusual immunodeficiency disease which, interestingly enough, looked very much like what we describe in AIDS patients today. The patient had elevated immunoglobulins and very low T cells. It didn't fit any pattern of previously described immunodeficiency.

So, having known about Eloise Giblett's discovery of this enzyme deficiency, we sent a blood sample from the patient to Eloise with a note which said, "Is this another enzyme deficiency?" And interestingly enough, it turned out to be a new genetic enzyme deficiency.

Now, that actually became a very important case, although rare, because the immunologic pattern in that patient was identical to AIDS. When we first saw that pattern in pediatric AIDS patients, we thought that they had the same enzyme deficiency. We measured the enzymes and found that they were normal, so we knew that we were dealing with a different disease. This had to be immunodeficiency disease with a cause that was different than that of either genetic enzyme deficiency.

II THE AIDS EPIDEMIC

Puzzling Cases of Immune Deficiency in Three Infant Sisters

Searching for Causes

Hughes: I noticed in going through your notebooks today an article in 1985 about the three female immunodeficient babies of a prostitute IV-drug user mother.[1] You began to wonder in 1980 about the cause of the immunodeficiency, although what later became known as the AIDS epidemic wasn't reported until a year later. What did you think in 1980 was going on?

Ammann: Well, we were clearly frustrated at that time, because we were trying to fit--and all physicians do--a patient into a category so that you can understand what's going to happen to the patient. And when patients don't fit into a category, you get frustrated, because one, you don't know what the cause of the disease is, and two, you don't know how to treat it.

So we had had this circumstance of the mother who was an IV-drug abuser and a prostitute, which we didn't think was related in any way to the immunodeficiency.

Hughes: Because you thought the immunodeficiency was congenital?

Ammann: Right. She had low T cells, but she was not severely immunodeficient. The first sister, who was very, very sick and was a graduate of the newborn intensive care nursery with multiple complications, was quite ill with severe immunodeficiency. The

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[1]Maternal transmission of AIDS studied. *Research Resource Reporter*, February 1985, 11-12.

second sister also had immunodeficiency. There was a healthy brother about ten years old. And then there was another sister who was born later.

So here we had an immunodeficiency disease that seemed to partially affect the mother (she had low T cells), affected severely two of the sisters, and a brother who was normal. Now, the mother said at first that they were all from the same father, but when we did genetic typing, they were all from different fathers.

Hughes: Why did you do the typing?

Ammann: Well, she was a prostitute, and the children all looked different.

I remember this well. We were puzzled, because at that time, there were only certain known forms of genetic immunodeficiency disease. There was an X-linked chromosomal form, autosomal recessive and sporadic forms. If you did studies on the X-linked form, the mother was normal but she'd be a carrier, as in hemophilia or X-linked hypogammaglobulinemia. In the autosomal recessive forms of immunodeficiency, the parents were always immunologically normal. It was only the infant that was severely affected.

So we couldn't figure out genetically how you could have a disease where the mother would be partially immunodeficient, and only the females inherit the immunodeficiency, and the male normal. I actually talked to a number of geneticists and, believe it or not, some of them came up with some theories as to how that could happen, none of which seemed sound to me.

So we began to think about how all of these female children could have gotten immunodeficiency disease. One of my articles reported the family and refers to the possibility that the disease could have been caused by Epstein-Barr virus infection.[1] We had worked with Robert Chang at UC Davis, and he found a very unusual pattern of antibodies which he said you just don't normally see. He thought that the children had some sort of unusual Epstein-Barr virus infection that they had acquired from the mother.

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[1]*Journal of Pediatrics* 103: 585-588, 1983.

Recognizing AIDS

Ammann: As we were wrestling with this, the AIDS epidemic started. We didn't really ask the question if it could have been AIDS until we had seen our first adult patients with AIDS. And about that same time, 1982, we also had an infant with another unusual immunodeficiency who we suspected had blood transfusion AIDS. And at that point, with the report of hemophilia patients who were felt to have AIDS via transfusion of factor VIII, we began to say, "This is a genetic disease? This is crazy. What we have are infants who have been infected [with HIV] from the mother by vertical transmission."

Hughes: Did you think that the mother had AIDS?

Ammann: Well, this is when we got into big arguments with the CDC [Centers for Disease Control]. Very early in our contact with the CDC, we objected to their definition of AIDS. They were coming from an epidemiologic point, and they were coming from describing adults. I was a pediatric immunologist who had spent my career dealing with immunodeficiency disease. They were trying to define immunodeficiency disease in such a restricted way that we said, "We totally disagree."

What we had seen in genetic immunodeficiency diseases were children who had immunodeficiency disease diagnosed by laboratory criteria but who were asymptomatic. The CDC would never accept the mother as having AIDS. We said she had acquired immunodeficiency, because she had low T cells and an abnormal T4/T8 ratio, and to us, that meant immunodeficiency.

Hughes: But none of it was severe enough to suit the CDC definition.

Ammann: No. The mother died probably five or six years after we had first seen her children. Only shortly before then did she start developing candida, thrush, and other symptoms of AIDS.

Defining AIDS

Accepting Cases as AIDS

Ammann: That was actually very characteristic in the early epidemic, because we were coming at it from a very different perspective. We were seeing a lot of the patients earlier in the course of

disease. For example, in the blood transfusion story, we were screening recipients of blood product which had come from donors with AIDS, and we had no viral marker. Some of the blood transfusion recipients only had reduced T4 cells. We would have patients that were tired and lethargic, and one woman who had candida of the mouth. She had abnormal levels of T cells.

The CDC rejected all of those patients as having AIDS, and we got into big debates with the referring physicians because they said we were over-interpreting, that they didn't have AIDS because they didn't have the classical features--*Pneumocystis carinii* pneumonia and so on.

You asked about the early blood transfusion cases. When we said that a patient who had a low T4/T8 ratio and abnormal immunologic function had early AIDS, nobody accepted that. These patients never appeared as blood transfusion AIDS cases early on, because there was no way of testing them for the virus. The number of blood transfusion cases was therefore grossly underestimated.

Some of them were tragic cases. There was a woman referred to us from Stanford who had had a blood transfusion. She was lymphopenic; she was fatigued; she had the wasting syndrome, which at that time was not known to be a symptom of AIDS. She did not fit the category of AIDS. She died of *Pneumocystis*, which was accepted as a criterion for AIDS, about six months after we saw her. But most of the early cases in pediatrics as well as of blood transfusion were not accepted as AIDS cases.

Problems with the Official Definition of AIDS

Hughes: Do you think that the problem of defining AIDS had something to do with the slow acceptance of blood transfusion AIDS? I mean, the fact that there just weren't many transfusion cases that fitted the official definition of AIDS?

Ammann: Yes, the numbers were not there. I didn't tally them up, but the number of blood transfusion recipients who had abnormal T-cell subset ratios and had mild symptoms of immunodeficiency but were not defined as AIDS cases probably were three to four times the number that actually had AIDS by official definition. So their numbers would have been much larger if the definition of AIDS had been expanded, and I think things would have moved ahead faster.

In some of our early publications, I had a classification of AIDS in children that was different than the CDC's.[1] It was never accepted, because the CDC kept pounding their definition, which they said was for epidemiologic reasons. But our argument early on was, if you want to find out the true incidence of this disease, you've got to define it immunologically, and that's what we always did. We said, "We are the immunologists, and we always define disease by laboratory criteria. We don't wait until a patient with hypogammaglobulinemia gets meningitis to make the diagnosis. And if a patient has low immunoglobulins, he has hypogammaglobulinemia. If a patient has T-cell depletion, he has acquired immunodeficiency. And we don't wait until he gets *Pneumocystis* or candida to call it AIDS."

We're now ten years into the epidemic, and bit by bit, the CDC is expanding the definition. Now, they include CD4 counts below 200 and candidiasis, and I heard recently that they may even go to using HIV infection as the only definition.

Hughes: Do you think it was strictly a scientific disagreement, or was there more to it?

Ammann: Oh, I think then and now there's more to it. At first, the CDC was correctly wanting a strict definition so that this [disease] didn't become some big, broad exaggerated problem by making the definition too loose. That was fine, initially. But I think once we started to learn about the disease, and then without question once the virus was isolated and you could test for it, the definition should have been changed to, "Are you infected with the virus or are you not?" That should be the only question.

But I think early on, the blood banks did not want to know the real numbers of [AIDS] transfusion cases. I think the medical care system did not want to diagnose AIDS, because that would have important ramifications for health care. I think there was a reluctance on the part of physicians to diagnose patients at early stages, and then probably a reluctance on the part of patients. It was very difficult. If you had a patient with immunodeficiency and low T4/T8 ratios, and you had no diagnostic test for the virus at that point, you had to spend a lot of time with the patient, answering questions and so on. Basically, there were many, many reasons why the definition wasn't expanded right away.

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[1]*Annals of Internal Medicine* 103:734-735; *Journal of Pediatrics* 106:332-342, 1985.

Framing AIDS as a Gay Disease

Hughes: Well, it's very interesting, the question of how a disease is framed, because virtually everything flows from that. I'm wondering about the impact of framing AIDS as a "gay disease." How limiting was that? You in pediatric AIDS must have felt the ramifications of that frame.

Ammann: Yes. I'm embarrassed by it now--but if you go through my research notes and a lot of my reprints, the early ones have "gay syndrome" written across them.

Hughes: Well, that's what many were calling it.

Ammann: Yes, many were calling it that. And I think it was really wishful thinking; people didn't want this disease to affect heterosexual people, and they didn't want it to occur with blood transfusions, and they didn't want it to occur in children, and they didn't want it to occur in women. So there was a tremendous resistance on everybody's part to expand the disease beyond a very restrictive definition.

Hughes: So perceiving the disease as centered on the gay population made it more difficult to accept other risk groups?

Ammann: Yes. When people ask, "Why was AIDS so slow in being accepted?" I can't think of any one reason. To me, it was due to multiple factors. The situation at UC was complicated by people not wanting to have the disease at the university hospital. AIDS was said to be a San Francisco General Hospital kind of disease. There was a lot of resistance to setting at an AIDS clinic at the university hospital.

A lot of resistance came from the medical community itself, which hoped that what some people said was going to happen was not going to happen. Maybe by ignoring certain things or not making the classification too broad, it wouldn't turn out to be this big epidemic that some people were talking about and enter into different populations.

However, there were some people at the CDC who said that this was a disease that was going to infect everybody, based on the epidemiologic pattern. Don Francis was one.[1] He clearly said that AIDS had all the patterns of other sexually transmitted diseases. Jim Curran said that as well.

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[1]See the oral history in this series with Donald Francis.

Hughes: Can you remember how early they were saying that?

Ammann: I think they began saying those things in '84, '85, when more was known about the transmission of the virus.

Hughes: But not at the time of your transfusion baby, before the virus was isolated?

Ammann: No. At that time, the concept that a woman could have a viral disease causing AIDS which was transmitted to her babies during repeated pregnancies was not even contemplated. We were not thinking in terms of a unique virus; we were thinking of viruses like cytomegalovirus [CMV]. We tried to find out from the literature whether or not anyone had ever described an immunodeficiency disease attributed to EBV [Epstein-Barr] or CMV that could be transmitted during more than one pregnancy, and we found none.

We kept coming up against these roadblocks. The immunodeficiency we were seeing in children couldn't be genetic, it was too contrived. Even though the girls had Epstein-Barr virus, the cause couldn't be that, because this had never been previously described. It would have to be something different about them. Cytomegalovirus couldn't do this, or Epstein-Barr virus couldn't do it.

Pediatric AIDS

Resistance to the Idea of Pediatric AIDS

Ammann: When we presented our cases of pediatric AIDS at the New York Academy of Science in November 1983, my previous mentor, Bob Good, got up and said that he didn't think that we were seeing AIDS in children, that he had seen this immunodeficiency with CMV before. I quickly responded, because I had looked up all the literature. I said, "If it's been seen before, no one's ever reported it."

Hughes: And he couldn't document it.

Ammann: He couldn't document that he or anyone else had.

Hughes: Was that resistance, or was that just a mistake?

Ammann: No, I think that was resistance. In fact, I just met with Arye Rubinstein recently at a meeting entirely devoted to pediatric

AIDS at the New York Academy of Science. He gave a paper on the history of pediatric AIDS. We were talking afterwards about some of the meetings that he and I had attended where there was over-resistance. People just didn't want AIDS to affect infants. They just didn't believe it. And they didn't believe it until HIV testing became available.

Hughes: Did this resistance have ramifications for your practice at UCSF?

Ammann: Actually, no. Amazingly, in a way, there weren't concerns about the children, and about nurses taking care of the children, or "catching" some unknown disease. I was always astounded by what was happening on the East Coast. Children with AIDS were being kept in the hospital because of community fears. I always said that we just didn't have that problem on the West Coast.

Hughes: I wonder if resistance to the idea of pediatric AIDS relates to the early construction of AIDS as a disease of the gay community, and an inability to think beyond those confines.

Ammann: I think you're right. Initially the idea was that this was a disease in adults and specifically in gay men. In fact, early on, as I said, many of us referred to it as the "gay syndrome," because many people felt that it wouldn't be spread by any other means. And I think "any other means" included heterosexual spread, casual contact, blood transfusion, and accidental inoculation.

At a meeting at the CDC, I first realized that the political aspects of this disease were going to be very significant, because some of the people there felt that you shouldn't notify anybody that got a blood product from someone that had AIDS because there was nothing you could do about the disease and it would create more problems. I was shocked at that. In fact, I remember I said, "My word, if we have a defect in an automobile, we're obligated to notify every car owner. Why wouldn't we notify a blood transfusion recipient, even if there's nothing you can do about it, because you certainly want to know if you had gotten a blood transfusion from an AIDS patient and whether you might have or get AIDS."

Defining Pediatric AIDS

Hughes: How were you initially defining pediatric AIDS?

Ammann: We set up the following criteria: you needed a source of infection, so that would be either a blood transfusion, or a mother that had evidence of immunodeficiency, or in a hemophiliac, repeated use of blood products. The source either had to be a blood product or a mother who was known to have AIDS.

At that time we were saying a source of infection, but we didn't know what virus it was, and evidence of T-cell immunodeficiency. Those were the only two criteria that we had. Then we had rule-outs. For example, you had to rule out congenital immunodeficiency. But our criteria for pediatric AIDS were never accepted.

Hughes: Never accepted by the pediatric community and by the CDC?

Ammann: By the CDC. And the CDC's influence was just overwhelming. I think it was unfortunate that more liberal criteria were not accepted. The CDC definition reduced the pediatric AIDS epidemic to only a small fraction of the whole problem, when the numbers were indeed much, much larger. And the epidemic was increasing at the same rate in children--the numbers were smaller, but it was increasing.

It was predictable what was going to happen: children did not receive appropriate medical care because they weren't diagnosed by an accepted definition of AIDS. They couldn't get *Pneumocystis carinii* prophylaxis or AZT. The ramification of sticking to the CDC epidemiologic definition was felt in all areas. The state would say, "Gee, we're not putting in extra money to take care of children with AIDS; there are twenty cases reported in the whole state," when the number probably was 200. So the CDC definition had very significant social-medical consequences.

The CDC kept saying, "This definition is only for epidemiologic purposes." But of course, the governmental agencies--Medicare, Medi-Cal, SSI [social security insurance]--said, "Well, the CDC says, by their definition, that there aren't many pediatric AIDS cases." It was a significant problem.

Suggestion for Simplifying the Definition

Hughes: How has the definition changed?

Ammann: Well, now my battle [laughs], a losing one again, is to get away from all of the contrived definitions, which most people can't

remember--P1, P2, P3, 2A, 2B, 2C. We need to treat HIV infection like any other disease and say, "Do you have HIV infection or don't you?" That's the only question that I think is relevant.

And the reason for that is that we have to get to the point where this disease is treated like any other disease. If people are HIV infected, they should be eligible for whatever medical care they need, just as if they had gonorrhea, syphilis, tuberculosis, cancer. We don't say, "If you have cancer 2A, you can get drug treatment, but if you have cancer 3B, you can't get treatment." We don't do that with any other disease. This is unique in the history of medicine.

Hughes: Are you getting anywhere with your argument?

Ammann: Well, slowly, the CDC is reversing it. I talked to Jim Curran nine months ago, and he said they were going to change the definition for women. I said, "Jim, why do you keep doing it on the installment plan?" [laughter] "Why don't you just ask: Are you HIV infected or are you not? And if you are, then you deserve whatever treatment is necessary, no matter whether you fulfill some epidemiologic criteria or not."

How stupid can we be to set up criteria for treatment based on a CD4 count when people don't even believe that the CD4 count is a marker for response to treatment? And we're basing treatment on a test that can vary by two-fold? You can use some tests to design a clinical study, but you shouldn't say, "Gee, I know you're sick now, but when your CD4 count reaches 200, come back and see me and I'll start treating you." I am convinced we'll be there soon and then it will be, "Are you HIV infected or not?"

When that happens, a lot of discrimination will go away, because then HIV testing becomes routine. Someone comes into the doctor's office, and he may say, "I'm feeling tired," or whatever. Someone will say, "Well, why don't we do an HIV test?" They're not necessarily going to go into a sexual history, a drug history, or asking: "Are you heterosexual or are you gay?" Testing for HIV, without even asking questions, will be part of good medical care. And if the patient tests positive, then counseling can be provided.

Treatment

Hughes: When you realized that something was being transferred from mother to infant, what could you do?

Ammann: At that point we could not do a lot. If infants presented with symptoms that were suggestive of immunodeficiency, with the appropriate immunologic tests, you could then make a diagnosis of immunodeficiency, and then you could institute supportive treatment--just like we did for any other immunodeficiency disease. The cause was not what was important; it was diagnosing the immunodeficiency. If the child had T-cell deficiency, we would start prophylaxis with Septra for *Pneumocystis carinii*, and we would give gamma globulin to prevent bacterial infections.

When we made an early diagnosis of immunodeficiency, we could treat quickly and we could change the prognosis for the patient. If one child was diagnosed, then we started testing other family members. If the mother had immunodeficiency, we said, "Gee, we don't know what the cause of this is--it could be a virus--but it's affecting your children and you have to consider that in terms of having additional children. Your child needs earlier health care when the child gets an ear infection. You can't treat it like an ordinary infection." Early identification is important for preventing complications. But now early identification is [based on] testing for the virus, rather than on immunodeficiency.

Chronicity

Hughes: Adult AIDS is now conceived of as a chronic disease. Does that concept have validity in pediatric AIDS as well?

Ammann: Yes, absolutely. Initially, it was felt that blood transfusion AIDS patients died more quickly. But we now are seeing newly diagnosed patients that had blood transfusions ten years ago.

We were filmed two weeks ago for the Dr. Dean Edell show. We had two asymptomatic children, a girl and a boy, both transfusion AIDS cases right around birth. They are now eleven years old. One of them has gone public; she wanted to tell her class that she had HIV infection, not AIDS. The boy has not yet told his classmates, but he was on a national television program. Here are two eleven-year-old kids talking about HIV infection, what it means, and what they're worried about.

We want to plan a conference in February to decide how we're going to approach this question of long-term survivors and chronicity. There's either something different about the virus or there's something different about the immune system. And we've got to find out which it is, because it may have very important clues in terms of vaccine development.

Hughes: Immunologists don't know if there are differences among people in terms of their immune reaction?

Ammann: No. But they are going to be very important studies. At this point, I don't know if the virus is different or the immune system is different, or a combination of the two. Probably up until about three years ago, when people asked, "When do patients with AIDS die?" we would have probably said just about 100 percent by ten years after infection. Now clearly, there are more and more surviving longer. And I don't know what the limit to that is because we are only ten years into the epidemic for most patients.

Surveillance

Hughes: In 1983, you were quoted by the *Oakland Tribune* as calling for a surveillance program for pediatric AIDS cases similar to the one for adult AIDS cases.[1] What sort of response did you get?

Ammann: It was not enthusiastic. I don't know what all the factors were. The CDC was content to have the surveillance come in by self-reporting. They were not doing active surveillance. Arye Rubinstein asked the March of Dimes to sponsor a meeting so we could get groups of pediatric immunologists together to ask, "How many cases of pediatric AIDS do you have?" I had written an editorial in *Pediatrics* saying, "Please send in any suspected cases," and I think maybe I got three responses.

The other problem was that in the AIDS community many groups don't work together. I think I was privileged to be in California and in the University of California system. This is not just my own impression; when [Harold] Jaffe came from the CDC, he was astounded at how cooperative people were in California, sharing patients and data and information, putting groups together. San Francisco is the best example of how people from different medical specialties got together and pooled information. The whole blood bank story evolved here in San Francisco: [Herbert] Herb Perkins provided us with blood samples from blood transfusion cases and worked with the city health department to match AIDS cases.

In San Francisco there were areas where people were cooperating and trying to get an idea of how extensive this problem was. But on a national basis, it began to divide up into

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[1] Children of female prostitutes more prone to contract AIDS. *Oakland Tribune*, September 26, 1983.

turf issues. It was a funding or academic issue: "We want to get the money to do this research, and if we share [cases], then we might not get it." That attitude was very prevalent in some areas of the country, to the detriment of making more rapid gains in AIDS research. No one had a large number of [pediatric AIDS] patients to begin with. But people just did not want to put the cases together and do a surveillance program. And when we applied to funding organizations for support for conferences in pediatric AIDS, we were told that pediatric AIDS was not a significant problem.

Hughes: In 1988, the *Chronicle* printed your warning that at least 20,000 children would contract AIDS in the next four years, and more than half of them would be orphans.[1] Has that statistic indeed been borne out?

Ammann: About 5,000 cases of pediatric AIDS have been reported to the CDC, and our estimate is that four to five times that number are HIV-infected. So that would be about 20,000 cases.

Now, the orphans issue: I saw an abstract recently that talked about how many orphans there would be by the year 2000. I think they were talking about 150,000 orphans. They include in that orphan picture non-HIV-infected orphans as well, because if the parents die and leave uninfected children, then they're orphans as well as the HIV-infected children. In fact, they'll be the long-term survivors, because they're HIV-uninfected.

Debate over the Time of Infection

Hughes: Is it known at what juncture infection occurs? Is it in utero?

Ammann: Now it's debated even more than it was before.

Hughes: Why is that such a difficult thing to determine?

Ammann: The main reason is because you can't take a blood sample from the fetus at different times during pregnancy. There are ways of getting samples directly from the baby during pregnancy. But the problem is that with over 60 percent of the infants being uninfected, if you were to take a needle and go through the abdominal wall and into the uterus, or do it vaginally, and you produced bleeding from the mother, you might infect an uninfected

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[1] *San Francisco Chronicle*, September 19, 1988.

baby. So nobody feels that it's ethical to do these procedures in an HIV-infected mother.

What it has meant is that we can't find an answer. Now, people say, "Well, why don't you just look at aborted fetuses?" But the problem is that tissue from an abortion is easily contaminated with maternal blood so that a positive might just be contamination with the mother's virus.

Hughes: What would be the range of timing of infection?

Ammann: It is still debated. A recent study on twins suggests that the first-born twin is more likely to be infected than the second. This has been used as an argument, a very strong argument, that infection is actually acquired at the time of delivery, because if it were in utero, then both twins would be infected. The reason that the first rather than the second is infected is because the first baby to be born usually undergoes the most trauma, going through a birth canal that is not yet dilated. It takes longer than with the second one.

Hughes: You're saying that the baby might contact maternal blood?

Ammann: Yes, the feeling is that maybe the baby swallows blood as it is born and gets infected at that point. If you look at the time you isolate virus in babies, there's a group where you isolate it very early after birth, and there's another group where you don't isolate it until two to three months after birth. So it's felt that the very early isolation of virus is in-utero infection, and the later isolation is [due to infection] when the baby was born. So we don't have a precise answer.

Problems in Drug Approval

Hughes: In that same article--it was really a protest--you called the FDA's delay in approving AZT for use in pediatric AIDS unacceptable.

Ammann: Well, I now know more about the system, and now I don't blame the FDA.

Hughes: Retraction! [laughter]

Ammann: Now that I've had some pharmaceutical experience, I know more about drug approval.[1] The FDA cannot approve something if they're not given something to approve. So the question is, how did it come about that AZT got approved for adults and it didn't get approved for children? And clearly, because the studies were not done in children.

Why weren't they done in children? Well, they were not done for two reasons. One is that the pharmaceutical company didn't go to the investigators and say, "We want to study this drug in children." They didn't do that because it's not easy to study drugs in children, there are a lot more questions to answer, and it's not a big market. Traditionally, pharmaceutical companies will do studies and get a drug approved if its main use is for adults. But they are not very interested in women, pregnant women, or children. So one reason was the pharmaceutical company didn't push to have the study done.

But the reason that bothers me the most is the pediatric community didn't push it. We're going through the same thing right now. I just got back from a meeting in Washington where I uttered the same frustration, except this time I didn't blame the FDA. It's like someone saying, "I didn't get something from you," and you say, "Well, you never asked. If you had asked me, I would have given it to you." The FDA can only approve what it gets. If a study was done in children, and the FDA didn't approve the results, then it would have been the FDA's fault. But they never got the study.

But what's happening now? I pointed out to the pediatricians that we all said when AZT was not approved for use in children until three years after it was approved in adults, we'd never let that happen again. But I want to remind all of you that an AIDS vaccine was tested in adults seven years ago, and not a single dose of a vaccine has gone into a child with HIV infection. We're now talking seven years. So what's going on? My personal feeling is that the pediatric community is not aggressive enough in saying that we want testing done in children: "Give us the drug or else."

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[1]Ammann was a research director at Genentech, a biotechnology company, from 1985 to 1992.

Faulting the Pediatric Community

Ammann: Why are drugs always available later for children than for adults? I think the pediatric community is not aggressive enough. My feeling is that if you had a middle-class, Caucasian population with this disease, there would be parents demanding from physicians, "Why is there no treatment available for my child?" But what you have is [a population that is] orphaned, economically-deprived, lower socioeconomic, prostitute, and IV-drug abusers. People do not become incensed that this population is not getting treatment.

Hughes: This population doesn't have the power structure to affect changes.

Ammann: Yes. But who's defending the children? Has the American Academy of Pediatrics taken a stand on this? No. Child welfare leagues? No. They're just now getting into AIDS. They're just now mentioning it, and I think the issue of pediatric AIDS was a no-no. These children had nobody who spoke for them with rigor.

One of the things that puzzles me the most, because I usually think of pediatricians as being the defenders of children, is that they never took up the cause as they did other issues. Now, some of the reason is that a lot of the pediatricians taking care of AIDS kids are overwhelmed, absolutely overwhelmed. But we're screening for thyroid disease and alpha-fetoprotein for spina bifida and PKU [phenylketonuria], and arguing that screening has got to be done routinely on a state level. These are diseases that don't have the impact and are not present in the numbers of pediatric AIDS cases. Why isn't the pediatric community screaming that we want routine screening for HIV? Why isn't it saying we want treatment for these kids at the same time as for adults?

Part of what I'm doing in my current existence is trying to change that. I'm meeting with the FDA and with legislatures through the Pediatric AIDS Foundation and saying that we, the foundation, want to change the laws for drug testing in children; we want drugs available at the same time as for adults. What's going wrong? What can we do in terms of legislation to make sure that this doesn't continue to happen?

The pediatric community has failed the kids. I'm getting emotional--but I think they have. These are poor kids. A lot of people say, "Well, they're going to die from the disease, and what difference does it make?" It's such a contrast to the other part of the AIDS epidemic involving the gay community, which is very vocal and very demanding, and well they should be. Good for them.

Maybe ACT UP should become the spokesperson for women and children, because other groups haven't been. Children need strong spokespersons because they have nobody to represent them, especially since a lot of these kids have no parents.

Kaposi's Sarcoma Clinic and Study Group

Ammann: My role at the university when the AIDS epidemic began was pediatric immunologist. We were set up in the laboratory to do all of the immunologic studies, including studies of T cells. That laboratory was part of what I had been doing since 1971, diagnosing infants and children who were born with congenital immunodeficiency disorders. There were few individuals at the university who were interested in immunodeficiency disorders because they were considered to be pretty rare and, for the most part, confined to children. For that reason, most of the immunologic tests were done in my lab, including adults with acquired immunodeficiency disease.

Acquired immunodeficiency disease was not a new concept to a pediatric immunologist, because we had been dealing with older children and adults who developed immune deficiency. We didn't know what the cause was, but we assumed that there were some sort of genetic problems. They were very rare but they had very definite characteristics. They usually had low immunoglobulins; they had decreased immunologic function; they were isolated cases; they didn't occur in clusters. I had never heard of Kaposi's sarcoma except as a rarity until Marcus Conant pointed it out.

Marcus called together a group of people to form the Kaposi's Sarcoma Study Group and discuss acquired immunodeficiency. Although Kaposi's sarcoma was new to me, it was not a strange notion that there might be some acquired immunodeficiency disorders. From a scientific point of view, pediatric immunologists had an easier time than other specialists in accepting the fact that there could be such a disorder. From what Marcus told me, I was very anxious to work with them and try to define the immunologic problems these patients had.

Marcus called together myself, Paul Volberding, who was at that time a young assistant professor, and John Greenspan, because John had been seeing a group of patients who had lesions in the mouth. I think Bill Wara was originally involved in the study group, too. He's a radiation oncologist at UC.

We met at the Faculty Club to discuss this disorder that seemed to be arising here in San Francisco but was also being described by Bijan Safai in New York, and then subsequently by Michael Gottlieb in the *New England Journal of Medicine*.[1] I knew Michael from immunology circles because he was an immunologist dealing with adult immunodeficiency diseases. I heard that Michael was seeing cases like we were then finding in San Francisco.

To me, this epidemic was very important, and it was something new. I didn't feel that all of a sudden we could have all of these cases of acquired immunodeficiency because for over a decade the cases that we were seeing were very sporadic and rare, never in this number.

Hughes: So you were immediately alerted that something strange was going on.

Ammann: Yes. People probably won't believe this now, but I remember the very first meeting of the Kaposi's Sarcoma Study Group, because we sat down and said, "What could this be? What could it mean?" One of the very early theories was that it was an infectious agent that was being spread through a homosexual lifestyle, and that if so, this could spread to other people as well. We were just conjecturing, not knowing really what was going to happen, but feeling that the epidemic was going to be very significant.

Hughes: Well, tell me more about the Faculty Club discussions, or was there just one?

Ammann: No, there were several, and then it became formalized as the Kaposi's Sarcoma Clinic and Study Group. I think the initial discussions were: how will we react to this epidemic, who should be involved, what should we do? In California, it became an important group. To this day, we all know what we're all doing, and we feel like we are a family--brothers who had worked through many obstacles.

Hughes: Did you keep attending the KS Study Group meetings?

Ammann: Yes, I kept attending them. Marcus gave us blood samples from Kaposi's sarcoma patients who belonged to the younger, homosexual risk group, and blood samples from older KS patients from the Mediterranean area with classic KS. We performed immunologic

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[1] M. Gottlieb, R. Schroff, H. Schanker, et al. *Pneumocystis carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men. *New England Journal of Medicine* 1981, 305:1425-1431.

tests and showed that you could tell the two groups apart: the first group had immunologic problems, and the latter group had no immunologic problems.

Where we contributed was in showing that KS in the homosexual group was different from classical KS, and that it probably had a different cause. So I kept involved in the KS Clinic in terms of reporting the immunologic aspects of it. Then gradually, as things became overwhelming on the pediatric side, I started pulling back from the adult side, except to continue doing the immunologic evaluations.

Immunologic Studies of AIDS Patients

Ammann: Money for research was a problem, because at that time, this epidemic was not something that people were interested in. And yet, we had to do studies on what this was and define it. My role became defining the immunologic problems. At that time I was in a good position to do this, because I was head of the Pediatric Clinical Research Center at UCSF. One nice thing about clinical research centers is that they have a laboratory associated with them that can be used very flexibly. You don't have to apply for a grant to do studies. So I immediately said, "Okay, we'll study these patients. Send the blood in."

I remember very well the results on the first patient we studied. We had a blackboard in the lab, and we would list the patients by name. Then as the lab got the results, we would write them down. I would walk past the blackboard every day and look up at the board and see what the results were. I remember looking at the board one day and I saw the name of a patient who had virtually no T cells and very low numbers of CD4 cells, a reversed helper/suppressor cell ratio, and hardly any immunologic function. I said to the head technician, "Oh, it looks like we have a new infant with severe combined immunodeficiency disease." Now, that's a genetic disease where the infant is born with virtually no immunity. When I looked at the numbers without knowing who the patient was, that's what it had to be, because I had never seen that degree of immunodeficiency in an adult who had acquired immunodeficiency.

She said, "No, that's not an infant. That's an adult from Marcus Conant's Kaposi's Sarcoma Clinic." So that was the first test that we had run, and that was probably 1981. We gave medical grand rounds on that--"Immune abnormalities in the gay population"--in 1981. There was a tremendous disbelief by people

in the audience that this was really as severe an immunodeficiency disease as the data showed.

Hughes: How could they doubt the data?

Ammann: Well, I think the feeling was that no one had ever seen anything like this degree of immune deficiency in this number of adult patients. Even though the numbers were there, there was considerable doubt. I think you will find that the scientific community is as resistant to new things as anybody else. They don't like things that are very new. Some people almost have to be pounded over the head. As a whole, the scientific community is very conservative, with a large degree of skepticism. I think for the most part that's appropriate, so that things that get into the medical literature are well documented.

Hughes: The Kaposi's Sarcoma Clinic first met on September 21, 1981.[1]

Ammann: Yes. I made a presentation of some of the early results at that clinic in 1981. Of course, we weren't the only ones. By that time, there were patients in New York and Los Angeles, and then Michael Gottlieb also published his cases of acquired immunodeficiency and PCP.[2]

I was dealing mostly with the adults, but at the same time we had children with immunodeficiency. The mindset was, here were the adults with acquired immunodeficiency and here were children with immunodeficiency. Initially they were not thought to be connected. Eventually, however, it was clear that children had an acquired immunodeficiency syndrome similar to that described in adults. This was especially true after we observed AIDS in the three sisters born to a mother with immunodeficiency.

The UCSF Infant with Transfusion AIDS, Fall 1982

Ammann: Then we had this second family, with an infant taken care of in the intensive care nursery, where the child had gotten multiple

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[1] Marcus Conant to William Epstein, Paul Volberding, Magdalen McMullen, Lucy Whybrow, September 2, 1981. Marcus A. Conant. Kaposi's Sarcoma Notebook 1981-2/1982. Conant's dermatology practice office, San Francisco.

[2] Michael Gottlieb et al. *Pneumocystis* pneumonia--Los Angeles. *Morbidity and Mortality Weekly Report* 1981, 30:250-252 (June 5, 1981).

blood transfusions for Rh hemolytic disease. We were asked to see the child, as often happened in immunology. When the neonatologists have a lot of unexplained problems, they ask the immunologists to see the child.

The infant eventually left the intensive care nursery well, but about six months later had gotten ill with fever, diarrhea, weight loss, lots of infection that couldn't be explained, fevers without a cause, and low platelets. We consulted on the child and said that we would perform immunologic studies. We also suggested that they do a bone marrow culture for unusual organisms. Now, this was happening in 1982.

We found the child was immunodeficient. We could not pin a genetic reason to it. About two months after the culture was taken, the laboratory called us and said that the bone marrow culture was growing out *Mycobacterium avium intracellulare*. Well, the first question was, "Why did you call us two months later?" They said, "Well, we've been working with this organism. It didn't grow out until about a month ago, and we didn't know what it was. So we've been trying to identify it, and we finally did."

I said, "Well, I've never seen this in any children with immunodeficiency disease, but it's the same organism as is now being reported in AIDS patients." So we said, "This must be a case of blood transfusion AIDS." That was in the fall of 1982.

Hughes: You diagnosed AIDS just on the basis of the presence of *Mycobacterium*?

Ammann: No, on the basis of an unusual organism in a child who had gotten blood transfusions and was immunodeficient with an unusual form of immunodeficiency. We said, "Maybe one of the blood transfusions came from someone who had AIDS." At that time we didn't know what the infectious agent was.

Now, your question was entirely appropriate, because some of the scientific community said, "Without knowing the infectious agent, how can you prove that this was blood transfusion AIDS?" I agree that it was circumstantial, but we had heard from the CDC in early 1982 about some hemophilia patients that looked like they had AIDS. It was thought that some infectious agent was transfused into them from factor VIII. So we put this information together, and said, "This must be blood transfusion AIDS, but how do we prove it? There's no test; we don't know what the infectious agent is. Well, let's go back and check blood donors, and see if any of them have AIDS."

That would have been a very tricky problem if it weren't for Selma Dritz and Herb Perkins. Herb was always cooperative. I had gone to Herb several times with blood transfusion problems in pediatrics concerning newborns and immunodeficient patients, and he was never a person who dismissed things by saying, "Oh, it's not a problem; don't worry about it." He always investigated things seriously.

In 1971, when I came to the university, we had the problem of graft vs. host disease in immunodeficient patients. As I told you, I had trained in immunology at Minnesota and Wisconsin, and we noted that when you gave children who had no immunity a blood transfusion, they often got a fatal disease called graft vs. host reaction or graft vs. host disease. Basically, when you give a blood transfusion, even though it's a red cell transfusion, there are also white cells in the blood. Those white cells will cause graft vs. host disease. When you give a transfusion to a normal person, their immune system recognizes the foreign white blood cells and it destroys them. So in a normal person there's no graft vs. host disease.

When we presented this information initially in 1971, people accused us of exaggerating the problem. They said that they never saw it in the hospital, and it wasn't until we had five or six fatal cases that people began to believe that graft vs. host disease really occurred.

Well, Herb believed it from the beginning, and he went along with radiating the blood products to kill the white blood cells and to prevent graft vs. host disease. He agreed that any patient suspected of having immunodeficiency disease should receive radiated blood. People across the country were critical of us. They wrote letters to journals that the problem of graft vs. host disease was exaggerated, and that blood banks shouldn't have to go through the extra expense of radiating blood products. Ten years later it was a deja vu with people saying that we were exaggerating the risk of blood transfusion AIDS.

About ten years later, the AIDS problem occurred, and I said, "Herb, I think that this immunodeficient baby may be a case of blood transfusion AIDS. Can we somehow find out the history of the donors and whether or not they have AIDS?" He said, "Well, we have the list of donors. Why don't we talk to Selma Dritz and have her cross-check it with her registry of people who have AIDS? We will keep the names confidential."

And that's what she did. One of the donors had AIDS. By the time they eventually tracked him down, he had died. But at the time he had donated blood, he was not known to have AIDS. This

child was about two years old in '82, so he was born in 1980. AIDS was just being picked up then. We felt that this was a very important observation. We couldn't prove that it was AIDS, but there was just too much circumstantial evidence there to ignore it.

We called the CDC, and wanted to have it published in the *Morbidity and Mortality Weekly Report*. The CDC sent out Harold Jaffe. He came to the office, and he went through all of the records that we had, including those of the three girls who we felt had AIDS from the mother, and the blood transfusion case. He meticulously went through the records, looking at the CD4 counts, the immunologic tests. He matched all of the blood donors against known AIDS cases. He didn't want to make a mistake.

Publication Problems

Ammann: Jaffe talked to Herb Perkins and to Selma Dritz to make sure that the blood donor numbers and names correlated with patients with AIDS. He was convinced that it was a case of transfusion AIDS. He agreed that we should put it in *Morbidity and Mortality Weekly Report*. Then he said kind of casually, "You know, if you publish it there, it may jeopardize your publishing it in a medical journal, because some of the journals," i.e. the *New England Journal of Medicine*, "will not publish anything that has prior publication. Let me go back and talk to Jim Curran about this, because you may, for your own personal reasons, not want to put it in the *Morbidity and Mortality Weekly Report*."

I said no, I thought we had to get the information out as soon as possible. So Jim Curran called me back and said that he had talked to Arnold Relman, the editor of the *New England Journal of Medicine*. He played a major role in terms of AIDS publications. In any event, Relman said that it wouldn't jeopardize publication, so we went ahead and published it in *Morbidity and Mortality Weekly Report* in '82.[1]

Then I wrote it up as an article to publish in the *New England Journal of Medicine*, and it came back rejected. The reason given was that they didn't feel there was sufficient documentation that this was an AIDS case in the child. My feeling

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[1] A. J. Ammann, M. J. Cowan, D. W. Wara, et al. Possible transfusion associated acquired immunodeficiency syndrome (AIDS). *Morbidity and Mortality Weekly Report* 1982, 31:652-653.

was that Relman was not abiding by what he had said. The case was published in the *Morbidity and Mortality Weekly*, and he didn't want to publish it in the *New England Journal* in spite of its importance in questioning the safety of the blood supply.

I felt that this information had to get out, because if the agent causing AIDS was transfused in blood transfusions, then AIDS could be transmitted to thousands of people. There are literally millions of blood transfusions given each year.

We decided to submit the article to *Lancet*. The editor of *Lancet* wrote back that it was a very interesting article, but it really should be published in an American journal because it was an American problem. So I wrote back to them and said that the *New England Journal of Medicine* had actually rejected it, because they didn't feel it was sufficiently documented, but that we felt that it was important enough that we needed to have it published in a journal with an international distribution. Interestingly enough, they accepted that explanation and they published it. So instead of '82, it was published in early 1983.[1]

Well, that's the beginning of my involvement in the AIDS epidemic. I got pulled into it at first from the adult side by performing immunologic tests, and then realized that we were seeing pediatric patients where AIDS was transmitted from the mother. Almost simultaneously, children with AIDS were being described in New York City; Newark, New Jersey; and Miami.

Hughes: Were you aware that others were interested in the problem of pediatric AIDS?

Ammann: Yes. I don't remember now how I had heard, but other pediatricians were seeing similar problems.

Cold Springs Harbor Conference on AIDS, Winter 1983

Ammann: In fact, in '83 [looking through papers] Ayre Rubinstein and I were invited to a Cold Springs Harbor symposium on AIDS. Arye Rubinstein and I were asked to be there because, by this time, people were aware that we were describing the same thing in pediatric AIDS as in adult AIDS. At this meeting was Luc

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[1] A. J. Ammann, M. J. Cowan, D. W. Wara, et al. Acquired immunodeficiency in an infant: Possible transmission by means of blood products. *Lancet* 1983, 1:956-958.

Montagnier whom I didn't know anything about, [Robert] Bob Gallo whom I had never heard of, Sam Broder whom I didn't know, and Lawrence Drew from San Francisco, and a bunch of other people. It was a very small meeting in the middle of winter.

Hughes: Was there any particular focus?

Ammann: Well, the focus was AIDS.

Hughes: But other than that?

Luc Montagnier and Robert Gallo

Ammann: This was the famous meeting where Montagnier showed an electron micrograph of what he thought might be a virus that he had isolated from blood cells of patients with AIDS. I was very naive; I didn't know about the competition that was going on between Gallo and the French to discover the virus. But I remember a conversation in the hallway. Sam Broder and Gallo were talking intently, and I remember Gallo saying, "I'm going to be the one that discovers this virus!" And I thought to myself, "And who is this person?" That conversation occurred right after Montagnier showed the electron micrographic pictures of a retrovirus.

Hughes: You were soon to find out! We all were.

Ammann: Yes, I was soon to find out. Arye's job and mine was primarily to present the pediatric portion of AIDS.

New York Academy of Sciences Meeting on AIDS, November 1983

Ammann: The next meeting where we officially presented pediatric AIDS was the New York Academy of Sciences meeting which was on AIDS in women, hemophilia, Kaposi's sarcoma, kind of the whole picture. It was the first really big meeting of scientists where the issue was being discussed from all perspectives: clinical, etiological, and so on. Jim Curran was also at that meeting. I presented AIDS in pediatrics.

That was the meeting where Bob Good, my previous mentor, got up after my presentation of pediatric AIDS and said, "I don't

believe any of this. We have seen immunodeficiency over the years in infants that have cytomegalovirus infection."

Hughes: Immunodeficiency as a result of cytomegalovirus?

Ammann: Yes. So in the question and answer period, I pushed him, and basically asked him, "Have you specifically seen immunodeficiency due to cytomegalovirus where you have elevated immunoglobulins and depressed T-cell immunity?" And he said yes.

At a subsequent meeting some six months later when he asked the same questions after a presentation, I said, "Dr. Good, I asked you for documentation of what you've seen before, and you've not given me any, nor has anyone else." He subsequently reversed the statement he had made, because, in fact, he had never seen this before and could not document it. He was going on his memory. [gets paper] That was this meeting. [Society for Clinical Investigation, 1984]

This meeting was in '84. You remember that the test for HIV really didn't come until two years after the virus was discovered in 1983. Routine testing for the virus was not available until 1985, March of '85, I think it was.

Transfusion AIDS

The Blood Banks

Ammann: By 1985, I was involved in a fairly extensive program of screening recipients of blood transfusions from donors that had AIDS. Because antibody testing for HIV was now available, Herb Perkins was doing a study to see how many transfused patients had gotten HIV infection. After performing immunologic studies, I noticed that many of the blood transfusion recipients had symptoms of immunodeficiency: their CD4 cells were low, and they had decreased CD4/CD8 ratios. I was again convinced that we were seeing a significant number of patients with "AIDS" but they could not be called AIDS because they did not fit the CDC definition of AIDS. If the CDC definition of AIDS was used, the numbers seemed smaller. I felt they were larger because of all the patients with immunologic abnormalities.

The resistance of the blood banks in admitting that blood transfusion AIDS was a major problem was related to the political ramifications of it, the scientific ramifications in terms of what blood banks had to do, what physicians had to do to make the diagnosis and the liability implications. It was just too new and too much for them to accept this readily.

Hughes: Randy Shilts' book [*And the Band Played On*] is critical of the heads of certain blood banks, particularly the head of the New York Blood Center who was slow in accepting that AIDS could be transmitted through blood and blood products.[1]

Ammann: The Red Cross was very resistant, too.

Hughes: Was that for economic reasons?

Ammann: Yes. I had gotten involved with the blood bank industry in this debate. I started using the term, "blood bank industry," because it was clear that most blood banks (Irwin Memorial excluded) were protecting their industry rather than their clients.

The Kushnick Family

Ammann: Helen and Jerry Kushnick lived in Los Angeles, and they were in the business of managing entertainers. About the time pediatric AIDS was being described--this was '83--they had twins who had gotten blood transfusions at Cedars-Sinai Hospital in Los Angeles.

They called me late one night because their son was in the intensive care unit with *Pneumocystis carinii* pneumonia. He had a history of blood transfusions. They had called Arye Rubinstein to see if he could fly from New York to see their child. He didn't want to fly to Los Angeles, but they kept checking around and finally called their cousin, Ted Kushnick. It turns out that Dr. Kushnick was my professor in medical school, and he said, "Well, a former student of mine in San Francisco is an immunologist. Why don't you call him?"

The Kushnicks called me, but I had a bad case of the flu. I remember I really felt awful. But I agreed to take a plane to Los Angeles that night and see their child and go through the records.

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[1] See for example, pp.410-11, pp.433-34. (Randy Shilts. *And the Band Played On: Politics, People, and the AIDS Epidemic*. New York: Penguin Books, 1988.)

Until two o'clock in the morning I went through the medical records, and it was all there again. It was like our first case: multiple transfusions in the nursery, low CD4 counts, immunodeficiency, *Pneumocystis carinii* pneumonia, and a perfect control--not just an identical twin, but a twin who had gotten multiple transfusions. One twin had grown well but her brother, who I had seen in the hospital, had multiple infections and was growing slowly. They had been very concerned about the twin who was growing well but had been told that they were "over anxious."

Hughes: How could you reassure them?

Ammann: You couldn't. Actually, they were experiencing one of the hazards that I think wealthy people often have with their medical care. Their physicians are afraid to tell them the truth or to treat them like "normal" people. In the end they don't get as good care as someone else, and that's I think what was happening. I didn't want to tell them that things were really not going well, but my conclusion was that the child had AIDS. I flew back home that night. Jerry called me later in the day, saying that Sam had died about six hours after I'd seen him.

Then the Kushnicks got into the blood transfusion AIDS controversy, because I started telling them the resistance in believing it. They had access to the Donohue show, the Good Morning America show, the CDC. Helen and Jerry went on a vigorous campaign, using their connections in Los Angeles and making public the fact that the blood banking industry was not paying attention to the fact that you could transmit AIDS by blood transfusions.

Hughes: When do you suppose this was?

Ammann: This started in '83.

Screening Blood and Blood Donors

Ammann: The blood bankers began listening to the scientific evidence, and they realized that indeed they had a problem; they had to start doing something about it. And that's when other methods of screening blood started. T4 cell screening, which was done by Edgar Engleman at Stanford; Herb Perkins looking at hepatitis core antibody screening to try to pick out high-risk donors, and taking the medical history of blood donors to find out if they had any risk factors for AIDS. At that time the risk factors were drug abuse and homosexuality. And that was a big controversy: Could

you ask someone's sexual orientation? Some blood banks didn't want to do that.

Hughes: I've read that the members of the gay community, particularly in San Francisco, are avid blood donors, and blood bankers were reluctant to designate homosexuals as a risk group for blood donation.

Ammann: Yes. In fact, I think Randy [Shilts] goes into that somewhat in his book,[1] showing that the homosexual community was particularly good about donating blood. Because no one knew what the cause of AIDS was at that time, something that was meant to do good became a tragedy.

Los Angeles, where the Kushnick child got AIDS via a blood transfusion, had an enormous number of AIDS cases from transfusions. The blood bank of Cedars-Sinai Hospital was located in the gay community of Los Angeles, so they had a large proportion of donors that were HIV infected.

The hospital was resistant to looking into that. Cedars is a private hospital where all of the wealthy and the famous of Los Angeles go. They had major problems, not wanting to believe that any of their patients got AIDS through blood transfusions. They said, "We don't believe this at all," until the evidence became overwhelming. Further, they didn't want their hospital identified as having a high rate of blood transfusion AIDS.

Hughes: The KS Study Group was petitioning on this subject, trying to get more publicity and some action from the blood banks. Do you remember any of that?

Ammann: No, I wasn't actually part of that.

More on Pediatric AIDS

Delayed Epidemic in San Francisco

Hughes: Well, how did the flow of pediatric AIDS cases go?

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[1] See *And the Band Played On*, pp.238-239.

Ammann: There were geographical differences. In the San Francisco area, most of our cases were blood transfusion AIDS, for reasons that are still not understood clearly. HIV infection in intravenous drug abusers did not enter San Francisco until three to four years after it became a major problem on the East Coast. I was in contact with Arye Rubinstein in the Bronx and Jim Oleske in Newark, New Jersey, and it became apparent that they were seeing something like five to six cases of pediatric AIDS compared to every one that we saw. They had many more mothers who were IV drug abusers. So the pediatric AIDS epidemic on the East Coast escalated much faster. It wasn't until HIV got into the drug abusing population on the West Coast that the cases began to escalate here.

Mostly what we were seeing in San Francisco initially was due to blood transfusion in children. But then we had one family, which I've already mentioned, where the mother acquired HIV so early we could really understand what the source might have been. We calculated that she must have been infected with HIV in 1976. Why she got HIV so early on, we never understood.

Hughes: She could have had a bisexual relationship.

Ammann: It could have been bisexual, or it could have been intravenous drug abuse.

AIDS in Haitian Children

Ammann: By '83, it was apparent that there was yet another group at risk for AIDS, and that was the Haitian population, which people couldn't understand because the Haitians with AIDS denied IV drug abuse and they denied homosexuality. A lot of people said, "Well, that's impossible, because AIDS can't be transmitted heterosexually." So for a long time, the CDC had Haitians as a separate risk category. It was finally taken out. But that was separate because it wasn't understood. In Miami, Gwen Scott was the pediatrician who began seeing AIDS cases in Haitian children.

By '84, I think it was well accepted in the pediatric community that there was pediatric AIDS. And in '85 there were several meetings on immunodeficiency where part of the program was on pediatric AIDS, even before the blood test became commercially available in March, 1985.

Testing Serum Samples for Pediatric AIDS

Ammann: And when the blood test became available, then we worked with Jay Levy first. We went back and tested all our stored serum samples on our immunodeficient patients to see if any were HIV positive. I had samples going back to 1966. I went back and tested all the serum samples prior to 1981, and found that we had no positives for HIV in these immunodeficient patients over a period of twenty years. We concluded that HIV-associated pediatric immunodeficiency was a new disease.

We felt that we had confirmed with that data that pediatric AIDS had not occurred prior to 1980. In '85, you had the test for HIV. Then everyone began accepting the existence of pediatric AIDS.

Hughes: But it took several years.

Ammann: Yes, it took from 1982 until '85, three years, before people really began believing that AIDS could occur in children.

Publishing on Pediatric AIDS

Hughes: Were there problems in getting papers published on pediatric AIDS?

Ammann: Yes. In fact, in the very first paper that we published on a family with AIDS, we could not call it AIDS in the article, because the reviewers wouldn't accept it. [looking at bibliography] It was the paper that was published in *Pediatrics* in March 1984, and it was called "Maternal Transmission of Acquired Immunodeficiency Syndrome."[1] What we had to do here was suggest that the cause might be Epstein-Barr virus, because the reviewers of the article would not allow us to speculate that this might be transmission of an agent that was occurring in the adult acquired immunodeficiency syndrome.

So we called it acquired immunodeficiency without suggesting that it was similar to adult AIDS. Well, here: [reading] "In this report we describe three female children who are half-siblings whose mother is a prostitute and drug addict with

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[1] M. J. Cowan, D. Hellman, D. W. Wara, et al. Maternal transmission of acquired immune deficiency syndrome. *Pediatrics* 1984, 73:382-386.

laboratory and clinical evidence for AIDS. The two children have diffuse lymphadenopathy and chronic Epstein-Barr virus infection. All three children had candida. Two children have died, both of *Pneumocystis carinii* pneumonia." And that's all we could speculate. So we had to be very conservative.

Hughes: And what had you wanted to say?

Ammann: We wanted to say that these conditions in the children might have been due to transmission from the mother of an infectious agent that was the same as that causing the adult acquired immunodeficiency syndrome. That's really what we wanted to say.

Hughes: Why did the reviewers refuse to allow you to do so?

Ammann: Well, again, there was no HIV antibody test in 1983. Since you could have acquired immunodeficiency in multiple children due to inherited disorders--we had described that before--that wasn't due to an infectious agent, they said, "You haven't proved anything." And we hadn't. But the point was that we had proven the three sisters were half-siblings. So from a genetic point of view, to have three children with immunodeficiency each with a different father made no sense, because there's no disease transmitted via the mother to all three female infants.

Considering Causal Agents

Hughes: Did you actually think that Epstein-Barr was a possible cause of AIDS?

Ammann: No. We didn't think it had anything to do with it.

Hughes: Why not?

Ammann: We had never seen any immunodeficiency associated with EBV except what's called Dunkins syndrome. Patients with Dunkins syndrome will get fatal Epstein-Barr virus infection. But we had reviewed those cases, and basically found that they got hypogammaglobulonemia, low immunoglobulins, but their T-cell immunity was not destroyed. This was the reverse phenotype of what we were seeing in AIDS, where you have elevated immunoglobulins and low T-cell immunity.

Hughes: Did you have an hypothesis about etiology?

Ammann: Yes. We felt AIDS was due to a new virus. I can't give you the date, but this was before I knew that Jay Levy was working on the virus, so it had to be early in the AIDS epidemic. It had to be like '82. I called a very well-known investigator at UC, who subsequently won a Nobel Prize for his work on retrovirus, and I said, "We've never talked before, but I'm working on acquired immunodeficiency syndrome in adults and in children. I have blood and spleens and lymph nodes frozen in the freezer. These people died of acquired immunodeficiency syndrome, and it's got to be due to a virus. I understand that you can isolate viruses. Can you help me try to identify a virus?"

There was a pause on the phone, and the comment that came back was, "It sounds like a very interesting problem, but I don't believe there's going to be any money in it."

Hughes: And that was the end of it?

Ammann: Yes, that was the end of it.

I had worked with Larry Drew, and initially we thought, well, maybe it was cytomegalovirus. But nothing panned out. Larry told us that 60 or 80 percent of the adult patients with AIDS had cytomegalovirus, but when we tested our infants who we thought had AIDS, we found cytomegalovirus in only a few. So I didn't feel it was cytomegalovirus. I thought it was some other agent.

The only clue was this Epstein-Barr virus infection, but when we tested our blood transfusion AIDS patient, he didn't find Epstein-Barr virus. So we said, "It's not cytomegalovirus. It's not Epstein-Barr virus. It's got to be some new virus," because I had never seen this syndrome before.

Recognizing Pediatric AIDS

Hughes: Dr. Ammann, I am interested in hearing how pediatric AIDS patients were treated.

Ammann: I think there were some differences between the treatment of children and adults. And there were differences between how the children were treated in San Francisco and in other areas of the country. So let me first address how the care of children with AIDS evolved.

As I've said, immunodeficiency was not a unique concept to the pediatric community, because we had been dealing with children

with immunodeficiency as a result of a genetic disorder. They were susceptible to infection, and they had *Pneumocystis carinii* pneumonia, and they would get other opportunistic infections. They had failure to thrive.

The discovery of pediatric AIDS came about because these children were being referred because of their symptoms to pediatric immunologists. The first three descriptions of pediatric AIDS came from San Francisco, Newark, and New York. I was seeing the immunodeficient patients in San Francisco, Dr. Jim Oleske in Newark, and Dr. Arye Rubinstein at Albert Einstein. We were all pediatric immunologists. Recognition of pediatric AIDS came about in the same year [1982], on the East Coast because of drug-abusing mothers, and in our case because of blood transfusions resulting in an AIDS-like syndrome.

Infection Control

Ammann: The first cases that we discovered were in very young children who had classic clinical symptoms of immunodeficiency, so they came to our immunodeficiency clinic. When they were hospitalized, they were hospitalized in the clinical research center or on the hospital ward of Moffitt Hospital, just like any other immunodeficient patient. There was no concern on the part of the staff about taking care of them, because for a decade, they had been taking care of immunodeficient children with the same clinical manifestations, but, of course, a different cause.

Children with AIDS had *Pneumocystis*, so we would isolate the children to protect them against infection, but not to protect other patients or staff from possibly getting some sort of infection which the children might have. And when the blood came into the laboratory to be studied by immunologic tests, it was handled the same way as we had done it for ten years. There were no special precautions taken. The cells were separated under an isolation hood, but we were doing that anyway because we didn't want to contaminate their cells with infectious agents from the air. It was more to protect the patients' cells from getting contaminated than to protect the people working with them, so people took no special precautions. The children with AIDS in San Francisco got medical care and management equivalent to that of any other immunodeficient child.

Now, you can ask, well, when they were found to be HIV-infected, when the virus was discovered in 1984, and then testing began in 1985, we could prove that the cause of the

immunodeficiency was HIV, did anything change? Well, at that point, AIDS had been around for a while, so there was no drastic change, except the hospital staff and the laboratory technicians now realized that infection through accidental inoculation was a possibility. So they took more caution; they wore gloves. Prior to this time, they did not wear gloves. But in spite of the fact that we took no special precautions, I know of no one to this day who got infected either from working with the blood products of the child or taking care of the patient.

Hughes: Before the actual isolation of the virus, people had suspected that the cause of AIDS was an infectious agent. Why weren't they more concerned?

Ammann: I think the general feeling was that patients get infection and they get over it. The entire field of medicine had gotten to a point where we no longer believed as seriously in the problems of infectious diseases as we used to. Infectious diseases services had dwindled, because a lot of diseases were prevented or were treatable. There used to be infectious disease wards--San Francisco General had a TB hospital that was closed, although it may be opened again. People got cocky about infectious disease. Physicians were not washing their hands as much as they used to and precautionary procedures were not being taken as much. People were becoming very cavalier.

Then the AIDS epidemic hit. But I think it took a while to sink in that perhaps you could get this virus, which might be lethal. With the long incubation period, you couldn't prove that someone had the virus before the test came out in '85. So there was nothing to alarm people, even though you knew that this was a virus. I also think that most people felt that you could only get AIDS if you were a drug user or homosexual.

Hughes: Yet the public response in certain areas has been exaggerated. I'm thinking of the HIV-positive children excluded from schools.

Ammann: Our approach, when the children got old enough to go to school, was that we didn't tell anybody they were HIV infected. That was somewhat of a risk on our part, because you could say, "Well, suppose there was transmission from this child to another child?" We were aware of how children were being isolated and ostracized in the Midwest, Florida, and New York. We were saying as scientists that this disease was not easily transmitted in a casual manner, and so there was no reason to not go to school, nor was there any reason for us to tell anybody that this child was HIV infected. We were more concerned about the school telling us whether chickenpox was in the school, to protect our patient, than the risk of our patient giving HIV to another child.

Hughes: How could you ask for that information without indicating that the child was HIV infected?

Ammann: We had other immunodeficient patients where we said, "This patient has immunodeficiency, and we feel he may be susceptible to chickenpox. We would like to know if there's chickenpox in the school." We had been doing that for over a decade. So we never said that these patients with AIDS were any different than our other immunodeficient patients. We wouldn't allow it to be raised as a question, because we saw what the media was doing. To me, the media was the villain.

Using Children as Scapegoats

Ammann: I have my own theory on this, but it's a theory only. My feeling is that a lot of people believed that AIDS was indeed contagious. They didn't believe science. People really were angry at the gay community, but they couldn't publicly come out at the gay community, because the gay community was very politically organized and it was dangerous to attack. So, instead they attacked this vulnerable population of children which couldn't defend itself.

I think that the media contributed to that, and they recognized that they could come in with their cameras and their videos and on national television say, "Here's a child with HIV infection going to school, and what's your opinion about this?" But you never saw the cameras following an adult saying, "Here's an HIV-infected adult going into the workplace. What do you coworkers think about it?" They couldn't do that, they couldn't attack adults, so they used the children. To me, it was a very insidious thing that I think created tremendous trauma to the children and to their families, perpetuated by the press. While the adult HIV-infected population enjoyed confidentiality, children's confidentiality was being violated repeatedly.

Hughes: It's interesting how the child seems to have been manipulated from both sides. I have read criticisms of the pediatric AIDS movement on the basis that it was shifting focus from less socially acceptable segments of the community with HIV to children whom everybody is supposed to feel sympathy for. The shift was obviously detrimental to the other risk groups.

Ammann: Yes. Last year, the Pediatric AIDS Foundation was criticized in a magazine article in *Lear's*. It wasn't a direct criticism of the foundation. It just said that it was easier to give financially

to a foundation that was doing research in pediatric AIDS, because people wouldn't give for research in gays, but they would do it for children. Because I work with the Pediatric AIDS Foundation, I was concerned about that, and I spoke to a lot of activists, basically saying, "We all know that if there is a cure or a new treatment in the adult area, it will benefit children, and we know that if it's in children, it will benefit adults. Let's not allow our community to be split." And to the credit of everybody in the community, people said, "We're not going to say, `This is a gay disease; this is a pediatric disease.' This is a disease that affects everybody--heterosexuals, homosexuals."

There was a rebellion in the gay community when people would say, referring to children with AIDS, "The innocent victims of AIDS." I still feel that children are innocent in the same way we feel children are innocent in an automobile accident. They're not driving the car; they're innocent victims. But I can understand what using that terminology meant to people, as if this meant that there were major differences in the disease, and who was responsible for the disease.

So you're right; it was played both ways. But in terms of medical care, I think here in San Francisco, it worked. In Florida and in New York, it was a big problem. The children were put in separate wards in the hospital; they were not adoptable; they weren't allowed to go to school.

Hughes: You mean legally they weren't adoptable?

Ammann: No, I think because there was so much of an issue made of the fact that they were HIV infected nobody wanted to take care of them. In addition, there were so many more HIV-infected children on the East Coast that it was very difficult to find the resources to take care of them. Usually the children in California found foster care very easily, maybe because the social service system in California, at least at that time, was fairly organized and used to dealing with a lot of chronic disease--better ratio of social workers to clients and so on.

Hughes: Foster care was arranged with full understanding of what the implications could be of taking care of HIV-infected children?

Ammann: Well, initially, no, because no one knew what the cause of AIDS was. But once they were known to be HIV infected, then the foster parents were told that it was an HIV-infected child.

Hughes: Were they given training?

Ammann: Yes. They were told the care they needed to give and the precautions they needed to take. As far as I know, a lot of the foster parents kept the children. After they found out they were HIV infected, they didn't say, "Well, I'm not going to take care of them any more."

Issues Raised by HIV Antibody Testing

Hughes: What steps did you take after a child with HIV infection was first presented to you?

Ammann: Once a child was identified as being HIV infected, he became eligible under the California Children's Services for special care, because he had a chronic disease.

Hughes: But wasn't the testing ambivalent?

Ammann: Yes, at least initially. The problem with the early testing was that it was antibody testing only. So if you had a child who was over nine months of age, the mother's antibody would be gone, and so if the antibody test was positive, you knew the child was infected. But if you had an infected child in the family, and now you had a newborn child, then the problem was that the antibody test of the newborn would be positive because of the mother's antibodies, but you didn't know if the baby was positive.

We developed a series of steps to go through that would allow you to make an early diagnosis or a presumptive diagnosis. There was mixed feeling in the community. Before AZT was available, people said, "Well, what difference does testing make? There's no treatment available for the children."

But then when treatment became available, it became important to make an early diagnosis of HIV infection. Antibody testing, though, could only be used with certainty sometime around nine months of age, and a lot of the children were sick before then. So basically you made the diagnosis on clinical grounds: if the child had a very low CD4 count, or if the child had *Pneumocystis carinii* infection, well, you knew the child was immunodeficient and had HIV, and then you just waited until he was nine months of age to prove it.

Diagnostic Tests: Viral Culture and the Polymerase Chain Reaction [PCR]

Hughes: Would you treat before nine months of age?

Ammann: Once AZT was available, most physicians would begin to treat if you had a child where you were certain of the diagnosis, based on clinical grounds and laboratory studies. As some of the more sophisticated tests became available, like viral culture and PCR testing, then that began to change things because you could say, "Well, this infant has a positive antibody. Let's culture the blood for the virus, and if the virus is there, then the baby is infected." Or if the PCR were positive. But these are developments that weren't around at the beginning of the epidemic; viral culture didn't really take hold until about 1986. And there wasn't as much testing done in infants, because viral cultures are very long and expensive tests to do, and they weren't readily available. PCR testing has only been available for the last three years.

Hughes: Was viral culture an outgrowth of work in Robert Gallo's laboratory?

Ammann: Gallo was not interested in viral culture as a diagnostic. Jay Levy had a lot to do with it, because he was the one culturing virus here [at UCSF], and he got some of the first positive cultures in infants and children. So we were very dependent on Jay for doing a lot of those cultures in children. But they took a lot of blood, so the method wasn't geared for doing widespread testing in children. You really didn't do it unless you had a really difficult case. Now PCR testing seems to be the fastest and easiest to do. It is usually positive in infants by two months of age.

Impediments to Research in Children

Ammann: We had just as many problems in treating children as in diagnosing infection. For example, how long do you wait before you start treatment? Since there were so many fewer children with HIV, we didn't have the extensive clinical trials as in adults to give some of these answers. We didn't even know what the normal CD4 cell count was in children.

Here in AIDS we were dealing with the immune system, and we knew in normal infants and children that their immune systems

changed as they got older. The newborn infant has a very high CD4 count, and it falls naturally. There's a rate of decline that occurs over the first six to nine months, and then it begins to level off. Well, a falling CD4 count in an adult indicates severe disease. So if you have a falling CD4 count in the infant, and you don't know what the normal rate of decline is, then is the disease progressing rapidly? Or is it static? There was no normal data, and it was impossible to get normal data, because none of the human subjects committees would let you draw blood on normal infants and children to get the data.

Hughes: Even after the recognition of pediatric AIDS and the need for such standards?

Ammann: Yes. So most of the data came from children who were having blood tests done at the hospital for other reasons, like they would come in for surgery or for minor illness, and they turned out to be normal. It took years to get that data. It really hampered pediatrics, as did the failure to recognize that, for the benefit of all children, we needed to get some normal data. What's a blood stick to get some cells so that you can benefit everybody? I think parents would give their permission to do that.

Hughes: Do you remember any of the arguments against doing that?

Ammann: Well, there was the general argument that you couldn't do studies in children just for the sake of doing research. There had to be some benefit to <u>that</u> child. So the argument was, if doing a stick to get blood is of no benefit to that normal infant, then you can't do it. It was that simple. So there was no altruism: parents couldn't volunteer their child for the future benefit of mankind.

Evaluating Drugs for Children

Hughes: Was using a drug in infants that presumably had only been tested in adults a problem?

Ammann: This is an interesting paradox. All of the experience with pentamidine and Septra for *Pneumocystis* pneumonia came from studies on children--immunodeficient children, children with leukemia--because prior to AIDS, adults didn't get *Pneumocystis carinii* infection. And there was no requirement that a study had to be done in adults for adults to use it.

Hughes: So drugs moved from child to adult with no problem, but not the other way.

Ammann: Yes, that's the paradox. It's absolutely incredible that society and pediatricians and the American Academy of Pediatrics and the groups that supposedly represent children stood by for three years while AZT was used to treat HIV-infected adults but was not available for HIV-infected children.

In 1962, new FDA rules were instituted which were meant to protect children. What they required was that before a manufacturer could say that the drug could be used in children, he had to do studies in children.

Now, people overinterpret the regulation as meaning efficacy studies; you had to prove the drug worked in children. And that's not really what those guidelines said. They were talking more about safety in children. But because of that interpretation, people said, "Well, you've got to protect children," and here children were dying because they couldn't get a drug. So I don't know what they were protecting against. It's a very strange concept.

I had a meeting with Dr. [David] Kessler [commissioner of the FDA] and some legislative aides to address the issue of exactly what needs to be done to get drugs to infants and children with a life-threatening disease. The FDA has been very progressive in this area. The FDA says, "The intent is to get drugs into children as early as possible for life-threatening diseases." So if the disease has the same cause and if the clinical features of the disease are similar in adults and children, then all a drug company has to do is the safety and the pharmokinetic studies, so that you know what dose to use in a child. You don't have to show the drug's efficacy. The AZT experience doesn't have to be repeated, if people keep that in mind.

There is still a problem, however. Why would a drug company want to do studies in children? The market is not big; it's going to cost them money; it might delay the development of the drug in adults. So the way it's phrased now, it's up to the goodwill of the pharmaceutical company to test in children, and they may choose not to do it. The challenge is to find a way to encourage pharmaceutical companies to test these drugs in children, and I would add women, because the safety of drugs is not thoroughly evaluated in women either.

Hughes: Do drugs act differently in children and women?

Ammann: Well, children for sure, because you've got the dose and metabolism problem. There are many, many examples of drugs acting differently in children, for example, chloramphenicol, an antibiotic which was often lethal to infants because they metabolized it differently. There are also examples of drugs in women behaving very differently.

Hughes: You told me that pediatric AIDS progresses in a different fashion than adult AIDS. Therefore, isn't a drug going to have a different effect in a child and an adult?

Ammann: You're correct on the progression; that's been an argument. But all of the ways that it's different suggest that we should evaluate the drug in children first, rather than last. Because the disease progresses more rapidly in children than in the adult population, clinical endpoints could be evaluated more quickly in children.

If you want to do a study of clinical endpoints in a person who's already on a drug, as most adult patients are, the study might take two to four years, with thousands of patients. If you had a population where the disease progressed rapidly to clinical endpoints, you could do the study faster with smaller numbers. The pediatric population would be where you want to do that.

Another example is AIDS dementia. It's known from the first study of AZT in children, by Phil Pizzo at the National Cancer Institute, that children have reversible dementia, which occurs more dramatically than in the adult population.

Hughes: You mean, the dementia is more extreme in children?

Ammann: It's more extreme, and it's more easily reversible than in the adult. Probably it's more extreme because the developing nervous system is affected by HIV. But children recover better. We don't know the explanation for it.

Testing Vaccines in Children

Hughes: Do some of these distinctions also apply to vaccines?

Ammann: Well, vaccines are another area where we've got a paradox, as Sam Katz pointed out. Sam Katz was chairman of pediatrics at Duke University, and he's a very senior infectious disease person who's worked with vaccines and infectious diseases for years. Sam spoke at the international AIDS meeting in Amsterdam in 1992. He

pointed out that AIDS vaccine testing is probably the first instance in the history of vaccines where the studies were not first done in children. Almost every vaccine that you can think of has been tested first in children and then it moves to the adults.

Now, is it logical? Well, no, because under what circumstances do you have a known exposure? Do you know who the person is that's transmitting the virus, the period during which exposure occurred, and then have the opportunity to follow the exposed person to determine if infection occurs?

Now, here's a situation: the mother is HIV infected. She may or may not transmit the virus to the infant. You know that the infant is going to be exposed, and you know that a third of the infants are going to become infected. So here's an ideal population where you know 20 to 30 percent are going to become infected.

Well, the CDC looked all around the U.S. for a population with a very high HIV transmission rate to be studied for a preventive vaccine to see if it works, and the biotechnology companies talked to people and had meetings. Some of us kept saying, "Look at mother-to-infant transmission." The most you can come up with in the United States is about a 3 to 4 percent transmission rate in adults, which is in young, very sexually active adults that go to sexually transmitted disease clinics. But these percentages translate into a study of thousands of patients, whereas 30 percent transmission translates into a study of about 800 subjects.

Theories about the Cause of Adult AIDS

Hughes: You said at the outset of this discussion that in the very first meeting at the Faculty Club, you and the rest of the Kaposi's Sarcoma Study Group suspected an infectious agent. Was there evidence for that early on?

Ammann: In this epidemic, there were two things that initially appeared to be common. One was homosexuality, and the other was something linking the disease to blood or blood product transfusion. And that was the hemophilia and intravenous drug abuse stories that began emerging fairly early. I don't think there are mysteries in medicine. I think mystery is too strong a word. There are problems that arise in medicine that may look mysterious

initially, but usually when you work them out, they're very logical.

I think that the AIDS epidemic was very much the same way. Initially it was felt that some drug was causing AIDS. I was aware that there was some evidence in the literature that drugs could cause immunodeficiency. I guess the reason I never got excited about that hypothesis was because I had looked at anesthesia and radiation fairly intensively in terms of their effect on the immune system. We had also performed immunologic tests on patients who had been treated for cancer.[1] But out of all of those studies that we had performed over ten years, none of the immunologic phenotypes we observed were that of severe T-cell deficiency with elevated immunoglobulins.

Hughes: So it was the combination--

Ammann: Yes, so the combination of depressed T-cell immunity and elevated immunoglobulins, and the fact that there was a group with AIDS that wasn't using drugs. So if it wasn't drugs, and yet intravenous drug abusers and homosexual patients were getting the disease, then it had to be an infectious agent. I think most of the Kaposi's Sarcoma Study Group were convinced of that. It was just how do you find out what the virus is?

Hughes: What was your reaction to the immune overload theory?

Ammann: Well, eventually, I didn't buy it either, because the T-cell immunodeficiency was too severe. At first I thought it was a reasonable hypothesis. For example, in a normal individual it takes sixty to seventy years to go from 100 percent down to say 40 percent of normal immunity. What was happening in an AIDS patient was that they went from 100 percent to almost zero in a period of less than ten years. It was so severe and specific for T-cell immunity that something had to be doing that.

And one of the theories was that you had too much stimulation of the immune system. Because of the lifestyle of an individual with AIDS, you had a repeated assault of viruses and other infections that could have worn out the immune system early. Now, one of the reasons that later on I thought, and most of us thought, that this wasn't a tenable hypothesis was that you had

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[1] W. M. Wara, D. W. Wara, A. J. Ammann. Immunosuppression and reconstitution after radiation therapy. Immunopharmocologic effects of radiation therapy. *Monograph Series of the European Association for Research of Cancer*, vol. 8. J. B. Dubois, B. Serrou, C. Rosenfeld, eds. New York: Raven Press, 1981, pp.169-173.

these blood transfusion AIDS cases where they got a single presumed virus insult and they wound up with AIDS. So it suggested that AIDS wasn't the result of multiple insults, but rather a single one.

Interestingly, however, even though we now know that HIV is the cause of AIDS, we're back to this theory again, because these multiple insults may actually explain why some patients deteriorate faster than others. For example, some HIV-positive patients have survived for ten years without any symptoms, and some patients accelerate very quickly to full-blown AIDS. Well, it's known that certain infections will cause the AIDS virus to multiply. The multiplication of HIV could result in further spread of virus and immune deterioration.

We learned a lot from the infants with AIDS. We felt we could eliminate CMV, we could eliminate EBV, we could eliminate drug abuse, and we could eliminate the multiple insults to the immune system. And what was left? A unique agent. And that's when I started calling this Nobel-Prize winner. I'm sorry I didn't know about Jay Levy at that time. If I had known about Jay's interest, probably Jay would have discovered the virus before anyone else, because he would have gotten into it from patient samples sooner.

Hughes: You would have given him biological material.

Ammann: Yes, he would have received material and gotten into AIDS research sooner.

The First California State Appropriation for AIDS Research, 1983

Ammann: So that's basically the history except for the meeting that [California Assembly Speaker] Willie Brown called. Marcus [Conant] had contacts with the [California] state legislature. Even though we were doing the studies in our laboratory, as we got more and more cases of acquired immune deficiency, it was obvious to everybody that more money was going to be needed, and where would we get it?

I don't remember the year [1983], but Marcus organized a meeting with Willie Brown and Paul Volberding, myself, John Greenspan, Frank Jacobson, and some investigators from UCLA. I don't remember if Michael Gottlieb was there.

We wrote what we thought was needed in the way of research and estimated the money needed to do it. We actually wrote it up

in Willie Brown's office, had it typed up, and gave it to him on the spot. He took it to the state legislature. The idea was to get a special appropriation to do AIDS research, and that it would go directly to investigators working in AIDS.

When the UC administration heard that we were going to get a direct appropriation, they wondered how they were going to control the distribution of the money--these potentially maverick individuals who might abuse this money given to them by the state. So the university administration, when they heard about it, said, "No, no, no. You can't give this money directly to the investigators. There's no such thing as giving money directly to the investigators. It's got to go through some channel where we can make sure it's being used correctly."

The university had no organization to review and administer funding for AIDS, so instead of using the people who were working in AIDS, who believed that AIDS was a real problem, they said, "Well, we'll put it through the only organization that exists between all the California universities," and that's the Cancer Coordinating Committee which was housed over in Berkeley. I said, "They don't even believe in AIDS! They don't even know what it is. They never heard of it, and they're going to coordinate the distribution of money?" So of course, it went to the Cancer Coordinating Committee. They didn't know how to distribute it. It got delayed. Months went by and we didn't have the money, and we still were having all these AIDS cases, and there were studies that we wanted to do.

Hughes: You had submitted applications?

Ammann: We had submitted applications. Nothing was happening. The people who were reviewing the applications knew nothing about AIDS. I was very upset. And the money just wasn't coming.

Then one day Randy Shilts called and said, "How are things going?" I said, "Oh, not so good." He said he wanted to talk to me, and that was when the headline came out, "UC Researcher Accuses University of Withholding Funding for AIDS Research."[1] [Dean] Rudi Schmid at UCSF got upset. Everyone who put in an application was awarded money except me. And then some six or nine months later when there was money left (can you imagine that?), they asked if I wanted to apply again.

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[1] See Randy Shilts, UC assailed for delay on AIDS funds, *San Francisco Chronicle*, August 25, 1983.

Hughes: Can you give me more information on how you think the blood transfusion issue impacted on AIDS?

Ammann: Blood transfusion AIDS had an enormous impact on the eventual acceptance of AIDS as a disease that could affect everyone and the need to develop a specific test for AIDS. I think it accelerated the whole issue of finding out what the cause of AIDS was. HIV was discovered and that led very quickly to antibody testing. Approval of the antibody test was accelerated. The FDA didn't wait months and months to approve the test, because it was needed right away to screen blood products and to identify risk groups for AIDS.

Hughes: Did people view children with AIDS differently?

Ammann: People often say [in reference to children with AIDS], "Why?" Many individuals in the gay community don't like the term, "the innocent victims," but parents feel that their children are innocent victims of this disease. And so, sometimes what I try to do with these families is say how their child's illness or death contributed to the health of others. You can never completely rationalize the death of someone in that way, but at least it helps the parent understand that maybe someone else was helped by what happened.

I've told the Kushnick family that I feel that literally thousands of lives were saved because they as a family wouldn't accept the death of their child from AIDS following a blood transfusion. They entered very aggressively into this whole thing of whether our blood supply was safe. And they raised major questions. Oftentimes when questions are raised by the nonscientific community, things happen faster, because scientists are accused of bias: "You're reporting that because you want research money and publications." But when someone who doesn't have any scientific gain to make says, "Wait a minute, you've got to do something about the blood supply," it sometimes moves faster. And that's I think what happened.

Hughes: Did pediatric AIDS swing opinion towards the idea of a virus?

Ammann: Yes, I think we did it in the pediatric community. I think that until the virus was discovered and antibody testing was developed, there were still people that felt that there might be other causes.

Co-factors in AIDS

Hughes: Currently, there's a lot of talk about co-factors.

Ammann: Well, the whole co-factor thing is not clear at all. That's been a problem ever since the beginning, and it is extraordinarily difficult to sort it out. For that reason, we don't have any answer. I think there are co-factors in terms of how quickly the disease progresses and whether a person gets infected or not.

But even the pediatric cases haven't helped us in sorting that out, even though children with AIDS have some co-factors similar to those of adults. Some of them have cytomegalovirus from their mother; some of them have the Epstein-Barr virus. Drugs are not as much of a factor.

Hughes: Do you think there was any downside to the switch from the earlier multifactorial, epidemiological approach to the simple infectious agent as the explanation for the cause of AIDS?

Ammann: I think that medicine does go in cycles. I think people like to grasp at what they can understand in very simple theories. The medical training that people get is to explain what you see in a patient by a single cause: Tuberculosis is caused by one organism. Cancer has one cause. It doesn't. But most scientists are trained to look for a single cause. It's just easier to understand everything based on one cause, until people say, "Well, there's too much variation here to have a single cause. What are the co-factors?" But that's some of the most difficult research to do, and it requires large numbers of subjects.

And now it's even more difficult, because patients are being treated not with one agent, but with multiple agents. So the research on co-factors is confounded by the fact that patients have had multiple treatments, which can alter the course of the disease.

There are clearly a lot of other factors. In pediatrics, the time from infection to onset of AIDS is on the average a year and a half, whereas in adults it's five to six years. So there is a big difference there, and it has been attributed to the immaturity of the immune system in the newborn. Well, we don't have any proof for that. That's conjecture. So there's a lot of things that need to be looked at in terms of genetic susceptibility, co-factors in terms of virus, co-factors in terms of environmental aspects. When there are no clear answers, that means to me that we don't have the techniques yet to look for them.

Seminal Discoveries Prior to the AIDS Epidemic

Ammann: AIDS is a classic example. We would still be debating about the cause of this disease if it weren't for the discoveries that preceded it--Howard Temin's discovery of reverse transcriptase. He went through a period when no one believed him. This idea was too much for some scientists to handle. I love talking to him, because when he describes what he went through in the early days of describing reverse transcriptase, it's what all the early AIDS researchers went through--scientific disbelief. But his discovery paved the way for research and discovery in AIDS.

As much as people malign Robert Gallo, Gallo's discovery of a virus, HTLV-1, that was associated with cancer and could infect T cells, was critical. Clearly, he understood very early in the epidemic that a real good possibility for the cause of this disease was a retrovirus. Despite all the politics and the ego and everything, you still have to give him a lot of credit for really pursuing that idea.

Hughes: Yes, and developing the growth factor for culturing the virus.

Ammann: Yes. HIV wouldn't have been discovered as soon as it was without the growth factor because you couldn't grow the virus and the cells.

Hughes: Did you suspect the cause was a retrovirus?

Ammann: No. I never even understood the difference among the retroviruses. That's why I called for help. There's no way I would have tried to isolate the virus in my lab. I was an immunologist. All I knew was that I had never seen an infectious agent that could do this to the immune system.

None of the known viruses ever did this to the immune system. So my feeling was it was a new virus, so I called this person at UC by the name of Bishop who I had heard was interested in viruses. I didn't know about Bishop; I wasn't following that literature. I didn't even know about Temin at that time. I had heard that Temin had gotten the Nobel Prize for discovering reverse transcriptase, but I had no idea what that was all about.

Origin of the AIDS Virus

Ammann: I really felt very strongly that this was some sort of a new virus that had somehow entered into the gay community, initially by some difference in lifestyle, and then had gotten into drug abusers and women. I didn't know at that time how it could happen other than through a virus. But it had to be some new virus that came from somewhere.

Hughes: Do you have any theories now?

Ammann: No, I'm like everybody else. One of my favorite quotes is from a Sherlock Holmes mystery. Watson is always pushing Sherlock Holmes for a theory on the murder or the mystery. Sherlock Holmes gets impatient with Watson and says, "Watson, I have told you before, we cannot have any theory without facts. First we must have facts, and then we can have a theory."

I think the problem with HIV is that we don't have all the facts. We can't go back far enough with blood samples to get all the facts about where this virus came from. If we could, then we would have the facts for a theory. So right now, a lot of this is conjecture. It seems to me logical that somewhere along the line this virus mutated drastically from another similar virus.

It's also now clear that this virus has been around a lot longer than most people think. They found the virus somewhere back in the sixties, I believe it was, in stored blood specimens from a guy in the British navy. So because of the way the virus is transmitted, and the fact it's not highly contagious, and the fact that airplanes weren't around in the fifties and sixties to the extent that they are now, it took a while for the virus to infect a critical number of people and allow for the recognition of AIDS.

I think the gay lifestyle contributed to the spread of the virus. It's been well documented that the virus first appeared in several countries in homosexual men. So I don't think there's any mystery about that. The rapid spread now, however, is by heterosexual transmission.

I did an awful lot of reading. I read about other epidemics; I went into the history of unknown epidemics that had been recorded years ago; I went to old medical books to find out if there was anything like this before. Because of the Haitian connection, I started reading books on voodoo to try to find out if there was some way that a virus could have been transmitted from voodoo practices. I remember going to the Haight-Ashbury

[District of San Francisco] and buying books on voodoo. None of it panned out. What it really shows was how desperate most of us were to try to find out what the cause was and where it came from, mostly because if you knew how it came about, then you could stop the spread.

Stigma

Ammann: UC didn't want AIDS at the university hospital.

Hughes: Why was that?

Ammann: Well, I think that AIDS had a stigma. The university administration didn't want AIDS, which was a disease of homosexuals and IV drug abusers. They didn't want those patients to be seen with other patients. Even though it's a state university, there are a lot of private patients at UC. I think the problem still exists today. There are different areas around the country where physicians don't want to take care of AIDS patients because if you have "an AIDS patient" sitting in your office, maybe the other patients won't come in. So that problem hasn't gone away.

Hughes: Another fear was that institutions serving large numbers of AIDS patients would suffer a drop in applications for residency positions.

Ammann: Early on, it wasn't a problem, because people wanted to learn about AIDS. But then, later it became a problem, at UC as well. Merle Sande at San Francisco General will probably tell you that the hospital had a fall-off in intern and resident applications because they didn't want their training dominated by AIDS.

Hughes: Is that still true?

Ammann: It depends who you talk to. If you talk to people in San Francisco, there's pretty much an acceptance of AIDS and the risk of working with AIDS patients. But if you go to other parts of the country, you go back ten years. People say, "I wouldn't go to any hospital where there are AIDS patients. I don't want to get AIDS." Or, "It's not a problem I'm going to deal with in my private practice, so I don't want to train in AIDS medicine."

Establishing Networks

Hughes: How were networks of people and agencies set up to deal with the epidemic, and who was involved?

Ammann: Well, I have good memories of the way AIDS worked in the San Francisco Bay Area. I think we were very fortunate here in that people worked together. They weren't as threatened by academic and scientific interests, so that almost everyone worked together. You approached somebody, and "Sure, we'll help you on that problem." Individuals in different specialties became involved. Jay Levy was very interested in isolating the virus. John Greenspan in the oral-dental community, where they were seeing a lot of AIDS patients with oral problems, was very interested in AIDS and continuing to work on it. Paul Volberding and [Donald] Don Abrams, of course, were also interested. The physicians in the community were very responsive in terms of obtaining patients for studies, and supplying samples and doing tests. The CDC always felt comfortable coming to San Francisco and knowing they would get cooperation. My impression is that people were working more as a community in San Francisco. The blood bank was helping in defining blood transfusion AIDS, and the city public health department was helping in terms of identifying patients anonymously for case finding studies. Overall, people were working together here in San Francisco. The AIDS ward was established at San Francisco General Hospital. AIDS conferences were set up. Things moved along very quickly. It was not as divisive as in some areas, like New York City. For that reason, a lot of the cooperative studies and data came out of San Francisco.

Hughes: Why was New York different?

Ammann: Crowding. [laughter] I'm an old New Yorker. You can't crowd people like they do. I don't know. People have expressed puzzlement. I just know that my own history was always one of cooperative, collaborative research. I always felt if I didn't have enough pediatric AIDS cases, that I could call Dick Stiehm at UCLA, and he would help me find more patients. For some reason, people here were not as threatened by working together. There was more of a feeling that we were working on this problem together.

As a pediatrician, I was asked to work with internists and dermatologists. But that I was used to from my previous experience at UC. So I think it was just something that evolved.

Hughes: The networking was an extension of what you were already doing.

Ammann: Yes. All of the meetings were multidisciplinary. Originally it was the Kaposi's Sarcoma Study Group meeting, and then it expanded into talking about AIDS in general. The meetings were attended by all these subspecialty people, feeling that it was a subspecialty problem. Of course, as the AIDS epidemic got big, then more and more infectious disease people became involved in it as well.

Federal Funds for AIDS Research

Hughes: Was there a problem obtaining funding for AIDS research at the federal level?

Ammann: Oh, yes. The federal system had no way of responding quickly, and it still has trouble. As a result of AIDS, I think their response has changed a little, but at that point, there was no such thing as a rapid response to a research problem or a new disease. The mechanism that had been set up, which has been that way ever since I worked with National Institutes of Health, was to apply for a grant, have it reviewed, and then get it scored, and then reapply if the grant didn't get funded. Again, who was going to review [an application for AIDS research funds] if most people didn't believe that this epidemic was a problem to begin with? So grants got rejected and individuals had to reapply--maybe a two-year process.

So research on AIDS was done initially by people who had funding which they could use flexibly. Gallo had intramural funds. In our lab we had the Pediatric Clinical Research Center which could be used for research on AIDS or any other new disease. Paul Volberding had no funds initially to do specific research on AIDS that I was aware of. A federal funding mechanism didn't get built until people accepted AIDS as a disease, and the government put money into that area. And I think it's still a problem.

One of the reasons I'm now with the Pediatric AIDS Foundation is because the foundation realized that in the area of pediatric AIDS we were going through funding problems similar to those back in 1982 and '83. How could you get funding faster into critical areas without having to go through these long, elaborate review processes?

Hughes: Do you think the organizational aspect is sufficient to explain the delay in federal funding for AIDS research?

Ammann: I think the federal funding mechanism is not conducive to a rapid response. The fact that it was a new disease and that many of the

people at NIH did not believe that this epidemic was going to be a major problem delayed funding. I also think there were ego problems involved. Once it was clear that AIDS was going to be a major problem, other people wanted in. I think the fact that this disease was being seen by people in New York and San Francisco and wasn't being seen by other people who were "influential" had a lot to do with it. They were not going to take money out of research they were doing and put it into AIDS.

Finally, when certain people realized that this epidemic was a problem, and they themselves got involved in it, they started pushing for more research money. But there was a lot of self-serving going on in the funding.

I had a very interesting conversation with a person in infectious disease who was complaining to me how he couldn't get any funding for infectious disease because of AIDS. I paused for a short time and I said, "What do you mean? There has never been more funding for infectious disease than there is now." Infectious disease was a specialty that was disappearing. Nobody was going into infectious disease. Now you've got funding for virology, you've got antiviral therapy, you've got opportunistic infection. There's never been more funding for infectious disease than now. There's never been more people going into infectious disease training and practice. In the seventies, there were hardly any people in infectious disease.

But I think initially, a lot of people were worried that this epidemic was going to take money away from what they were interested in, and they couldn't see what they were going to get out of research in AIDS.

So it's a complex answer in terms of why the response wasn't quicker. I think we need historical perspective to ferret out what all of the problems were.

Hughes: Well, the epidemic coincided with the Reagan administration cutbacks in funding. The CDC, for one, was severely cut back.

Ammann: Yes. We have the same situation now, where if you target one area for funding, basically under the Gramm-Rudman Act, you've got to take it out of another area. With the tuberculosis epidemic starting now, that's exactly the problem. If you take AIDS money and put it into TB, then it's got to be cut somewhere else.

The TB epidemic is an example in which the federal government responded quickly. Basically, I think people in the government said, "We're not going to be caught again." So when the TB epidemic broke, the CDC, the Public Health Service, the NIH, and

the NIAID [National Institute of Allergy and Infectious Disease] all got together and immediately jumped on it, saying, "Yes, this is a problem. This is what we're going to do. This is how much money we're going to put in." It is an example of the government now being able to respond because it had learned from the AIDS epidemic how to be more flexible.

AIDS Vaccines

The Need for a Vaccine

Hughes: Do you want to talk about vaccines?

Ammann: Yes. The development of a vaccine for HIV is a very tough issue. Without question, I think if you asked most scientists, they would tell you that the only way to stop this epidemic is with a vaccine. Theoretically, the AIDS epidemic is completely preventable by behavior changes--theoretically. But behavioral change may be as difficult as developing a vaccine. If behavior can't be changed, then the vaccine becomes the only other way for preventing infection.

In terms of prevention, I think most people in the public health area feel that a vaccine offers the best hope of stopping the pandemic. It also offers the best hope for health care workers who are dealing with HIV-infected people. That's becoming a bigger and bigger problem as a result of accidental inoculations. There's no evidence that treatment with AZT prevents HIV infection. As with hepatitis, people in the health care profession should have a vaccine to try to prevent infection from occupational exposure. There is a need for a vaccine; no one argues with that.

Scientific Problems

Ammann: There are two problems related to the virus. The problem that's most commonly mentioned is that the virus keeps changing. So if you had an effective vaccine now, would it be an effective vaccine six months or a year from now? Would it be effective in the U.S., in Africa, in Thailand? Most scientists admit that more than one vaccine will be needed, because the virus varies enough that one vaccine probably won't do it.

Hughes: Could you have a combination vaccine?

Ammann: Yes. There are precedents for combination. Polio vaccine is a combination of three different polio virus vaccines. The best example of multiple combinations is the pneumococcal polysaccharide vaccine, which has twenty-two different types of antigens or immunogens in it, and people are immunized all in one shot.

The problem is that the AIDS virus varies more than the pneumococcus. The problem is similar to the flu virus and vaccine. Every year there's a new flu vaccine that people get for the current predominant flu type. But AIDS doesn't go in waves like that. It's not like the flu where you get a winter epidemic. It's an all year-round thing, and the virus varies from person to person. So the big question is, is there enough constancy to the virus that you could develop a vaccine that would protect against infection? And the scientific community is divided. Some people feel yes; some people feel no.

Hughes: Do you have an opinion?

Ammann: Well, my feeling is that there is enough constancy that there's hope for a vaccine. There are still a lot of problems with the vaccines currently being developed, but there have been some advances that make us optimistic. I think if you talked to people five years ago, they would have been more discouraged than now.

Hughes: What is the second major problem?

Ammann: The immune response to the virus is poor. It suggests that there is something inherently difficult about eliciting an immune response to parts of the virus.

Hughes: What are some of the advances?

Ammann: One is if you immunize with a vaccine, you can see protection in an animal model, the chimpanzee. People thought that would not be possible. If you immunize with a vaccine in humans, you see the development of antibodies which neutralize the virus. You also see the development of immunity which cross-reacts with viruses taken from different people in different geographical locations. You don't see neutralization of all viruses; a single vaccine won't neutralize viruses from Africa and from the U.S. and from Thailand, but it will neutralize a lot of [viral] isolates from the U.S.

The other encouraging thing is that the vaccines that are being tested most intensively are being developed by recombinant

DNA technology, which means they're pure, they're available in large amounts, and can be studied in detail. There are different adjuvants that are being looked at which are not just the standard aluminum hydroxide or alum.

But with all the encouragement, some bad news always follows. The most recent is that antibody taken from immunized donors doesn't neutralize virus taken directly from patients, even if the antibody is concentrated.

Competing Vaccines

Ammann: We know a lot more about what kind of immunity is needed to prevent infection. We need both antibody and cellular immunity. The major vaccine candidates are produced by Genentech, Chiron, MicroGeneSys, Immuno-AG, and the vaccine of Jonas Salk.

Hughes: Salk's is not a recombinant vaccine.

Ammann: Salk's vaccine is the only one in the U.S. that's not recombinant.

There are at least five or six different vaccines that have some promise. Initial results were encouraging. They showed that if you give a vaccine, it's safe. No one so far has gotten an autoimmune disease or anything like that. The vaccines induce neutralizing antibodies, they do cross-react with different isolates, and they protect chimpanzees. Now, not all of them do that, but some of them do that. And those are all advances.

Now, the question that remains is, is the immunity enough to protect people?

Hughes: And is it long-term?

Ammann: Right. If a person gets infected and he got the vaccine nine months ago, is the immunity down at a level where it's no longer protective? Well, a lot of those questions you can't answer until you do the trial; eventually a clinical trial will be required.

Problems Raised by Vaccine Trials

Hughes: Starting clinical trials brings up another set of issues.

Ammann: Right. Where should the trial be done? Who should be the vaccine recipient? When do you give a population a vaccine? Are you going to give them counseling? And if you give them counseling, is the rate of infection going to go down because you're telling them about AIDS and how you get AIDS? Or is it going to go up because they think they are protected? So it's an enormous issue. The liability issue, the indemnification issue--if you immunize someone and they test positive for the virus but they're not infected, are they going to be denied health insurance, life insurance, a job?

So a vaccine trial raises enormous questions. But like many problems, these are things you just have to take one at a time. We don't know today whether or not there's an effective vaccine, but progress is being made. We're not at a point where people say, "We can't go ahead with vaccine development because all of the information we get now is negative." There's a good amount of positive information.

I think discouragement will come--if it comes--at the stage of the efficacy trial if it is found that a vaccine does not protect. The biggest question that has to be faced is when to do the vaccine trial? How much information do we need to begin?

Hughes: There is talk of starting phase III efficacy trials in a year or so. Is that going to be possible?

Ammann: Yes. I think phase III could be tried in a year, if people agree on what criteria you need. I think the big problem is what kind of results do you need from phase I and II to give you the confidence to do phase III? And there's going to be some debate there.

Dan Hoth, when he was at the National Institutes of Health, made an interesting presentation at an advisory vaccine meeting. He calculated the number of cases of HIV infection that would occur each year for the next five years, and then said, "What if we had a vaccine that prevented half the cases?" If we started with a vaccine now and it only protected 50 percent of the people, versus waiting five years for a better vaccine, where would we be? The answer is pretty obvious: We'd be better off protecting 50 percent of the people. But right now we don't know if a vaccine would be 50 percent or 25 percent or even less, or if we need one or more vaccines.

Hughes: Will the FDA listen to that sort of argument?

Ammann: Yes. I think the FDA will not be the problem. I think the problem is within the scientific community, deciding whether or

not a vaccine is good enough to move ahead, and which one will it be. I don't think it's as difficult as people are making it out to be. Most traditional vaccine trials proceeded after you showed the vaccine was safe and immunogenic. At some point, you had to go ahead and do the vaccine trial. Some of them, like the measles vaccine trial, were probably done too soon. The vaccine was effective, but it had some side effects. By the time they found the side effects, a new preparation was available that was safe and efficacious.

An Institute of Medicine meeting on AIDS vaccines will occur in two weeks, and one occurred two years ago. The one that occurred two years ago ended with tremendous pessimism. "We don't think that there will ever be a vaccine; the results are not good."

Hughes: For scientific reasons?

Ammann: Yes. The upcoming meeting will not so much address the scientific reasons; it will address more the issue of where and when should the trial be done. It's a subtle shift, but clearly it means that people are becoming more comfortable with the idea that a vaccine is possible. People are being appropriately cautious, saying, "We don't know how much it would protect, if it would protect."

But there is going to have to be a trial fairly soon to test the hypothesis. And if it meets with failure, then I think there's going to be a lot of questions about why the trial went ahead, why didn't they wait.

Hughes: It may delay future trials.

Ammann: Yes, that's the risk. But I don't think you're going to be able to avoid it, because there's only one way of finding out, and that's to do an efficacy trial, take that risk. People are going to have to be courageous enough to do it, and say, "Okay, we'll be willing to take the blame if we went ahead too soon."

MicroGeneSys, Genentech, and Chiron Vaccines

Hughes: Please talk about the commercial vaccines being developed.

Ammann: MicroGeneSys was the first company to get permission to immunize humans with an AIDS vaccine. It's hard to believe it was started in 1985.

When I was at Genentech [1985-1992], as associate director of pharmacological sciences, and later director of collaborative medical research, we went to the FDA and to the NIH saying we wanted to start a vaccine trial. It was with a recombinant HIV-3b envelope vaccine. This is a laboratory-adapted strain of the virus. MicroGeneSys was slightly behind Genentech at that time [1985]. They were not yet ready to do the trial.

We had immunized some chimpanzees and then challenged them with this HIV-3b, a laboratory strain of the virus--because that was what was available, it had been standardized, and it was shown that chimpanzees could be infected. This must have been about 1986.

The chimpanzees turned out not to be protected; they got infected. That result bothered us a lot, because if you couldn't protect chimpanzees under optimal conditions, then what chance did you have with a human vaccine? You could argue, "Well, let's go ahead and look at the safety and the immunogenicity."

But Genentech made the decision to back off and not to pursue the vaccine. We had already gone to NIH; we had written a protocol for testing the vaccine. I remember speaking to the people at the NIH and saying, "This is what the vaccine does. These are the results in rabbits and baboons." We had immunized forty baboons, had developed a lot of data on this vaccine--its safety and purity and everything. It's a difficult thing when you say you're going to back off of a study. But we did.

MicroGeneSys at that time had enough of their gp 160 vaccine available that they wanted to go ahead with vaccine trials, and so they started the vaccine trials for safety and immunogenicity in humans. Meanwhile, Genentech and then Chiron and other groups began working on other vaccine preparations. Phil Berman at Genentech continued doing studies on purifying the vaccine more and did another chimpanzee study. Now we're talking about three years down the line [1989], and this time he got chimpanzee protection. So the feeling was, three years later, Genentech was ready to go ahead with human trials.

Well, about this time, a lot of information started coming out that HIV-3b did not represent anything except a laboratory strain and had no relation to the real world.

Jay Levy was working with Chiron. He isolated a viral strain called SF-2 [San Francisco-2], where the antibodies seemed to cross-react with different isolates from different people. Chiron initially was working on an HIV-3b vaccine, but they decided to work on developing this recombinant SF-2. Genentech started

working on a recombinant MN, which was again more representative of strains outside the laboratory infecting patients.

Well, when the SF-2 and MN vaccine results began to appear, some differences were seen. MicroGeneSys had a lot of trouble with their immunization schedule, even when they went up to very high doses. They had trouble getting neutralizing antibodies, no matter how much vaccine they gave or how frequently it was given. So questions were raised: Is it gp 160 versus gp 120? Is it adjuvant? Is it glycosylation? Chiron was doing a study with a different adjuvant, and they got more cellular immunity, but began seeing neutralizing antibodies. And Genentech with a gp 120 and an alum adjuvant began seeing neutralizing antibodies.

It appeared that you got better neutralizing antibodies with glycosylated versions of gp 120. Gp 120 is not just protein. It's 50 percent sugar. The different recombinant proteins, even though they sound like they should be the same because they're highly purified, actually vary considerably in sugar content, depending on the type of cell used to produce the recombinant material. It began to appear that the sugars were very important for the structure of the vaccine.

Soon criteria for evaluating vaccines began to be discussed. Did they protect chimpanzees? Did you get neutralizing antibody? The result was that scientists began setting up criteria and insisting that these be met before large clinical trials were performed.

Most companies had invested millions in vaccine research, and certain people working with the companies, such as Bob Redfield, are very aggressive individuals. His idea was that the immune response in an HIV-infected person is not adequate but could be boosted by immunizing with parts of the virus presented in a different way. So the MicroGeneSys story got complicated because Bob Redfield introduced the concept of using a vaccine to prevent progression of the disease. Now, we're not talking about prevention; we're talking about progression. So the vaccine functions as a therapeutic, rather than as a prophylactic.

Currently, a therapeutic vaccine doesn't exist. There's no such thing. People always quote rabies, but that's really not a therapeutic vaccine. Although you give the vaccine after the person has become infected, the incubation is so long and the virus grows so slowly that when you give the vaccine, you're accelerating the immune response. By the time the virus takes hold, you can prevent infection of critical nervous system cells.

Hughes: Right, so the principle is really the same.

Ammann: It's still preventive, not therapeutic. Hepatitis B vaccine given to infants who are exposed in the newborn period by an infected mother is also a preventive, because you're basically boosting the immune response before infection takes hold. So there is no therapeutic vaccine in existence. If a therapeutic vaccine works, Robert Redfield will get the credit for pushing the idea of a therapeutic vaccine. If it doesn't work, he will be pounded by the scientific and AIDS community.

Now, Redfield started with MicroGeneSys, because MicroGeneSys was the only company that really was receptive to his idea. He started doing studies with the MicroGeneSys gp 160 as a therapeutic, not as a preventive, vaccine. Questions came up about his early reports, about the interpretation of the data. I was one of the ones that actively questioned him at the international AIDS meeting in 1992 after his presentation, because I didn't believe that his data really showed a decrease in viral load. It looked to me like viral load had actually gone up and then went back down to baseline. I thought he was overinterpreting his data.

Hughes: It's going to be looked into.

Ammann: Yes. It really shows the importance of having scientific criteria.

In 1992 the FDA had a meeting at which I testified. I was still with Genentech. I put up criteria for an AIDS vaccine which Genentech could not meet at that time, saying that these were the criteria for moving a vaccine into the phase III efficacy trial. If six out of eight or whatever number could be met, then you'd move the vaccine to a clinical trial. I suggested that you should not do a trial unless you meet criteria that the scientific community agrees upon.

Hughes: What happened next?

Ammann: Well, we were caught by surprise because MicroGeneSys had successfully lobbied to receive a defense appropriation of $20 million to study a therapeutic AIDS vaccine. I got a phone call the morning Congress was voting on the $20 million appropriation. Everybody heard about it the same morning that it was being voted on. By the time people on the West Coast learned about it, it was a done deal. It was discouraging.

Hughes: You mean because it shouldn't be done that way?

Ammann: It shouldn't be done that way. I guess if you're the pharmaceutical company that gets the money, you're happy about it. But it's just not the way to do research.

Hughes: It seems a really crucial issue. It's much wider than whether or not we test an AIDS vaccine. It is, who is going to decide scientific policy in this country? Is it going to be Congress, or is it going to be the scientific establishment, or a combination of the two?

Ammann: Right. It points out that if the scientific community is not taking a lead on this, then someone's going to step in and take it away from you. So there's fault on both sides.

NIH was urged to set up criteria for vaccine trials for several years before this happened. And it was, "Oh, we will do it," or "we're not ready yet," or "we don't know what the criteria are." MicroGeneSys deserves credit for taking the risk of being the first to try the vaccine, but just because you're first doesn't mean that you've got the vaccine. If scientists stick to judging vaccines by scientific criteria and ignore political and profit issues, I think it will be clear which vaccine candidate will be the best.

Liability

Hughes: What about the liability issue?

Ammann: The liability issue is under serious consideration once again, and the example that everybody brings up is the swine flu vaccine, which is taken as an example of the worst possible scenario, a nightmare for the pharmaceutical company. It's always used as an example of why liability protection is needed, especially for vaccines.

What happened with the swine flu vaccine is there was an influenza epidemic, as is not unusual, and so a vaccine was developed for preventing influenza. It was nothing new. But in this particular instance, the vaccine that was used was felt initially to be associated with a disease called Guillain-Barré syndrome, which is a paralyzing disease. Merck, Sharpe & Dohme, which was the company manufacturing the vaccine, decided that they wanted government protection against any liability.

I spoke to Maurice Hilleman about the liability issue just a month ago, December 1992, at an AIDS vaccine meeting. He told me

that had Merck not gotten government protection in the liability area, that probably it would have gone under. That is a surprising statement about a company which is considered the most successful pharmaceutical company in the world. Merck added up all of the liability that was awarded as a result of that vaccine, and it was more than they had in terms of insurability. So Hilleman uses Merck as an example of why vaccine research in particular is fraught with major liability problems, and why there has to be government protection against liability.

Now that that swine flu epidemic is over, and people have reanalyzed the data, most people agree that there was never a clear association of the vaccine with Guillain-Barré; the vaccine was being blamed for what was occurring spontaneously without the vaccine. But the money has been awarded to the victims of Guillain-Barré.

To me, the issue is not whether or not liability protection is needed, but at what point is it needed. That's where the discussion is going on now. There's a liability protection bill pending in Congress by Pete Stark. The Childhood Vaccine Protection Act covers any injury as a result of a childhood immunization, <u>if</u> the childhood immunization was mandated. Most are mandated--polio, measles, mumps, DPT [diphtheria, pertussis, tetanus]. Money from the sale of vaccines goes into a pool, and from that pool these awards are made. As I understand it, that pool covers most of the claimed liability as a result of vaccine administered to a child. It does not cover adults. So for an AIDS vaccine, the bill would have to be amended or some new bill would have to be put in place. My feeling is that the easiest way to do it is to amend the existing act to cover adult vaccines as well.

Where I think there may be a mistake is the point at which you enact the protection. In the Stark bill, which is not passed yet, there's a recommendation to extend the liability protection to the experimental phase of a vaccine, and I think that would be a mistake. My feeling is that liability protection should be given, but only after a vaccine has been approved by the FDA and used in large numbers of patients.

When a vaccine's in the experimental phase, there are just too many unanswered questions to say that we're going to cover all of the potential adverse reactions. I think it raises very serious questions for research if you say that somebody has to cover liability for every drug that's in the research phase. The purpose of doing phase I and phase II studies is to look at drug safety, and oftentimes drugs are withdrawn because they're unsafe.

Hughes: Are drugs in phase I or phase II trials subject to a suit?

Ammann: Well, they never have been up to this point, and that's what I am concerned about. I am concerned about the extension of liability in medicine period, but, up to this point, there has never been a suit against an investigator, a university, a pharmaceutical company, for a drug in the experimental phase, because everybody's understanding is that the risks are high and informed consents are usually very detailed.

And you say, well, if the risks are high, then shouldn't there be liability? Patients who are treated in phase I studies are primarily patients who have a lot to gain, so it's felt that they can take a higher risk. As the drug or the vaccine is shown to be safe, then it moves into populations where you don't want to take as much risk. So liability becomes more of an issue.

However, some drug manufacturers want liability protection at all levels. In July or August, 1992, Abbott Laboratories said it was not going to develop hyperimmune intravenous immunoglobulin for use in the prevention of HIV transmission from mothers to infants. They said it was because they thought that there was significant liability for using this drug in children and pregnant women even though this was in the experimental phase.

When the Pediatric AIDS Foundation and Project Inform (Martin Delaney) heard about it, we were all very upset because we felt that this was an attempt of a pharmaceutical company to extend liability protection into an area where it had never been, in particular to groups that weren't being adequately evaluated for AIDS drugs, and that was women and children.

So the Pediatric AIDS Foundation and Project Inform jumped on it. We put a lot of pressure on Abbott. The ACLU [American Civil Liberties Union] actually drafted a suit against Abbott.

Hughes: Prompted by your group?

Ammann: No, prompted by Dick Stiehm from UCLA and Diane Wara from UC San Francisco, both of whom joined in the suit as physicians to force Abbott to provide the drug as they had promised.

But the ACLU, the investigators, the Pediatric AIDS Foundation, and Project Inform felt that allowing a company to say that there was a liability issue during this experimental phase would essentially prohibit the development of a lot of drugs in any population. We felt it was a test case. Fortunately, Abbott backed off.

So the question was, is liability a problem of sufficient magnitude to keep companies from developing an AIDS vaccine? Well, interestingly, in spite of what I said, no. There are at least twelve AIDS vaccines under development. Pharmaceutical and biotech companies say, "This is potentially a lucrative market, and we want to go after an AIDS vaccine." They're not in it for altruistic reasons. The cry for liability protection is really a cry for absolving them of any risk at all. That is unreasonable.

However, I think before any of those twelve or fourteen AIDS vaccines are used after final approval, the companies will ask for liability protection. They will use pressure to get it, and at that point I don't think it's unreasonable. People could sue, saying, "I thought the vaccine was going to protect me so I engaged in sexual activity, and I got HIV infected." Or someone who's already infected could say, "My disease has progressed, and the vaccine was supposed to keep me from progressing."

Approaches to Vaccine Development

Hughes: Are AIDS vaccines being developed mainly by biotech companies, as opposed to pharmaceutical houses, largely because of the potential liability problem?

Ammann: No, I don't think so. I think that the main reason for that is because of the science. The large pharmaceutical companies have used traditional approaches for drugs and vaccines. By traditional I mean, if you have a virus and you make an attenuated vaccine, you simply grow the virus and treat it so it is not infectious. Nobody who is rational feels that you can give an attenuated HIV vaccine. There's speculation, but I seriously doubt it will happen.

The easiest and safest way to make an AIDS vaccine is to give a purified part of the virus. Well, one way of getting a purified part is to grow large amounts of the virus, then kill the virus, and then purify the components. But to grow enormous amounts of virus would be a risk for the people working with the virus, so that isn't possible.

That leaves using recombinant DNA technology. Early on, the big traditional drug companies, such as Merck and Smith, Kline, & French didn't have recombinant DNA technology. So that's why the small biotech companies got in it. They saw DNA technology as a means whereby they could produce successful vaccines. And in fact, they did.

Remember that the first hepatitis vaccine was made by Merck using the traditional approach. The virus was obtained from the plasma of infected people, they inactivated the virus, and fortunately unknowingly inactivated HIV as well. It was an inactivated hepatitis B vaccine obtained from the plasma of infected people. That vaccine has now been replaced by a recombinant DNA vaccine, which was developed by a biotech company, Chiron, and then sold to Merck.

State of California Vaccine Legislation

Hughes: Did you have any role in the passage of a vaccine bill in California in 1986?

Ammann: No, that was when I was still at Genentech, and Genentech decided that it would not participate in forming the bill, although it was passed. The bill contained many restrictions, which Genentech didn't want to get into. As soon as a company accepts money from the federal or state government, it's got to follow all of the requirements that come along with it--OSHA [Occupational Health and Safety Act], affirmative action, forms that you fill out, what's the composition of your employees, how many. So Genentech said, "It isn't worth it." It was a small amount of money for the work that needed to be done to conform to state regulations. It was very much a disappointment of the people that pushed the bill through, because they really didn't have any takers on it. The bill languished, and the money was not used.

Two years ago, it was reintroduced and passed as a bill for a vaccine for pregnant women. The bill was much better. Chiron pushed to get it passed. Genentech again took a pass on it because they did not want to get into immunizing pregnant women.

Hughes: Was the bill largely to provide money for vaccine research?

Ammann: The first bill gave money for research. It also provided that if the vaccine were successful, there would be a payback to the state for the amount of money that it had given so the state wouldn't lose out. But it was primarily money for doing the research.

The second bill was similar. However, it contained an incentive that the vaccine could be approved by a California equivalent of the FDA. But it could be used only in California. I felt that was one of the weaknesses of the bill, because I don't think it's a benefit to have vaccines passed only in a state; you want them passed nationwide. There could even be repercussions in

having it passed only in a state, since some people might say, "Well, the vaccine wasn't good enough to be passed on the federal level."

The California State Legislature reintroduced the bill this year, and it again passed. They wanted the support of the Pediatric AIDS Foundation. I discussed it with the executive committee, and our feeling was that we did not want to support the bill since it gave the appearance of bypassing the FDA.

My question to the legislature was, "Who are the pharmaceutical companies going to use for the test population of HIV-infected pregnant women?" They said, "Well, the patients being taken care of in the state of California." I said, "Well, I would like to take you through the obstetrical clinics of the state of California and point out to you what the state is not doing for these pregnant women."

The care of pregnant women who are HIV infected is terrible. Highland Hospital [in Oakland, California] delivers many women without any prenatal care whatsoever. I said, "If you really want to do something for HIV-infected pregnant women, then provide basic health care for them. There are more reasons why they're not getting care, and just putting in some money and giving it to a biotech company to do a vaccine trial, when you're not even going to be able to get the pregnant women into the trial because you don't know who they are because they have not been tested for HIV."

So the foundation didn't support the bill. We said that we would support a bill if it was linked to identification and provision of care for HIV-infected women. But they didn't change it.

Update on AIDS Vaccine, AIDS Vaccine Evaluation Group, Bethesda, Maryland, 1991

Hughes: Please tell me about the conference you recently attended.

Ammann: It was an NIH conference on ethical, scientific, and social issues on a preventive vaccine. Individuals got together to talk about identifying the problems in moving a vaccine ahead. It was a one-day conference, but pretty broad, and I think very successful in identifying what the major problems are.

The main difficulty is what vaccine would you use for a 5,000- to 8,000-patient trial to prove that a vaccine works. There was a lot of discussion about what kinds of immune responses would the vaccine have to elicit to move it forward, to avoid some of the political problems that had occurred with the gp 160 MicroGeneSys vaccine.

There was a clear mandate for a scientific group to set up standards for a vaccine. What should it do in terms of antibody level, the type of the antibody, the type of virus that it neutralizes, and so on, before you study it in large populations? The present situation is unlike polio or measles, where there were a limited number of vaccine candidates and companies. Here you've got all these biotech companies saying, "My AIDS vaccine is the best." A decision has to be made if any of them are any good.

The second question was--and there was no agreement here--where do you do the study? Where do you have a high enough rate of transmission of HIV? You have a high rate in developing countries, but the current vaccine preparations are not the correct ones, because the evidence is that the virus is different in developing countries than it is here.

Identifying the population for vaccine testing in the United States is very difficult. I made a plea, saying that if you want to test a population with a high HIV transmission rate, where you know what strain the virus is, where you know the timing of transmission, then that's the infant and pregnant woman populations. It was strange to me that people were talking about developing countries and rates of less than 5 percent transmission in the U.S., and nobody was talking about the population that we knew in the U.S. which had a high transmission rate.

Hughes: How do you explain that?

Ammann: Well, I think it's related to who is currently leading vaccine development. This is a quirk of history, which is the point that I actually made when I made my comments. I said, "We forget that all of the major vaccines that we now have, with very few exceptions, have been developed, tested, and proven to be efficacious in children. And then they go into adults. You're looking for a population in which to test an AIDS vaccine, not realizing that children are the population which historically and traditionally has been used for vaccine development." Children still are one of the easiest populations in which to test efficacy, with much smaller numbers.

It depends who dominates the field--internists, infectious disease people. The AIDS field is dominated by adult specialists,

most of whom don't even use vaccines in their practice. They don't know how to immunize, whereas pediatricians immunize all the time.

Hughes: Did you get any response?

Ammann: When you become an advocate for certain groups, I think others sometimes have the feeling, "Oh, here we go again." But I think when they look at it realistically, they can't avoid the fact that the highest transmission rate in the U.S. is in mother-to-infant HIV transmission.

Community Representation

Ammann: Representatives of the community at the afternoon session were asked, "What is the community's concern about vaccine development for prevention?" The panel had someone from the black community and someone from the Hispanic community and someone from the gay community and someone from the lesbian community. There wasn't a single person on the panel who represented the pediatric community, nor a single person that represented pregnant women, which I pointed out as well.

Hughes: The very fact that there was representation from the community is one of the changes that the epidemic has instituted in American medicine, and largely because of the vocal advocates of the community groups.

Ammann: Yes, and I think a lot of people get upset by the vocal AIDS community, because representatives sometimes say things that are not relevant to the matter at hand. Even I get annoyed once in a while and say to myself, "What does this have to do with what we're discussing?" But community representation does bring out people's concerns, which in most cases are valid and important.

One very obvious thing that came up at the meeting is the public's expectations concerning the next big vaccine trial. They expect that a group of scientists will meet, pick vaccines A and B, test them in 2,000 people, and find out at the end of that trial whether or not the vaccines work. If that's the community expectation, then we're in for big trouble in the scientific community.

To me, the expectation that has to be set is that this is an experiment. You have to do a trial to find out if a vaccine works. It's as likely going to fail as it's going to work. If

people assume that the vaccine is going to work, and that 80 percent of people are going to be protected against HIV infection, then I think that's going to be very wrong and the right expectations have to be communicated.

The community panel asked, "When are you going to test the vaccine? Are you going to move it too quickly, as with the MicroGeneSys gp 160 vaccine? Is this going to be a political issue where you spend the money that's been allocated no matter what, or are you going to wait for a really good vaccine?"

We talked about some of the problems of immunizing people who are not infected, who are HIV-negative, and what happens to those people when they seroconvert because they've gotten the vaccine, but they're not HIV-infected. When they donate blood, they're going to test positive for HIV. People at first didn't understand what that really meant. Now I think the community is beginning to understand, because they understand with the health care crisis that it's hard to get insurance when you're HIV-positive. In some cases you can tell by a laboratory test whether you've gotten the vaccine or whether you've been infected. But still, the first time around, you've got a lot of explaining to do. And how does that information get across to the insurance company so that the insurance company will accept that?

There was an insurance company representative at the meeting to discuss some of the issues from their perspective, and I think the informed insurance companies understand the problem. They also know that it's in their interest to have a successful vaccine, because that eventually cuts down on their health care costs. But that certainly doesn't mean that the insurance representative who spoke at the Institute of Medicine meeting spoke for every single health insurance or life insurance carrier in the United States. So that's going to be a big issue.

Hughes: Were there other issues?

Ammann: Yes. There was some discussion about the question: "Suppose the vaccine doesn't prevent infection but delays disease progression?" That would be somewhat of a nightmare if that were to happen, because to delay progression of disease means that you would change an eight- to ten-year incubation period to fourteen to twenty years. You could never follow people for sixteen years and find out if there was a difference between immunized and non-immunized. During a sixteen-year period, just too many things happen. So everybody hoped that if a vaccine were tried, that it would be simply a question of a yes-no, "Are you or are you not infected?" There were more questions about duration of immunity.

Congressional Testimony

Hughes: Well, our next subject is congressional testimony, and as we worked out off-tape, 1987 was the first time that you gave testimony before the House of Representatives--for Barbara Boxer's committee, which was called what?

Ammann: She was on the house health committee, which was part of [Los Angeles Congressman Henry] Waxman's committee, who was chairman of the House Appropriations Committee.

The theme that ran through all of these committees was the relative distribution of research dollars. Initially, it was a question of money for AIDS research, and then it went to how is the AIDS research dollar competing with research dollars for other diseases? And then it went to questions about what was the distribution of money relative to women, to children, to adults, to animal studies, to clinical trials, and so on.

The first congressional meeting that I went to was on AIDS itself. Testifying was almost a deja vu. The first meetings that Marcus Conant, Paul Volberding, myself, and others had in '83 with Willie Brown had to do with, was this epidemic really a problem in California? We were trying to convince Brown's committee that yes, it was a problem, and we presented hospital bills showing how much it was costing to take care of AIDS patients. That was when the first infusion of state money went into AIDS research in California.

The meeting with Barbara Boxer's committee, which happened to be held in the Los Angeles City Hall, was on the relative distribution of AIDS research versus other research dollars on a national basis. It was to point out that yes, indeed, AIDS was a very significant problem and that there wasn't sufficient money to do all of the research that needed to be done.

My subsequent testimony was kind of the same thing each year, because each year there was a new budget being appropriated for AIDS research. We were always very careful to say that more money for AIDS should not mean taking money from other areas. My feeling is still the same.

Hughes: How did the [President George H. W.] Bush administration respond to that argument?

Ammann: I had the feeling that we needed to continue to justify the distribution of AIDS versus other research dollars, instead of "Here come the pediatricians again," "Here come the AIDS people again," saying they need more money and there's never enough money. I felt less that way during those initial testimonies, but certainly in my most recent one before Senator Thomas Harkins's appropriations committee [Labor, Health, and Human Services], I felt that that meeting was called because they were under the gun of other activist groups who had learned tactics from the AIDS activists. They were saying, "What about heart disease? What about breast cancer?"

I think their tactics are correct, because I think people have got to call attention to what are the real problems and get them in the right priority. But it's not just a simple, straightforward, "There are more people with this disease than with this disease," because I think you can't extrapolate from one disease to the other. For example, there are issues concerning lung cancer that I think are very different than those concerning breast cancer or AIDS.

The Need to Reprioritize AIDS Research

Ammann: Congress is coming under more and more criticism about the money spent on AIDS, and that it is disproportionate to that spent on other diseases. My own feeling is that the money appropriated for AIDS is now a very significant amount. What I argue for today is more money for AIDS, coupled with saying that the AIDS community has got to look at what's been done and reprioritize some of the research goals. In any system that has been around for over ten years, things can become institutionalized; people can get money to do research and it may not be good research.

One of the major problems that we have in the academic research community, which is in contrast to what happens in the pharmaceutical industry, is that you don't have someone saying, "Well, did the results that you got after one year of research really answer the questions you initially asked? If not, we might not give you money for the next year."

At Genentech, I learned accountability, which I would like to see happen in all research, not just AIDS, because there will never be enough money to fund every research project. You've got to use research funds very wisely. If your research isn't giving you the answers, you drop it and you go on to other questions, or

if you have nothing else to go on to, then that's the end of the funding.

Hughes: Do you think some of the problem has been lack of coordination at the top?

Ammann: Yes, absolutely.

Hughes: Which relates to [President William J.] Clinton's idea of creating the Office of AIDS Research [OAR].

Ammann: Yes. The Pediatric AIDS Foundation has been asked to give some input into the structure of the OAR, and our recommendation is to have people who are not in AIDS research per se but who are very good at understanding science, who understand how to move things, and how to set priorities. They have to evaluate what research has been done, what needs to be done, and how to do it. If they find that a research group has been working for two years and there have been no answers, then they say, "Well, this research isn't getting anywhere; that's the end of it. Let's go on to a new area.

Hughes: There hasn't been that mobility?

Ammann: No, not at all. In fact, the good old boys' network is making the decisions, presenting things at meetings. Younger, more aggressive people with new ideas are not being given as much of the funding.

There's a real danger now at this point in AIDS history. When you try to control things too much, then you lose freedom to do innovative research. You have to go back to the history of AIDS and ask how some of the original discoveries were made. They were not made by someone sitting at NIH saying, "Here's this new syndrome that's going to affect everybody, so let's allocate money here and here." The initial work for the first three years of the epidemic really was done by people who were applying research from other areas and who were being innovative. So you have to allow a certain amount of freedom, through investigator-initiated research in order to come up with new ideas.

AIDS Politics

Hughes: How do you feel about the highly politicized state of AIDS research, and the fact that as a spokesman for pediatric AIDS you've had to assume a political role?

Ammann: Well, mixed emotions. There's part of me that rebels against the whole political system, because I can see how things can get influenced in the wrong direction. Of course, the other person thinks it's the right direction. What politics is really about to me is people with discordant ideas saying, "Do this," or, "Do that," and trying to figure out who they really represent.

But because you can't get rid of politics, my attitude is that you have to learn to work with the system, but then put it in perspective. The biggest imbalance occurs when you don't allow outside review. Outside review to me means obtaining the opinions of people who have nothing to gain personally if they say yes or no; the only question they answer is, is it correct? So in terms of my interaction with politics, I say, "I'll present to you my view on pediatric AIDS funding and priorities, and what I ask of you in return is to make a judgment based on whether you feel it is correct, not on whether or not it's politically expedient."

Politically, how much money needs to be spent on AIDS? Well, it's clear that the AIDS activists are always going to ask for more money. So when I talk to the activists I say, "All right, if it's more money, tell me for what? Secondly, have you looked at what is being done and decided whether priorities need to be changed?" When a child asks for more money, the parent says, "Well, what did you do with the money I gave you?" It's no different, I think, in terms of the government. "What did you do with the money I gave you?" You have to be accountable for it.

Regarding the Ariel Project for Prevention of HIV Transmission from Mother to Infant, which I'm working on as director for the Pediatric AIDS Foundation, I was worried about accountability because we're not a big organization and we're working with a very select group of investigators. I organized what we call the board of scientists, which is composed of very well-respected scientists--Howard Temin, Joe Sodrosky, George Shaw, John Coffin--these are well-respected HIV and non-HIV scientists.

I asked them if they would review the initial proposal for the Ariel Project and the ongoing results and progress. They agreed. The board is not funded by us, nor do we influence

whether they get research funding of their own. So they can be very frank with me and with the scientists, because they have nothing personally to gain. The opinion of the board allows the foundation to get a good idea of whether or not valid research is being performed.

Service on AIDS Committees

UCSF Task Force on AIDS, 1983-1986

Hughes: Well, the next topic is your service on AIDS committees. From 1983 to 1986, you were a member of the University of California Task Force on AIDS.

Ammann: The questions that the committee addressed had to do with research, some of it at the state level, and on safety precautions. When we first formed the committee, it was mostly trying to reassure people that AIDS was not a highly contagious disease which could be transmitted casually. The task force also instituted surveillance studies among health care workers for anyone who had an accidental inoculation from an HIV-infected individual. The latter problem really came under Merle Sande and Julie Gerberding. In fact, Julie was doing most of the work on that.

Out of this committee came practical recommendations which helped document that AIDS was indeed not a highly contagious disease, and that even with accidental inoculation, there were very few individuals that became HIV-positive. Initially, we did not have extensive data to support our views. Fortunately, what everyone felt was true, based on anecdotal information, was subsequently supported by epidemiologic data. And it was substantial. By the time '85 came around, HIV antibody testing was being done, so you could document the fact that you didn't have a lot of health care workers who had converted to antibody-positive.

Hughes: What was the initial mandate of the task force?

Ammann: The initial mandate was to take care of clinical issues related to AIDS.

Hughes: Issues that arose spontaneously?

Ammann: Yes. Someone would tack up a sign on a door saying, "This patient has AIDS." A hospital infection committee existed, but they could not deal with the AIDS issue, primarily because AIDS was so much more complicated, not only scientifically but also sociologically and politically. Years ago, you could say, "Patient has tuberculosis," and put up an isolation sign on the door. We put up isolation signs on the doors of patients who had immunodeficiency because we didn't want them to get a hospital-acquired infection. We didn't go through any hospital committee to do that; we just did it.

With AIDS, if you did something like that, then you heard from the public, everyone with an opinion--the press, the gay community. So there were wide ramifications. I think that committee worked because it had representation from pediatrics, surgery, internal medicine, and so on, to deal with the issue of infection control. The first policy paper in the nation [on this subject], published in the *New England Journal of Medicine*, came from the recommendations of this committee.[1]

Hughes: Have those recommendations stood their ground?

Ammann: Yes.

Casual Transmission of AIDS

Hughes: Were you taking a stand against casual transmission of AIDS, partially to allay fear in the medical and lay communities?

Ammann: It was probably coupled with two things. I personally didn't want AIDS to be casually transmitted, for one, because it would have been an even more devastating disease. But I think I also felt very strongly that had AIDS been casually transmitted, we would have seen it in other circumstances and transmitted more rapidly. But we just weren't seeing it. I think HIV testing confirmed what we had felt.

During those years, one of the major questions at every lecture I gave and at every meeting was, "Well, isn't it, couldn't

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[1] J. E. Conte, Jr., W. K. Hadley, M. Sande, and the University of California, San Francisco Task Force on the Acquired Immunodeficiency Syndrome. Infection-control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). *The New England Journal of Medicine* 1983, 309:740-744.

it be...?" It went from mosquitoes to kissing to saliva--questions which you never even thought of until somebody in the audience asked them.

But I knew families where, before they knew about HIV, for three or four years they had been eating together, and the kids were brushing their teeth with the same toothbrushes, and there were no special precautions being taken. Yet no one in the family got AIDS. Even with our own patients, the saliva would get on your hands; you didn't wash your hands. Between eating in the laboratory with blood samples and contact with secretions and no one getting AIDS, all of those things were telling most of us that it couldn't be casual transmission.

Hughes: Did you ever fear personally for your own health?

Ammann: Well, sometimes I would get a viral infection, and if I didn't quickly get over it, I would think, Could this be HIV? I was oftentimes a "normal" laboratory control, and a technician would say, "Well, your immunologic test didn't work this time; you weren't a good control." Or, "Your helper/suppressor cell ratio was not quite normal." Through my mind would go, "Gee, did I get AIDS?" Then the HIV test became available and I tested negative.

Hughes: Was some of your motive for serving as a control to monitor your health?

Ammann: No. It was just accessibility. The lab was there on the other side of the room.

But I do think there are two reasons to be tested for HIV. One is to know personally. The other--which I think we have to emphasize more in our society--is if a person thinks he has HIV infection, he should be tested, because under no circumstances should HIV be given to anyone else. I think there are good reasons from an ethical point of view to know HIV status, which we need to emphasize more. It's a lethal disease. People die from it. It's not like giving someone herpes or a cold.

Universitywide Task Force on AIDS, 1983-1988

Hughes: Well, from 1983 to 1988, you were on another UC committee, the Universitywide Task Force on AIDS.

Ammann: For me it was not an active committee. There were funding controversies probably as a result of Rudi Schmid being dean at that time. He was not my favorite dean.

Hughes: Would you like to say why?

Ammann: Well, he clearly did not want AIDS at Moffitt Hospital. I disagreed with Rudi's policy of trying to keep AIDS patients out of UCSF.

It was the same issue that goes on now in private practice, where some doctors don't want to take care of AIDS patients because they don't want their other patients to know that they take care of AIDS patients, because maybe the patients who don't have AIDS won't come back to them. I think there was a lot of that attitude at UCSF. So AIDS patients wound up at San Francisco General. But I think, in the long run, that was to their benefit because they got better care and more attention.

Hughes: Did you express your concern about the lack of AIDS facilities at UCSF?

Ammann: Yes, we talked about that at a couple of meetings. My feeling was that UC was serving the community, and one of UC's problems was that it was not always perceived as serving the community, and AIDS was part of the community. The response was, "Well, we're serving AIDS patients at San Francisco General Hospital." But space was not given for research or for clinical care at UC and there was no AIDS clinic set up at UC.[1] Marcus Conant had a Kaposi's Sarcoma Clinic, but no AIDS clinic at UC.

Chairman, Scientific Advisory Committee, American Foundation for AIDS Research [AmFAR], 1986-1994

Hughes: In 1986, you became chairman of the Scientific Advisory Committee of the American Foundation for AIDS Research.

Ammann: My role there was to be the chairperson of the grant review process and guide the scientific priorities of the foundation.

What I liked about the Scientific Advisory Committee was that it was a group of scientists from all disciplines, unlike the NIH review process. We had people like Mike McGrath and Jay Levy, and

[1]In 1984, the Adult Immunodeficiencies Clinic was established at UCSF.

also people nationwide from psychosocial areas and epidemiologic research. The group was very supportive of new researchers. The idea was to fund new investigators.

California AIDS Leadership Committee, 1990-1992, and Routine HIV Antibody Testing

Ammann: There's one other committee, the California AIDS Leadership Committee, which I was asked to join in 1990. This committee was established by the California State Department of Health Services to draft policy on HIV testing of women and children. Dr. Moses Grossman was chairman of the committee and we met only a few times. [produces list of members]

Hughes: A diverse group.

Ammann: Yes. Deliberately, I think. I was asked to be on it primarily because of my experience with pediatric AIDS. It turns out that I was again the maverick, because the committee's primary task was to give recommendations to the state about HIV testing of women and children. I had very strong feelings, and still do.

The committee's final recommendation was that HIV screening for women and children should be voluntary. They went through all kinds of discussions, like testing by zip codes, all of the ways of avoiding the real issue.

I dissented on the issue of voluntary testing. The primary obligation of a pediatrician is to diagnose disease. We screen newborns for thyroid deficiency and phenylketonuria and so on, without permission. But for AIDS, which kills the infant, we still don't routinely screen infants for HIV.

There were two reasons initially given for not routinely testing mothers or newborns. One reason was the confidentiality issue, that when you test the baby and the baby's positive, you know the mother's positive. I don't accept that, because when the baby becomes ill and is diagnosed as HIV-positive, you will know at that time that the mother is positive. So all you're doing is delaying the diagnosis, which is to no one's benefit.

The other reason which was valid for a period of time was, if you test the baby and discover that the baby is HIV-positive, there's no treatment to give the baby. You wouldn't do anything differently, so what difference does it make to know HIV status? That's not true any more. In fact, there is evidence now emerging

that the sooner you diagnose and treat, the more likely the baby's going to live longer. In fact, we have HIV-positive children living to fourteen and sixteen years of age now. So HIV remains the only disease in the history of pediatrics in which you can tell that the baby's infected at birth, or certainly after birth, where we don't routinely test with permission.

[This paragraph was added during the editing process, spring 1996] Now it's even more urgent to test, since for the first time in the history of AIDS, infection can be prevented in an exposed individual. Giving AZT to an infected mother can reduce HIV transmission to the infant. So prenatal testing should be done routinely.

So for those reasons, I said that it was unethical for the AIDS leadership committee to make a recommendation against routine testing. Now, everyone's afraid of the word "mandatory." I don't think you have to use the word "mandatory." I think you just have to say that routine prenatal testing should be the standard of medical care.

Another argument was that well, if you test, you're going to identify all these HIV-positive babies, and the social structure, the medical care structure, is not in place to take care of them. So don't test because you have to first have in place the support structure. And I say well, come on, did you not diagnose AIDS until the whole medical structure was in place? So to me these were very, very strange arguments. But I lost out. And I think the reason I lost out is because AIDS is a political and social issue, and it remains so to this day.

I've been talking to some of the activists, and not to my surprise but to a lot of people's surprise, the activist community is not as against prenatal testing as it used to be. The feeling now is that there's a real negative side to not testing. First of all, we don't know the real numbers of women and children who are infected. Secondly, early access to treatment and health care can only be provided when an individual is known to be HIV positive.

The policy of not testing routinely for HIV is contrary to everything that we do in other areas. That's what's so strange about it. I think I'm a logical person, and that gets me into trouble. But if a woman goes to a doctor to have routine Pap smears, or if you have mammographies done, aren't you having those tests to detect a disease before it occurs? The answer's yes. Then I say, "Why is HIV different? If this disease is ever going to be accepted as affecting everybody, you've got to get away from saying that testing should only be done in certain high-risk patients."

What I would really like to see now is that the standard of medical care will become that you offer HIV testing to every patient you see. That would mean that when a woman comes in for a gynecologic check, the physician would say, "Oh, by the way, we're recommending that you get the HIV test. I don't know anything about your sexual lifestyle, IV-drug use--" I think this has to happen, because the spread of the disease now is increasing among adolescents, heterosexuals. They have to be made aware that AIDS is something that could happen to them; it doesn't happen just to an IV-drug abuser or a homosexual or a bisexual.

Hughes: Is there any movement in that direction?

Ammann: Yes, slowly. We had a recent pediatric meeting where we recommended that the standard of care should be that prenatal HIV testing should be done routinely. But I think what's really going to change the policy quickly is when the first few successful lawsuits are instituted because a physician saw a patient and did not offer a test for HIV, and then that person transmitted it to another person or an infant. And then the person who got HIV infection or had an infected infant will sue the doctor and say, "You didn't do the test when you should have done it."

Hughes: That hasn't happened?

Ammann: That hasn't happened yet.

The Pediatric AIDS Foundation

Formation

Hughes: The next subject is the Pediatric AIDS Foundation.

Ammann: Well, when I was on the American Foundation for AIDS Research board of directors, Michael Gottlieb, who is one of the early figures in AIDS asked if I could assist in starting a pediatric AIDS foundation for a person, who at that time was anonymous. Michael became the co-founder of the Pediatric AIDS Foundation, along with Mathilde Krim from New York. Elizabeth Taylor had started the foundation, which was the first large foundation dealing with AIDS. I worked with the foundation from 1988 to 1992 as a "volunteer", weekends and evenings, and it took a lot of time while I was at Genentech. I had negotiated with Genentech 10 percent time where I could do whatever I wanted. Grant

applications that had to do with pediatric AIDS were reviewed along with the applications for adult AIDS.

Elizabeth Glaser

Ammann: In 1988, Michael was taking care of a patient who was HIV-infected and did not want anyone to know. That person happened to be Elizabeth Glaser. Because she wished to remain anonymous, he asked if I would come down to Los Angeles and have dinner with this patient of his, who had HIV infection and who had two children who were HIV-infected. That was 1988.

Michael said Elizabeth was interested in starting a pediatric AIDS foundation. Michael had recommended that she not try to create a whole separate pediatric structure, which could be costly, but that she take whatever money would become available and put it directly into research, and maybe use the American Foundation for AIDS Research infrastructure to administer the grants--which I thought was a good idea. So, since I was chairman of the scientific advisory board of AmFAR, would I talk to her about that possibility? So I had dinner in Santa Monica with this person who was previously unknown to me.

Hughes: Did you know her history?

Ammann: I knew she had HIV. I agreed to help her start the Pediatric AIDS Foundation. I would help with the administrative part and set up a group of scientists who would review grants and replicate for the Pediatric AIDS Foundation what the American Foundation of AIDS Research had. Elizabeth Glaser was very intense and was much more involved in what was going to be done and what was important than anyone I had ever met. She is a unique person.

She wanted to cut through bureaucracy and get right down to what needed to be done. She wanted to know the priorities in pediatrics AIDS research. Why wasn't there more research being done, and why did pediatric AIDS always get the lowest priority and lowest amount of research funding? AZT was available for three years before she could give it to her own child, which didn't make any sense to her. So she had lived the reality of what happens with pediatric AIDS.

Elizabeth has a different time line than anyone else. She's going to die of HIV infection.[1] She knows that; everyone knows that. So when she goes to a meeting, she gets right to the core of the issues. She's not gentle. She ends each meeting by saying, "This is what we've agreed to do. Now, when will this happen? Give me a time, a date. And when can we call you to see if this has happened?" Many times I heard her say, "I don't have time to wait for an answer."

Concerns have been raised about whether money has been taken away from adult AIDS for pediatric AIDS. I don't think that's a real issue. Elizabeth has been a very important advocate of obtaining new money for pediatric AIDS and stating that it has to be new money and can't be taken away from other research.

Setting Research Priorities

Ammann: We decided that to find out what the priorities were, what we should do is have a group of pediatric AIDS people meet and identify what needed to be done. Our first meeting was December 15, 1988, at the National Cancer Institute. We got together Phil Pizzo from NCI, Mickey Golbus from UCSF, Warren Andiman from Yale, Yvonne Bryson and Dick Stiehm from UCLA, Norval King from the New England Primate Center, Steve Wolinsky from Northwestern University, and myself. We focused on the areas of neurologic disease, transmission of the virus from mother to infant, and treatment issues. We had one person--this was a one-day meeting--address each of those issues, and we outlined the priorities of what had to be done.

We took the priorities and wrote up an RFA (research request for applications) saying that these were areas that we were going to award money for, and we wanted people to apply. And that was what we called our first think tank. We were excited about the response. People who were funded subsequently felt that we had put out research money for areas that were very much needed. We set up a group of people to review the grants, like we were doing on AmFAR, trying to fund people who didn't have big dollars, but who really could concentrate on these specific areas of research.

We scheduled another think tank, and this one was held in Santa Barbara [February 1990] on Ted Field's ranch, Ted Field the movie producer. It was a very informal atmosphere, only twenty-

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[1]Elizabeth Glaser died of complications from AIDS on December 3, 1994.

five people, from outside of AIDS research this time, as well as people within AIDS research, and a mix of M.D.s and Ph.D.s.

Hughes: Who invited them?

Ammann: At this point I was the nominal chairman of what was called the health advisory committee, to whom we had said, "Now you're going to become the Pediatric AIDS Foundation advisory board." The original board has remained pretty much the same.

We formed a subgroup consisting of Michael Gottlieb, Yvonne Bryson, Dick Stiehm, and Phil Pizzo, and myself, who would think through plans for future think tanks. We've just now planned the eighth think tank; there are two a year.

We've learned to have a single topic. The next one is mucosal immunity. We have a researcher in animal medicine from UC Davis, we have Hans Ochs from Seattle, we've got [Constance] Connie Wofsy[1] who has nothing to do with pediatric AIDS but deals with AIDS in women. She knows a lot about mucosal immunity and transmission from male to woman and woman to male.

We usually don't have people attend twice, because we try not to invite people who think the same and agree with one another. In fact, we like a little controversy. We do not allow slides. You can't believe how uneasy people get when you say, "You cannot show slides." Because scientists are used to showing slides.

Hughes: What about blackboards?

Ammann: No. We have an overhead that you can write on at the end of a session to summarize everything that you have identified as important. After the participants go through it--it's like castor oil--they realize how valuable it has been to talk about the issues rather than, "On this slide we showed a 23 percent increase in CD4 count." The question is not, was there a 23 percent increase in CD4; the questions are, why did the CD4 count go up or down, what might be the pathogenesis, what might be the mechanism, how can we find out about it?

The Ariel Project

Ammann: The first think tank the foundation had in '92 was on maternal-infant transmission of virus, and out of that think tank came the Ariel Project. We realized that we had spent three years funding

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[1]See the oral history in this series with Dr. Wofsy.

research; we had a lot of things that we thought were very positive, but we still didn't know why some babies got infected and why some babies didn't. So we said, "Well, let's get together the key people that can discuss this issue and tell us what needs to be done." At the end of that think tank we got a very clear indication of what needed to be done. Most of these researchers were outside of pediatrics. How could we get them to do the research? Obviously, give them the money and require that they work together.

So the researchers put together a research plan; we put together a budget. That part was not too difficult. But how would we make sure the research got done and that it was the right research to do? It would take a person to sit on top of everybody and say, "How's progress?" And everyone agreed it needed a full-time person. I happened to be leading that particular think tank, so people said, "Why don't you do it?" I said, "Not me. I've got a very well-paying job at Genentech. Enough."

But as time went on, I thought, Well, maybe this is something I really want to do. So I met with Susan DeLaurentis, Elizabeth Glaser, and Susie Zeegen, the three founders of the Pediatric AIDS Foundation, and said, "Okay, I'll do it." I left Genentech in July of 1992 and took on the direction of the foundation research projects full-time.

Hughes: Any regrets about leaving Genentech?

Ammann: None. I love what I'm doing. Because what I'm involved in now, Sally, is not just in saying what the research priorities are, and helping push them, but I also now have the time to get involved in health care issues critical to HIV/AIDS. Because of the experience that I had working at the university, with NIH, and then with a pharmaceutical company, I have a good idea of who can do what, and what the advantages and disadvantages are of programs which set out to accomplish certain goals.

For example, I'm a very strong proponent of having drug companies do most of the fast-track drug development and testing, because once they lock into it, they will move much faster than people in the university who've got conflicting responsibilities. On the other hand, if there's no money to be made in a specific area which is nevertheless important to HIV/AIDS, the university researcher can do it best.

Some examples. Where are the vaccine candidates? They're all in pharmaceutical and biotech companies. Why? Because the universities can't move quickly enough. They don't have the resources to make the recombinant material. Why are the

pharmaceutical companies interested? Because they see big dollars down the line. So let them move it as fast as they can.

But what about other issues? Who moves the testing of AZT into pregnant women or children? Well, that's where you have to bring in the NIH. They have to pay for the studies, because the drug companies aren't going to do them. And you need the academic researchers to answer fundamental questions.

Hughes: Do you see yourself as a facilitator amongst these different elements?

Ammann: Yes. I feel comfortable with the NIH people; I feel comfortable with pharmaceutical people; I work with the activists. In fact, I went with Martin Delaney of Project Inform to Abbott. I'm going to go with ACT UP Golden Gate [AIDS Coalition to Unleash Power, Golden Gate Office] to Genentech to talk to them about moving Genentech research more quickly.

San Francisco Model of AIDS Care

Hughes: Please comment on the San Francisco model of AIDS care.

Ammann: I'm not really sure what the model is, but I think what people mean by it is trying to find out why the entire AIDS effort in the city of San Francisco was so much more organized and less fraught with divisions than in other parts of the country. I'd like to take partial credit for it [laughing]. It was somewhat a consequence of the early history of how the AIDS problem was identified, and the people who identified it.

If you go back to that first group that met at the [UCSF] Faculty Club [in 1981], there was Marcus Conant, who was a faculty member at UC but had a private practice in dermatology. He represented the gay community. Paul Volberding was a young professor who came out of cancer research and was seeing patients with AIDS. John Greenspan was an oral surgeon who was seeing patients who had oral lesions. Bill Wara was a radiation oncologist who was interested in the immune system and was seeing patients who were developing malignancies and required treatment. And then the pediatrician--myself--who had not really identified a child with AIDS at the time of the first meetings. I was actually seeing them at that time but didn't really know they had AIDS until months later.

So here you had these different specialists saying, "We see this epidemic as an emerging problem and we think we should be doing something about it." We kept meeting on a regular basis, talking to people in the dermatology clinic and in the community, and trying to convince other people that this was indeed an emerging problem. We were not meeting with some of the opposition that was occurring elsewhere in the country about this being identified as a gay disease. Homosexuality was more accepted in San Francisco.

And then the group went down en masse to Los Angeles to the meeting that Willie Brown had organized to say, "We need research money to look at this epidemic." The San Francisco group divided up and wrote different parts of the proposal. I would like to think that that cooperation set the stage for what happened.

The next thing that happened, which was probably good in the long run, was that the program was put at San Francisco General. San Francisco General is an interesting place. It is somewhat isolated, but there's a lot of working together on problems. So there again, I think it set the stage for saying, "Okay, this is a problem; we know how to take care of it; we can set up our own clinic; we can set up our own hospital ward." It was debated at first whether or not this should be done, because it would isolate patients with AIDS. The AIDS ward, however, turned out to be a positive thing.

It was just very natural for people to work together in these multiple-specialty areas. And then once it became apparent to everybody that this epidemic indeed was a significant problem, that it required a lot more manpower, and that you couldn't take care of all of the patients through the university system, by that time there were a lot of private physicians who were involved. Geographically, this is a very small city, and the community people could easily attend the meetings at San Francisco General. So it evolved into this San Francisco model which is really people working together on AIDS.

As the AIDS effort got larger, there was more splitting and separation into different programs. But when people talk about the model, it means rather than fighting over who's going to get the money, what hospital gets it, where the patients are taken care of, people work together. If you look at the authors on the manuscripts that came out of the San Francisco area, they're very representative of the community. Probably half of my papers are with community internists and pediatricians. It was never a problem getting patients to do studies, and who they belonged to. People really had the initial vision that this was going to be a bad disease, and we've got to solve some of the problems, and

weren't so worried about the academics or the credit or anything like that. So to me, that's the San Francisco model for all new diseases. But whether or not it could be replicated, I don't know.

Publishing on AIDS

Hughes: Do you care to comment on peer review and publication of important results in reference to the AIDS epidemic?

Ammann: Initially, there were problems in people accepting AIDS as a new disease. On the pediatric side, nobody accepted it at first. We couldn't get anything published. As the epidemic progressed, AIDS was enough of a curiosity and people wanted to know about it that publication was not a major problem. Everything about the disease was important and published as long as you had enough patients and observations.

As time went on, however, there was a tremendous amount of competition about who reported what first, whether something should or should not be published, perhaps because it contradicted what another person reported. So as always exists in academics, there was an evolution in AIDS research from skepticism to everyone wanting to know about AIDS and finally to intense competition.

Hughes: The community activists, of course, had a role in the FDA drug approval process. Did they have a similar role in terms of publication? Was there pressure from the community to get information out faster?

Ammann: Well, I think not so much for publication. What I sensed was, the community wanted to know the information before publication. If something was of benefit, they couldn't wait for publication; they needed it before.

The Ingelfinger Rule

Ammann: That was a contradiction for certain journals, like the *New England Journal of Medicine*, which had its Ingelfinger Rule: If the data was published in the lay press, the *Journal* wouldn't publish it. They considered themselves caretakers for any important information that might come out of the AIDS area, or for

that matter, any other area. Therefore, they could set the rules and would actually punish investigators by not considering their articles, just as was true for my blood transfusion AIDS paper, if they let the information out early.

Hughes: Does the *New England Journal* still stick to the Ingelfinger Rule?

Ammann: Yes. People who don't want to hold to that rule publish elsewhere. But then, in the view of some people--not me--they're accepting a less prestigious journal for publication. The *Journal* still holds the position of purveyor of some of the best articles. It also holds the position of having published some of the most dishonest articles. Fabricated or questionable research has been published in the *New England Journal of Medicine* probably just as often as in any other journal.

Hughes: Are you saying that an article published in *Nature* or *Science*, which, of course, make the information accessible faster, doesn't have the scientific prestige of an article published in the *New England Journal of Medicine*?

Ammann: Yes. But I'm talking about clinically related articles. If you're talking about basic science, then *Science* or *Nature* get information out quickly.

Most of the critical articles in AIDS research have been published in the *New England Journal of Medicine*, *Science*, and *Nature*. Articles in other journals don't have the same impact. *Science* has a wide distribution, *Nature* has a wide distribution, and the *Journal of Medicine* has a wide distribution.

Peer Review

Ammann: Now, the scientific community argued that a paper had to be peer reviewed before it was put out in public, because otherwise you'd get all of these crazy results coming out that hadn't been proven, and it's not for the benefit of the patient or anyone else for that to happen. But activists also reviewed the research results of published articles and often pointed out weaknesses. They also insisted that important information be made available prior to publication.

So I think activism again played a positive role. If information was critical, it was appropriate to make that information available, without it having to go through a full peer review documentation which might take a year or year and a half to

complete. I view it as positive, just as I view the activist role in drug development as overall positive.

FDA Drug Approval Process

Hughes: Do you want to say anything more about the FDA approval process?

Ammann: Yes. Here's probably the most concrete example of the benefit that activism plays. A lot of the questions that the activists were asking about drug development turned out to be very appropriate. My initial response was probably like that of a lot of moderately conservative people: "What do activists know about this process? It takes a long time to develop a drug, and you've got to do studies, and this is the process." It turned out a lot of those things were just not true, and the activists said they weren't true. The approval process didn't have to take so long. Now I'm asking some of the same questions: "Why does this process have to take so long?"

Most life-threatening diseases affect individuals who are not members of an organized community. But the AIDS activists belonged to a community, and the bonding there was the homosexual lifestyle. It was like multiple people in a community dying of the same disease. This group of individuals just would not accept things as usual, and there's power in numbers. They began to question a lot of the FDA drug approval process.

I think most people would say that the changes the FDA has instituted have benefitted people outside the area of AIDS as well. There's a more rapid approval mechanism; diseases are categorized now according to whether they're life-threatening. There's a fast track for drug development, depending on the disease. You can get drug approval at phase III of development instead of waiting for phase IV large efficacy trials. Drug companies like that, because of course, they can start charging for the drug sooner. The community doesn't object to it, because it's to their benefit. Investigators don't object to it, because basically it confirms their clinical trials sooner. So everyone seems to have benefitted from it.

The only problem is, of course, it requires more staffing at the FDA. But the FDA needed more staff anyway. This is really a positive as well, because it has allowed the FDA to say, "We have to look at these drugs more quickly; we have to have more rapid turnaround time on these drugs." The FDA now says, "Well, how do we approve combination drugs? How do we get a drug approved if we

don't have classical endpoints? What kind of endpoints should be used?" So the FDA has more interaction with advisory committees. There are community representatives on a lot of the FDA committees.

Hughes: Would you attribute all those changes to the effect of the AIDS epidemic?

Ammann: Yes, I really would. I think the epidemic has raised questions of why do things have to be done this way? And other advocacy groups learned from the AIDS activists. The epidemic has pointed out discrepancies: there's insufficient drug testing in infants and children, insufficient drug testing in women, insufficient drug testing in pregnant women. It's raised questions: are there any differences in reaction to drugs in ethnic minorities, racial minorities? We don't know.

The Epidemic's Impact on American Medicine

Hughes: You are talking about the impact of the epidemic on the health care system. Are there other aspects that you want to talk about?

Ammann: Yes. I think AIDS has brought out many of the problems in our American society--prejudice, and the weakness in our health care system. We've got a very expensive health care system that, when you have money, you can access it. But even the AIDS patients who have money that can access it early on become destitute later and then have trouble accessing the system. HIV-infected children, of course, have virtually no access to the same health care as adults.

A pediatrician in Santa Cruz, who was on the IOM [Institute of Medicine] committee, told me that children with AIDS are like the canary in the coal mine. Now, a lot of people don't remember the coal mines or the canaries, but the canaries are the first to succumb to carbon monoxide poisoning in the mine and they were used for indicators of danger. I think that analogy can be extended to pediatric AIDS. How children with AIDS are treated is showing the weakness in the health care system in the United States.

The weakness is that our health care system is linked to whether or not you work. If AIDS patients are employed, they have access to the health care system. When they get so sick they can't work, they lose their health care. Children, of course, don't work at all, and if the parents don't work, then they all

lack access to health care. We are the only developed country that links our health care to whether or not you work, which makes no sense, because of course, when you're sick and you can't work, that's when you need health care coverage the most.

I think it is clear to the people taking care of patients with AIDS that the medical system is deteriorating. It is too costly; it is difficult to access; drugs are reimbursed only if they are approved; the health care system denies certain drugs because they are too expensive. Obstetricians enroll a woman in a clinical trial because they want to see if AZT keeps the baby from getting infected. But when the baby's born, the mother gets no further care and is not eligible for any trials. That's injustice. What are we doing about taking care of this large population of young, pregnant women who have HIV infection?

The epidemic has pointed out that we have to look at clinical trials very carefully. They have to be designed carefully; they have to have statistics built in; they have to have very clear answers, because the public is going to scrutinize the results. I think that's a benefit. The scientific custom in the past has been, "Well, we're going to do our studies, and we will interpret them, and we will tell you whether or not the drug works."

I would like to think that the questioning of how you treat breast cancer--do you do mastectomy, do you treat with chemotherapy, do you treat with radiation, what's the outcome of different treatments--is because people now feel the courage to say, "Well, as in AIDS, we're going to ask the scientific community to provide us with proof as to which is the better treatment."

Hughes: "And then I will make the decision."

Ammann: "And then I will make that decision," right.

Finally, I'm very worried about the institutionalization of AIDS, because I think that the benefit that AIDS has enjoyed is because it hasn't become institutionalized. If it becomes institutionalized, then it will fall into the same pattern that other diseases fell into, timelines that are driven by less committed individuals.

Hughes: Well, thank you, Dr. Ammann.

Transcribed and Final Typed by Shannon Page

Regional Oral History Office
The Bancroft Library

University of California
Berkeley, California

The San Francisco AIDS Oral History Series

THE AIDS EPIDEMIC IN SAN FRANCISCO: THE MEDICAL RESPONSE, 1981-1984

Volume III

Paul A. Volberding, M.D.

ONCOLOGIST AND DEVELOPER OF THE AIDS CLINIC, SAN FRANCISCO

Interviews Conducted by
Sally Smith Hughes
in 1992, 1995

Paul A. Volberding, M.D.

INTERVIEW HISTORY--by Sally Smith Hughes, Ph.D.

This oral history series begins with interviews with Paul Volberding, the most visible presence in AIDS medicine in San Francisco. His prominence rests on several factors. He has been an actor at the front line of patient care in the epidemic since its first recognition in the summer of 1981. He was a member of the original three-physician "AIDS team" which staffed the AIDS Clinic and saw service in the inpatient AIDS ward at San Francisco General Hospital.[1] He has had a hand in constructing and promoting the "San Francisco model" of comprehensive, community-based AIDS care, a model which has been translated to communities around the country and the world. Beginning as early as 1982, he directed clinical trials of new AIDS drugs, including those of AZT and the new protease inhibitors.

Who is the man behind these and other achievements? The oral history provides some clues. By training, Volberding is an oncologist, a specialty tending to attract those comfortable with death and dying. He relates in the oral history how early experience with cancer patients revealed his attraction to the clarity and directness of those facing death. He found he had the personal skills and interest to help--skills which were to be of use in the AIDS epidemic, the devastation of which continues without cure or effective vaccine.

Smooth and polished in social interactions, Volberding's genuine concern and humane treatment of early patients, often frightened and stigmatized, became the standard of those identified with AIDS medicine at the San Francisco General. The oral history provides a sense of the dedication and isolation of the team of health care providers first drawn to the new disease. But Volberding also admits to recognizing a good thing when he saw it. An assistant professor at the outset of his career when the epidemic broke, he knew he needed a "hook" to advance his academic career, and AIDS was it. It was a risky "hook" at first, because until 1983 patients were few, research funds virtually nonexistent, and the duration and importance of the epidemic problematic. All that has of course changed, propelling Volberding to a position among the first rank of AIDS clinicians.

Perhaps the most important information in this oral history relates to the development of the AIDS Clinic and the multiple services it provided. According to Volberding, what has always been unique about AIDS medicine at San Francisco General is its location in one multidisciplinary unit, the Division of AIDS Activities, which Volberding directs. Other institutions indeed offer a multidisciplinary approach to HIV disease, but the various specialists retain affiliation with their original specialty

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[1]The other team members were Donald I. Abrams, M.D., and Constance B. Wofsy, M.D., both of whom have oral histories in this series.

rather than to AIDS per se. Volberding emphasized this point in the oral history:

> It's my own conceit as much as anything else, but this [AIDS Activities Division] is still a pretty unique place. We are really truly multidisciplinary in one division. In a lot of other places, there is a network that's been formed of oncology, infectious disease, pulmonary medicine--of people who see themselves as still primarily in their own divisions, but who come together and take care of AIDS patients.
>
> Here, we have in one division oncology, infectious disease, pulmonary medicine, psychiatry, general medicine, family medicine--people who have that as their background and training, but who work full time in the AIDS program....
>
> I think it's unique. I haven't heard of any other place that's done that. If I had to pick one thing that really sets us apart and has been part of our success, it's the multidisciplinary nature of the program. The multispecialty medical care is really fully integrated. [p. 185]

The Oral History Process

Three interview sessions were conducted with Dr. Volberding in May and June of 1992. A fourth session was requested, and kindly granted in April 1995, as a result of questions raised by research in Volberding's professional correspondence, newly acquired by the UCSF Library's AIDS History Project [AHP]. We met in Volberding's pleasant corner office in Ward 84, the administration floor of the AIDS Activities Division, located in one of the old brick buildings some distance from the new hospital in the San Francisco General Hospital complex.

Darkly handsome and friendly in manner--"Call me Paul"--Volberding responded readily to questions but at first in generalities, perhaps because of his frequent exposure to the media. When he realized our purpose was to recreate a period of history in detail, his answers became fuller and deeper. In this regard, the reader may wish to compare the first and last interviews. Edited transcripts of the interviews were mailed to Volberding, who edited them lightly and returned them promptly.

Oral history and traditional archival sources should be used in dialectic: written documents providing the basis of research for the interviews, the oral histories adding critical new information about the written record. In the case of the AIDS oral histories, we are fortunate to have access to documents in the private possession of the interviewees as well as to the rich resources of the AHP at the UCSF Library. In the case of this oral history, the AHP's recent acquisition of Volberding's papers was a stroke of good fortune, providing an immensely useful source for, and indeed prompting, the final interview.

In this oral history, we have a voice from the heart of AIDS medicine in San Francisco. The reader will find that it speaks with authority, sensitivity, and compassion.

Sally Smith Hughes, Ph.D.
Senior Interviewer

Regional Oral History Office
The Bancroft Library
October 1996

Regional Oral History Office
Room 486 The Bancroft Library

University of California
Berkeley, California 94720

BIOGRAPHICAL INFORMATION

(Please write clearly. Use black ink.)

Your full name Paul A. Volberding

Date of birth 26 SEP 1945 Birthplace Minnesota

Father's full name Walter Volberding

Occupation Retired - Food Services Birthplace Iowa

Mother's full name Gloria Volberding

Occupation Retired - Housewife Birthplace Minnesota

Your spouse Molly Cooke M.D.

Occupation Physician Birthplace Philadelphia

Your children Alex b. 1981 Ben b 1984 Emily b. 1987

Where did you grow up? Rochester Minnesota

Present community SF.

Education A.B. Univ. Chicago 1971 M.D. Univ. Minnesota 1975
Medicine Residency Univ. Utah 1975-78 Oncology UCSF 1978-81

Occupation(s) Physician

Areas of expertise AIDS, HIV Therapy, HIV Malignancies

Other interests or activities Music (Opera - not singing)
Travel, Sailing.

Organizations in which you are active Past Am Soc Society - USA

I EDUCATION AND EARLY CAREER

Early Attraction to Medicine

[Interview 1: May 8, 1992] ##[1]
Location: Dr. Volberding's office, Ward 84, AIDS Activities Division, San Francisco General Hospital

Hughes: Dr. Volberding, I know you were born in Rochester, Minnesota.

Volberding: Right. I didn't think there was any other Rochester.

Hughes: [laughs] Oh, yes, there is. There's a Rochester, New York, also.

Volberding: There are a lot of them.

Hughes: Was your family associated with the Mayo Clinic?

Volberding: No. The Mayo Clinic was our doctor. My dad was a dairy farmer, and we lived outside of Rochester. It sounds completely hokey, but a view of the Mayo Clinic was framed in my bedroom window. As I looked out in the morning, I could see the Mayo Clinic. Growing up in a town where medicine was so much what you saw all the time, and also with the social elite being all physicians and physicians' kids, I think it was a natural enough thing to see medicine as a suitable goal for myself. So I decided to go into medicine when I was still in high school.

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[1]## This symbol indicates that a tape or tape segment has begun or ended. A guide to the tapes follows the transcript.

Hughes: Were you good in the sciences?

Volberding: Yes, I was good in sciences, and had a high school biology teacher who said, "Gee, you have talent." No one had ever really said that before. He suggested that I go to a college during high school for a summer science program sponsored by the National Science Foundation. So I did that, with high school kids from all over the Midwest, and it was challenging, but I did fine. So science seemed what I wanted to do, and biology seemed an area to focus on, again because of my teacher's interest. Medicine became a logical connection to make from biology.

Undergraduate, University of Chicago, 1967-1971

Hughes: And then you went on to the University of Chicago. Why did you choose Chicago?

Volberding: [laughs] This is literally true: I was riding up an elevator in a store in Rochester when I was in high school, and I overheard some friends of mine talking to another guy who had graduated the year before and gone off to college. This was the time when I was thinking about which schools I wanted to go to, and he was saying, "Oh, God, school is so awful; the pressure is terrible; everyone's committing suicide--." He kept going on and on about how hard it was. I said, "That's the place for me." And I asked him where he was going--University of Chicago.

Hughes: Why did that attract you?

Volberding: I really wanted to be pushed, I guess. I didn't frame it exactly in those terms. So I applied at Harvard, Yale, Stanford, Chicago, and a couple of schools in Minnesota, fallback schools. I remember going to my high school guidance counselor who said that it was really inappropriate for me to be applying to the schools that I was, because with my background, it was not reasonable to advance more than one step above where your parents were in life. So I said, "No, I don't believe you." [laughs] So I went to Chicago. It was a great school. It was everything that my friend said: it was very challenging, very tough. But I think surviving that gave me a lot of confidence.

Hughes: Were there any professors that you were particularly influenced or impressed by?

Volberding: I needed some extra money; I was there on scholarships, and also I wanted to get my hands into medicine and science a bit more. I found a part-time job in one of the virology research laboratories at Chicago, and worked for a person named Mark Beem, who was just a wonderful human being. He later became the head of pediatrics at Chicago. He really took me under his wing. I got to do virology, both clinical and research.

With everything going on, with the [student] "revolution" and everything else, it was great to have a centered place like that to be working. So I worked in the lab all the time during college. I actually got another National Science Foundation grant in college to spend a summer working on neutralization of rhinoviruses, the viruses that cause colds.

Hughes: Which Beem was working on?

Volberding: Which he was working on; that was his area, colds.

I got to be good friends with some of the people working in the lab next to mine. That was Werner Kirsten's lab, and Kirsten was one of the first people to discover retroviruses. So even in college, I was intrigued by them, because there seemed to be a lot of excitement in that field. Actually, rhinoviruses were kind of a dying specialty, and retroviruses were the emerging hot science.

Medical Student, University of Minnesota, 1971-1975

Volberding: So then when I went to Minnesota for medical school, again sought out work in a virology lab, and this time it was in RNA tumor viruses, retroviruses. During medical school, which I pretty much hated, the lab was a really wonderful exception. I really loved working in the lab.

Hughes: Why did you hate medical school?

Volberding: I'm not sure if it was me or if it's medical school in general, but I found it not very challenging. It takes a lot of work, but it's really rote memorization for about two full years. After coming from a place like Chicago, digging into ideas and--

Hughes: You wanted something more conceptual.

Volberding: More conceptual, and medical school was absolutely nonconceptual. So I found it disappointing, especially because medicine was what I had always imagined doing my whole life.

Hughes: Did you begin to question whether you really wanted to pursue medicine?

Volberding: Well, I came away thinking that I was really not very interested in clinical medicine. I was working in a research environment the whole time, and most of what I was interested in at Minnesota was in the lab. I fully expected to be one of the very typical people in medical science: having an M.D. but not really using it, and being a bench scientist.

I got wonderful support in Minnesota from the person whose lab I was in, Charlie Moldow. He had just arrived at Minnesota from Bellevue [Hospital, New York City] and was a great character and a young assistant professor. He's now head of medicine at the VA [Veterans Administration Hospital] in Minneapolis. He was just another one of these enthusiastic people and sort of adopted me into his family. I got to see science, and again the feeling from people around me was that I was capable, I was competent, I could do it if I wanted to.

Charlie really urged me to go to Bellevue for an internship, and I really wanted to. For some reason, I was really drawn to big cities, real urban life, and the challenge of blood-and-guts places. Not so much because I wanted to be an M.D.--I was confused as to what I wanted to do at that point.

Intern and Resident in Medicine, University of Utah Medical Center, 1975-1978

Volberding: My wife at that point was from the West, and she really wanted to move back to the mountains. The joint decision we made as a couple was that I would not go to Bellevue, but I'd go to someplace in the West. Utah was recommended by the people at Minnesota as having good classical hematology, exposure even as an intern and resident. I anticipated working in a hematology division, which is where I was working in Minnesota. So I went to Utah for my internship and residency, again expecting it just to be a stepping-stone to a lab.

Hughes: You had no contact with viruses at Utah?

Volberding: No. It's pretty hard as an intern and resident anyway, and I think even here at UCSF, which is a very academic and bench-oriented medical school, interns and residents rarely do much in the lab.

It was a good time. I wasn't expecting to work in a lab during those three years, and wasn't really at a place where research was a major part of the focus.

Hughes: Were your ideas changing about patient care?

Volberding: I had a couple of experiences at Utah that made me think that it might be interesting to take care of patients. I really have to say I did not excel in medical school. I got by. I was more interested in jazz and in the lab.

One of my first patients at Utah was an Assembly of God minister and missionary, and a faith healer. He had advanced thyroid cancer that had spread throughout his body, and was in really an end stage of his disease. He was young, and his wife was young. She in particular couldn't accept that he was dying. It didn't connect with their faith that praying and belief in God would not heal anything. So while he was dying and knew it, she really couldn't face it, and their friends couldn't get to a place of letting him even talk about it.

One day when I was by myself with him, he said, "I feel terrible because I know I'm dying, but my wife can't handle it." So I found myself in this weird position of being an intern just out of medical school, being told these incredibly confidential, honest things. And it really made me think: this is an amazing position to be in, that I could be there for him; I could be somebody that he could talk to, and I could help him in what little way I could to deal with what was going on.

So that was the most striking thing I remember about my internship and residency--he was one of my first patients. And it really did change me in a lot of ways. At that point I said, "Well, instead of doing a hematology fellowship, I really am more interested in doing an oncology fellowship," because I really liked working with cancer patients. While I was at Utah, I sought out more oncology elective time. So I did quite a bit of oncology as a resident.

Clinical Fellow in Hematology/Oncology, UCSF, 1978-1979

Volberding: I divorced during my internship and residency. My private life was absolutely miserable, and I am not especially proud of my overall performance as a resident. [laughs] But I did well in the area that interested me the most, so I was able to pick a competitive oncology fellowship afterwards.

This is a story I've told before but it's true. I was not all that happy living in Salt Lake City; it's a very conservative place, and I'm not a very conservative person. I sat up at night working on patients and looked out the hospital window; all the patients talking about their illness and then falling asleep, and I looked out across the valley floor, because the hospital sits up on the foothills looking west. It's a very flat valley floor, and I saw this red streak going across it, which was the tail lights of the cars on Interstate 80 heading towards San Francisco.

Hughes: That's where you wanted to be?

Research with Jay A. Levy, M.D.

Volberding: Really many nights, I said, "I want to be in one of those cars with red lights heading West." I came out here on holiday for a couple of days, and loved San Francisco. So when I was looking for fellowships, it was the logical place to look. And also the person [Charlie Moldow] in whose lab I'd worked in Minnesota had a good friend from college [Stuart B. Levy] whose identical twin brother is a virologist here--Jay Levy. Charlie Moldow said, "Jay's working on some really interesting viruses." In Minnesota, my interest was the connection between viruses and cells, what characterizes the receptors for viruses on the surface of cells. It's a very important issue in all of virology, because viruses have to gain entry into the cell before they can do anything. They don't gain entry into every cell.

Jay was working with a virus with a very bizarre feature. It was a mouse virus that could only infect cells from species other than those from which it was originally grown. It was called a xenotropic virus. He was one of the few people in the world working on it; he was one of the people that discovered the family of viruses. It's a retrovirus.

So I came to San Francisco specifically to work with Jay, to work in his lab. I did the oncology fellowship because that's the institute [Cancer Research] he was in. I was sort of interested in oncology after residency, but really came here expecting that this was where I was finally going to learn real science and become independent.

Instead, what happened is I really fell in love with medicine for the first time. [laughs] I am so sympathetic to people in training who don't know what they want to do, because it sometimes doesn't happen until years later.

Hughes: How did it happen?

Volberding: I really like taking care of cancer patients; I think the feelings that I had for those patients at Utah were telling me what I really wanted out of this. I really enjoyed the sense of responsibility for taking care of cancer patients, and the honesty and communication that I think is unique with dying patients. The same with AIDS, which I'll get to. It's just a unique situation.

As a fellow, I had a lot of responsibility, and I particularly loved the county hospital [San Francisco General], because here I could really take care of my own patients, which isn't something you usually get much experience with as a resident. You're always doing things for somebody else; it's always some other physician's patient.

So that first year here in San Francisco, my life was better. I was away from a place that I associated with not such a wonderful period, and San Francisco's a wonderful city. I loved it the minute I came here. I met my [future] wife during the first year. Molly Cooke was a resident in internal medicine on the cancer service when I was a fellow, so really things were going well.

Hughes: How quickly were you married?

Volberding: Oh, I guess we lived together for about a year or so before we got married. We went on vacation in Jamaica, and the brochure said, "It's easy to get married in Jamaica; just ask at your hotel," and so we did, and it wasn't. [laughter]

The other thing I found out about Jamaica--and it's probably true of all poorer countries--is anything can be done for money. They say, "Well, it's not that easy, but instead of you having to go to Kingston, we'll send somebody if you pay them." So we said, "Okay." We got married on the beach

and had to knock on doors to find witnesses for the wedding. [laughter] Very fun. We got married in 1980.

At the end of my first year of fellowship [1978], I then went into the lab, and it was a real disappointment.

Hughes: Why?

Volberding: After preparing for the lab my whole life, I had fallen in love with medicine. I really felt bad being in the lab all the time; my heart was really more with the patients.

Hughes: So it was more that than the fact that research didn't interest you?

Volberding: Jay was on sabbatical a lot of the first year that I was in the lab, so the person that I came to work with wasn't there. For whatever reason, whether it was my growth or changes in me, it just didn't feel right. I found myself during the last year looking at my watch at the end of the day, and leaving at five o'clock. Then I finally said, "What's going on here?" Going into a career, looking at a clock, and wishing I was somewhere else--this is not what I expected out of life. I then decided that the lab wasn't where I wanted to spend my life.

II THE AIDS EPIDEMIC

Kaposi's Sarcoma [KS]

Volberding: A clinical position opened up here at San Francisco General, and I really leapt at it, because this was the hospital that I loved. I could do what I wanted; I could start my own program. There was no oncology here at all so I would be the first chief of oncology just out of my fellowship.

Hughes: Why was there no oncology?

Volberding: There had been no chief of medicine here for quite a while. The former chief [Hibbert Williams] had left several years before; they hadn't found a replacement. Merle Sande had been hired just the year before [1980]. As one of the conditions for him coming, he wanted to create an oncology division. The cancer patients here had been managed by the [postdoctoral] fellow. A staff physician had come down from Moffitt [Hospital, University of California, San Francisco] once a week to see if there were any emergencies that needed attention. So it was really a pretty remarkable opportunity.

Hughes: Do you know why a decision was made to make a formal oncology division?

Volberding: Well, Merle was an infectious disease person, and in many places there's a close relationship between infectious disease and oncology, because oncology patients are immunocompromised and get very strange infections, and they generate business for infectious disease. So I think in part, Merle wanted to have the oncology division as part of an infectious disease program. Also, there are a reasonable number of cancer patients here, and it was awkward having to rely on Moffitt to take care of them.

So I took the job. I walked from a retrovirus lab into a retrovirus epidemic literally my first day.

The First Patients

Volberding: John Klock, who was a hematologist at Moffitt, had been looking in on the cancer service here for the last weeks of June, 1981, before I came down here to organize the service. On one of my last days at Moffitt he patted me on the back and said, "Paul, there's the next great disease waiting for you at San Francisco General Hospital. There's a patient with Kaposi's sarcoma." He said it as a joke; this was before any word had come out from anywhere about Kaposi's sarcoma [in gay men].

Hughes: When was this exactly?

Volberding: The end of June, 1981. There was a patient with Kaposi's sarcoma that he had looked in on just before I took over. He commented, because it's a very unusual tumor, but it's a no-big-deal tumor.

Hughes: But you did know about Kaposi's.

Volberding: No, hardly at all. I had just finished my oncology fellowship and really knew nothing about it. I knew the name.

So I came down here July 1, 1981. I was the attending [physician] and I had a fellow, Ray Stricker, to work with who had just gotten to San Francisco from New York, where he had done his internship and residency. On the first day, we saw this patient, a twenty-two-year old man with Kaposi's sarcoma. We went to the books like anyone would and found that this patient shouldn't have Kaposi's sarcoma; it absolutely did not compute. He was too young, didn't have an organ transplant, wasn't from Africa--those were the only kinds of conditions where you'd expect to see it.

Ray said, "Gee, I think we'd seen some of these cases in New York City." This was before any announcement at all.[1] So

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[1]The first announcement of Kaposi's sarcoma associated with what later was known as AIDS appeared on July 3, 1981, in a Centers for Disease Control publication. (Kaposi's sarcoma and *Pneumocystis* pneumonia among homosexual men--New York City and California. *Morbidity and Mortality*

we called his friends at Roosevelt Hospital in New York City--I really wish I could remember now who they were--and traded notes back and forth.

Hughes: Other fellows?

Volberding: Yes.

Hughes: None of the big names that eventually were associated with the AIDS epidemic in New York?

Volberding: Well, I don't know. Could well have been because all the big names were fellows at that time. We were all babies.

So I saw a patient with Kaposi's sarcoma, and, remarkably, the *MMWR* [*Morbidity and Mortality Weekly Report*] on Kaposi's came out just a week later.

Hughes: July 3, 1981.

Volberding: Yes, that was the first mention of Kaposi's. The June 5 *MMWR* just two weeks earlier had been just on PCP [*Pneumocytis carinii* pneumonia],[1] and we didn't make connections between those two reports at all at that point.

I was absolutely ideally trained to be taking care of some of these early patients, and I didn't know it at the time. Obviously, we didn't know for years that it was a retrovirus [causing HIV disease]. I owe a real debt to that prior training in virology. It still helps me understand the process of science, and I respect it enormously. I've done a lot of virology myself; I've grown viruses and am pretty good at tissue culture. At least I was. Hence I know a lot of the techniques that have been very instrumental in AIDS research, and still are.

Hughes: Even though you weren't particularly enjoying that period in Jay Levy's lab [1979-1981], were you adding to your knowledge of virology?

Volberding: Oh, sure. And knowledge of techniques. So I absolutely think it helped prepare me for what I would be doing, especially

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Weekly Report 1981, 30:305-307.)

[1]*Pneumocystis* pneumonia--Los Angeles. *Morbidity and Mortality Weekly Report* 1981, 30:21, 250-251 (June 5, 1981).

after a couple of years when we began to realize that it was a retrovirus.

My oncology fellowship had prepared me very well for taking care of the medical problems, which is what really dominated all of our thinking for the first couple of years of the epidemic. Here was a twenty-two-year-old man who was dying, and we knew how to deal with that as oncologists.

Possible Etiologies

Hughes: Did you speculate about what might have been the cause?

Volberding: I don't recall; I don't think so. It was weird; it was an unusual cancer. I don't give myself any credit in retrospect for that. I think we realized pretty early that there had to be an immune problem at some level. But the idea that this was transmissible wasn't much thought of at first. It was more lifestyle issues that were thought to be responsible.

Hughes: And that was after more cases had been diagnosed.

Volberding: Right. Well, I was here at San Francisco General, and there were gradually then a few more patients with Kaposi's sarcoma. I was at a point in my career when I didn't really have anything else to do. I had just left the lab. I had done some clinical research during my fellowship, but not very much.

When I came here, I really needed to be involved in something academic, so I agreed to help run the melanoma clinic at UCSF. It's a very good multidisciplinary clinic. I was the medical oncologist on that team, which meets in the dermatology clinic as opposed to the oncology clinic.

Marcus A. Conant and John L. Ziegler

Volberding: The significance is that in the course of going up there and taking care of melanoma patients, I ran into Marcus Conant one

day. As I recollect, it must have been early '82,[1] so there were still just a handful of Kaposi's patients in the entire city. We started chatting, and he said he had a couple of patients with Kaposi's sarcoma. I said, "Well, I've got a couple of patients with Kaposi's." So he took me over and showed me his patients in the [Moffitt] hospital at the time. We compared notes and decided--I think pretty remarkably given that there was only a handful of patients--that this disease was going to be important.

Hughes: Why did that occur to you?

Volberding: Well, because it was in gay men, and San Francisco has more gay men than most places. And we'd already seen a few cases, so we knew it was here, whatever was causing it.

Hughes: Were you thinking about transmissibility at that point?

Volberding: No. We thought, This is an interesting problem. Marcus has connections in the private dermatology community where all the initial cases were detected, because Kaposi's is obviously the most visible manifestation of HIV disease. He let it be known to the dermatology community that we would be willing to evaluate their patients, systematically, at UC.

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Volberding: Another person emerged on the scene as having an interest, and that was John Ziegler, who had just arrived at the VA [Veterans Administration Hospital in San Francisco]. He had worked at the National Cancer Institute, and he had been stationed in Uganda where Kaposi's is a common problem--not related to HIV at all.

Kaposi's Sarcoma Clinic and Study Group

Volberding: Then the three of us formed a small group and collaborated closely. John wrote a small grant to the American Cancer Society to get us some money for a staff person. We got that grant in '82. I think it was the first AIDS grant in the

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[1]The meeting had to have occurred before September 21, 1981, the date of the first KS Clinic, at which both Conant and Volberding were in attendance. (Marcus Conant to William Epstein et al., September 2, 1981. Marcus A. Conant's Kaposi's Sarcoma notebook 1981-2/1982, Conant's dermatology practice office, San Francisco. Hereafter, KSN.)

world. We hired a nurse practitioner, Helen Schietinger,[1] who then worked with us in the dermatology clinic, where we evaluated patients once a week. We met Thursday mornings, and then at noon had an informal discussion group [the KS Study Group] where we'd sit down and talk about the patients that we'd seen and compare rumors and notes. There were a lot of rumors; there was a lot of excitement building in a very small circle of people on campus.

Hughes: Were you reaching any further than that group?

Volberding: Not really. Through Marcus we had connections in New York with dermatologists there. Bijan Safai and Alvin Friedman-Kien were good friends of Marcus' through dermatology. We had talked to them; Marcus could do it over the phone. There were some early connections with the CDC [Centers for Disease Control] who were already in San Francisco to investigate this outbreak. There were connections right away with immunology and virology, and Jay Levy became interested early on. Dan Stites, who's now head of the department of laboratory medicine at UCSF, got interested early on.

We would just sit and talk, and that became the regular discussion group. For about the first year and a half, I think, that was the only regular forum for coordinating what we were doing.

Hughes: Regarding?

Volberding: All focused on KS.

Hughes: And all focused on the clinic?

Volberding: Not really. There wasn't really much research in the clinic. Dan Stites was working with the helper/suppressor T-cell ratios. I think there was one [cell-sorter] machine on campus that was able to count T cells.

Hughes: Had it been used for clinical work?

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[1]See the interview with Schietinger in the San Francisco Bay Area AIDS Oral History Project: Contributions of the Nursing Profession, 1981-1984. Department of the History of Health Sciences, University of California, San Francisco, and the Regional Oral History Office, University of California, Berkeley. Hereafter, AIDS nurses series.

Volberding: It had been purely a research instrument. But Dan had access to it because he was an immunologist, so we were using it on some blood from his patients.

Hughes: No other clinicians had been using it prior to then.

Volberding: No.

Hughes: Why did you think of counting the helper/suppressor cells?

Volberding: Because of the constellation of malignancies and infections. We had our blinders on very strongly. We saw Kaposi's sarcoma, but we saw a lot of *Pneumocystis* as well. When you see cancers and unusual infections in the same patient, you have to think immune deficiency. Enumerating the T cells had become available as a research tool quite recently, and so that was used. Dan and his lab, including Conrad Casavante, who was later to die of AIDS, made some very important early observations on the helper/suppressor abnormalities in patients with HIV.

Hughes: Were you setting up guidelines for--

Volberding: For clinical evaluation. We were really focused on clinical evaluation, learning more about the disease process. But we started talking very early about systematizing our [patient] management, and so we really walked right into clinical research.

Treating Patients at the Oncology Clinic, San Francisco General Hospital

Volberding: A very important early decision that we made was that the dermatology clinic was really only suitable for evaluating patients. It wasn't a suitable place to provide long-term care. It's just not set up to do that. Whereas my oncology clinic here at SFGH was capable of doing that, and here I was. So Marcus made a deal that we would continue to evaluate the patients at Moffitt, but when they required therapy, he would refer them to me here. It was really that arrangement that resulted in this clinic growing very rapidly. Otherwise, there would have been a very small number of patients that would have happened to come to San Francisco General Hospital.

Hughes: This clinic you're referring to is the general oncology clinic here at San Francisco General?

Volberding: Yes.

Hughes: Give me a feeling of what it was like for a patient to appear at the KS Clinic for the first time. What happened?

Volberding: We had a routine evaluation, complete physical exam and history. We asked a lot of drug-use questions and sexual-exposure questions--how he did what he did with whom.

Hughes: Selma Dritz and the epidemiologists with CDC apparently had very elaborate questionnaires.[1]

Volberding: We didn't do anything quite that elaborate, but we did our best at standardizing the evaluation, more than we would have done for routine medical care. So there was an academic approach to this disease really from the start.

Hughes: Was the lifestyle hypothesis of the cause of AIDS one of the reasons for getting a full history?

Volberding: Oh, sure. We asked people how many [sexual] contacts they'd had. We focused a lot on drug use, poppers [amyl nitrite] and the rest, hoping that we were collecting information that would help us identify what was going on.

Hughes: Were you getting any ideas?

Volberding: Not really. We thought a lot about CMV [cytomegalovirus] infection. Larry Drew was one of the early participants. His interest is CMV. There was reason from data collected in Africa to think that CMV might be involved in Kaposi's, so CMV was one of the things that we looked at early. I'd have to say I don't think we had any particular belief system then in what was going on.

Fear of Infection

Volberding: One thing I don't remember us thinking was that it was infection. Even though in retrospect it should have been obvious, I don't think it was. Now, some of the people that were there might remember it very differently.

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[1]See the oral history in this series with Dr. Dritz.

There are a lot of important early milestones, and one of them was in December of '82. Art Ammann, who was also an important early member of the group, then a professor of pediatrics and an immunologist at Moffitt as well, identified the first case in the world of HIV that was blood-transfusion related. The infant had a donor who had died of AIDS and the infant had what looked like AIDS.

Hughes: The baby who was transfused so many times for Rh incompatibility?

Volberding: Right.

Hughes: Well, what did you think at that point?

Volberding: We knew it was infection. I think at that point it was inescapable that it was going to be a virus. Blood transfusions transmit viruses.

[tape interruption]

Volberding: Perhaps we should have been more convinced earlier that it was infectious. But the reason that I don't believe we were is because I don't think any of us had any real personal fear of taking care of patients until the end of '82. My recollection there is that during the very earliest part of this epidemic, we took care of patients exactly as we took care of anyone else with cancer. We were really taking care of them as cancer patients.

The oncology clinic was meeting on Ward 5B at the main hospital at San Francisco General, and for examining tables we were using beds. The housestaff would sleep in those beds at night. We were evicted at the end of '82. The hospital found us Ward 86 [in Building 80] mostly because one of the women residents had become pregnant at the very end of '82 and raised concern about the safety of sleeping in a bed that had been used as an examining table by AIDS patients all day long. But really most of the concern was CMV.

I just don't recall any personal fear of taking care of patients until Art Ammann's case, and then for the next year and a half, we lived in real dread. There was a period in that part of the epidemic when all of us were variously convinced that we were already infected with whatever this was.

Hughes: Because of your poor technique?

Volberding: Well, and we just didn't know anything about it. We became convinced it was transmissible; it was a virus, but we didn't have any way to test for it. We'd been working with patients; we'd been touching them; we'd been drawing blood and all these things--not being sloppy, but not being careful either.

Hughes: How did your procedures change?

Volberding: Well, for a while gloves were used more frequently during exams. We debated back and forth whether it was necessary or not. For the most part, we decided it wasn't, but we didn't know for sure.

There was about a year or year and a half period where the anxiety was so great that AIDS was just not permitted as a discussion item at home. There was so much anxiety attached to it that if I'd say, "Gee, I'm worried about taking care of these patients. I'm worried I have a fever, maybe this is PCP," my wife, Molly, wouldn't let me talk about it. I got calls from other people. Jerry Groopman when he was still at UCLA called me once and said, "I've got it." He had developed a hepatitis and a fever, and was absolutely convinced (incorrectly, of course) that he had caught AIDS. So I really do think that that period at the end of '82, and then all of '83, into '84 until we had the [HIV antibody] test available, was a high stress period for us, with a lot of anxiety.

Hughes: What reduced your anxiety eventually?

Volberding: Well, it wasn't very well dealt with until we had the antibody test. Jay had an antibody test with immunofluorescence in early '84, as I recall.[1] As soon as it was available, we were among the first to be tested. All of that anxiety was dealt with completely, because then we could say, "Well, look. We took care of these patients without any additional precautions and none of us are coming back infected."

It really was very important, because then we could say with real confidence, "I've been there; I've been scared. But there's no reason to be scared." And it made us not very willing to put up with much of this AIDS panic. I think it helped us then to act in a way that really did help reassure the public that in fact there wasn't any reason to be panicked about this disease. And I don't think it would have been as easy to do that if we hadn't lived with our own personal fear.

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[1]See the oral history in this series with Dr. Levy.

Support from UCSF

Hughes: What sort of institutional support were you getting from UCSF in these early days?

Volberding: Well, they were willing to let us meet in the dermatology clinic. We didn't really push for much clinical management there--at least I didn't, because I was here at San Francisco General, and I wanted these patients. They were part of my career now, so I was happy with the arrangement.

There was an early patient at UC, a man [Simón Guzman] who had been hospitalized for several months with cryptosporidiosis, horrible diarrhea. Only at the end of his long hospital stay was it recognized that he was a Kaiser member and that Kaiser wasn't going to pay his bill. I think that UC ended up getting stuck with a major bill. It's my perception that that made the university early on a little less than eager to be taking on any more AIDS patients than they needed to.

Hughes: It was more that reason than reluctance to spend money and energy on a disease that was affecting only a small percentage of a minority population?

Volberding: I don't know. I don't think UC was particularly eager to have a lot of AIDS patients in Moffitt Hospital. I think early on it was seen as sort of a fringe-y thing. You know, we're in San Francisco, but gay men are stigmatized here as elsewhere, and this was seen as a disease of gay men. So I think it was a marketing issue in part. But maybe more importantly, I think UC as a medical center really revolves around the laboratory bench, and being very active in working with a disease is not really what it's geared best for. So I think it's understandable that a clinical reflex wasn't the first one from UC, that the science was, and the support of the institution through the science was quite strong. There were already a growing number of people working on AIDS in the labs there, and the institution doesn't provide any specific support, but it encourages that.

Hughes: Now, were those people associated in some way with Jay Levy?

Volberding: Well, not directly. Jay was involved in the KS Clinic, again Art Ammann, Dan Stites, Selma Dritz coming over from the health department, Herb Perkins, who was involved, especially around the blood transfusion issues.

Hughes: I was really meaning in basic research at UCSF.

Volberding: Not very many other people were really very involved. There's still a fairly small number of people actually working on AIDS in labs at UC.

Hughes: How were you keeping in contact with Selma Dritz at the health department?

Volberding: Through the Thursday KS Study Group primarily.

Hughes: Did Herb Perkins come pretty regularly?

Volberding: Yes, pretty regularly. Selma was religious. Other people from the health department, whom I don't really remember any more, would regularly come. Dean Echenberg was in the health department. I don't know where he is now, but he was involved with communicable diseases and was an active person early on.

In terms of institutional [UCSF] support, I think it was there. It was convenient that I wanted the patients down at the county [San Francisco General Hospital], because in a sense UC could then be involved without having to really organize more specific clinical services. Again, it suited me just fine, because then I could have a lot more patients.

Clinical Trial of Recombinant Alpha Z Interferon

Volberding: I did my first clinical research in the middle of '82, with just a handful of patients at that time. I was approached by Schering-Plough, the drug company that then had some of the very first recombinant alpha-interferon available in the world. So they approached me and Jerry Groopman, when he was at UCLA, and asked whether we would like to collaborate on a clinical trial of alpha-interferon in Kaposi's sarcoma. It was the first clinical trial for either of us, but we got together and did it.

When you're designing a clinical trial, there has at some point to be a face-to-face meeting with the investigators and the drug company where you plan the trial and form the relationship. So I invited them here to the General to a meeting. And here I am again just a baby, never having organized any kind of a meeting in my life, and all these people come from Schering-Plough in suits and ties. Jerry

Groopman and Ron Mitsuyasu, who was a fellow with him at UCLA, came up.

When it came time for lunch--maybe I should have thought about this, right?--I said, "Well, I don't know, there's a restaurant across the street." So we went across to the Vietnamese restaurant across the street, and it was full or something, so I said, "Well, there's another one around the corner." This whole group of people from a business meeting ended up walking to the Mission [District] looking for a restaurant. We ended up at Roosevelt's Tamale Parlor. [laughter] Jerry Groopman was sort of aghast, because he's an ardent vegetarian, and kept asking was it animal oil that was used. So this was my introduction to high finance in clinical research.

But it was really an important step, because then it established me as an academic clinical investigator working in this area [AIDS], and one of a handful in the whole entire country at that time. It was the first clinical trial on AIDS in San Francisco, and a time of real naivete, too. We just were convinced interferon was going to cure the disease, that interferon was magical.

We did the study in the clinical research unit, and my patients took a vial of the interferon. One of them took a vial down to a shop that makes T-shirts, and they blew up the label and had T-shirts made with the label on them from the interferon vials. It was also the first contact I'd had with the media really, because one of the nurses on the unit was a friend of Bill Skane, who was working for KQED at the time. He came down and did a TV interview: what were we doing with the interferon and this Kaposi's sarcoma thing? It was interesting.

Hughes: You liked that part?

Volberding: It strokes the ego, and it brought visibility, and also brought more patients. Patients said, well, San Francisco General Hospital is doing this research, and so we were really then flooded with patients with Kaposi's sarcoma.

Hughes: Was there a scientific rationale for thinking that interferon would work with a retrovirus?

Volberding: Well, not specifically necessarily for retroviruses, but interferons are natural antiviral proteins. They work against a broad variety of viruses. They have anti-neoplastic capabilities, and this was a cancer. It was thought that

interferon worked through the immune system somehow, so we had a disease that we were beginning to think was infectious. It certainly was a malignancy, and it was a disorder of the immune system, so it seemed like interferon was the logical thing to use. Still is; it's still used.

Chemotherapy in Kaposi's Sarcoma

Hughes: What had you been doing before the interferon became available?

Volberding: Nothing in particular--chemotherapy in patients with more advanced disease.

Hughes: That you had extrapolated from the work in Africa?

Volberding: To some degree, yes, by going through that. Ray Stricker, who was my fellow, and I reviewed the literature. I remember the first paper I wrote as a first author was for the *American Journal of Medicine*,[1] not a great place necessarily, but where we summarized the chemotherapy of Kaposi's sarcoma.

[tape interruption]

Volberding: In the KS Study Group, there was controversy right from the start. We said, "Well, this is an immune deficiency; how can you treat this with chemotherapy?" Because chemotherapy makes immune deficiency worse. We said, "Yes, but it's a cancer, and it's killing people, and it looks awful and destroys patients' lives." So really right from the start we said, "Well, let's try something kind of cautious," so we looked for cautious chemotherapy. In African Kaposi's, kind of everything you can give them works great. So we chose some mild chemotherapy--vinca alkaloids, vincristine, vinblastine--and concocted a scheme where we'd give one drug one week, one the next week. The idea was to really minimize the side effects, especially the immune side effects.

We did that as a clinical trial with no support from anyone. That was published early on, too [1984], and it's still our standard approach to chemotherapy.

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[1]P. A. Volberding, M. A. Conant, R. B. Stricker, et al. Chemotherapy in advanced Kaposi's sarcoma: Implications for current cases in homosexual men. *American Journal of Medicine* 1983, 27:315-325.

Hughes: No support because you couldn't get any, or you hadn't tried?

Volberding: There was no mechanism for supporting clinical trials at that point, except by drug companies, and the chemotherapy drug companies weren't and still aren't interested in Kaposi's sarcoma because it's just too small a market.

Hughes: What did you find in that first study?

Volberding: Oh, we found that using vincristine alternating with vinblastine really did work. It helped slow down the course of the disease. It didn't cure it, but it didn't have any real side effects either, so it became a very manageable sort of thing, and still remains our standard treatment. So it wasn't earth-shattering, but we published it in the *Annals of Internal Medicine*,[1] which is a good place. And again, I think it added to the sense that we were leaders in this area.

Hughes: A good place because of the audience, or a good place because of the prestige?

Volberding: Prestige of the journal. Well, both. They're related. All serious internists read the *Annals*.

Hughes: Did you have any trouble in these early days about getting research published?

Volberding: No, I don't think so. The real trouble we have is that we don't write enough, like a lot of people. I'm not really a natural writer. There are a lot of things that we should have written, and that still is the case. Now, when we get around to writing something, we don't have any trouble getting it published.

More on Interferon

Hughes: Well, I pulled you away from the interferon study. What was the result there?

Volberding: It worked. It worked about as well as chemotherapy worked, although with a lot more side effects.

Hughes: But not the immunosuppression.

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[1]J. E. Groopman, M. S. Gottlieb, J. Goodman, et al. Recombinant alpha 2 interferon therapy for Kaposi's sarcoma associated with immunodeficiency syndrome. *Annals of Internal Medicine* 1984; 100(5):671-676.

Volberding: It didn't really do anything to the immune system. Interferon remains an enigma. It does work, but it's quite toxic, it's quite expensive, it's cumbersome; it has to be given by injection. We still don't really know even after ten years from our first trials how best to use it. We don't know the best dose; we don't know the best schedule. It's a pretty cumbersome drug to use, but it's achieved a position as a useful drug. It got FDA approval in part from our studies.

Also doing the trial put us in contact with the FDA. We became much more aware and conversant with the bigger world out there. We got more contacts in the clinical research community, more contacts in the cancer community. So all of those early trials were really critically important.

Hughes: Can you name some names, or would that be relevant?

Volberding: Well, it's a later part of the story, but we worked with Sam Broder, who's now director of the National Cancer Institute; got to be close friends with him.

Hughes: Where was he then?

Volberding: He was in his lab at the NCI.

Hughes: Were you sticking closely to Kaposi's in these early days?

Volberding: Yes. A critical part of the story there is that as I was seeing patients in my oncology clinic with Kaposi's sarcoma, almost inevitably I'd run across patients with a weird infection, and I'd have to call in Connie Wofsy[1] to help me deal with the infections. John Mills was the head of infectious disease, but he was on sabbatical that whole first year [1981-1982] that I was working at SFGH, and Connie was the acting chief of infectious disease. I so regularly called her from my clinic that she started just coming to my clinic, thinking, Why wait for the call?

Hughes: She was getting interested?

Volberding: She was interested, I think. It really became the nucleus for what we still have at this hospital, which is a multidisciplinary comprehensive approach to these patients.

Hughes: It wasn't planned; it just sort of happened.

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[1]See the oral history in this series with Dr. Wofsy.

Volberding: Yes, it really just happened. Connie and I were working by ourselves and with one nurse, Gayling Gee.[1]

Ward 86, the AIDS Clinic, San Francisco General Hospital ##

Volberding: When Ward 86 opened on January 1, 1983, there was me, Gayling, and Connie. I was then allowed to hire an administrative person, and hired a woman from UC that I'd worked with in the cancer clinic, Roberta Wilson. That was it. We were the AIDS Clinic. I hired a couple of other people early on. J. B. Molaghan, who's now our head nurse, and Gary Carr,[2] who's a nurse practitioner, came in the first six months, I think. Donald Abrams[3] then joined us in July of '83, and we really grew by adding services that our patients seemed to need. So the growth was organic in the best possible way.

Early on, without a formal conceptualization of it, we said, "Well, we've got the patients here. We're stuck over in Building 80 at the corner of the campus. Rather than having to send our patients to the main building for services, let's try to bring as much of what our patients need to one place as we can." So it became a place that was really client-centered, in terms of services. As we saw more cancer patients, we added more oncologists; as we saw more infectious disease problems, we added more infectious disease people. What we've ended up with today now is probably the best balance of any program in the world in terms of being truly interdisciplinary. We have oncologists and infectious disease people, pulmonary specialists, general internists, family practitioners, all working together in the same clinic, as part of the same administrative group, which is pretty unique.

Hughes: Because of these historical roots.

Volberding: Because of these historical roots. Because we said, "We don't want to hassle our patients any more than we have to. We want this to be as comfortable an experience for them as we can make it." I think that grew out of my training in oncology, where you're sympathetic to the plight of the patient; you don't want to intrude any more than you have to. You want to

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[1]See the oral history in the AIDS nurses series with Ms. Gee.

[2]See the oral history in the AIDS nurses series with Mr. Carr.

[3]See the oral history in this series with Dr. Abrams.

make the patient as comfortable as you can. Even if you can't do anything to reverse the underlying disease process, there's the feeling in oncology that there's a lot you can do. You can be there for the patient, you can understand things, and you can try to create an environment that the patient feels supported in.

For us that meant multidisciplinary medical care. It meant psychosocial care right from the very start. It meant knowing who our patients were, getting to know the gay community, getting to know the services that were available in the gay community, and bringing those into the program.

Working with the Shanti Project and the Gay Community

Volberding: Really right from the start we had Shanti working with us in the clinic.

Hughes: How did that come about?

Volberding: Well, again it goes back to the KS Study Group. One of Marcus' friends was a gay clinical psychologist, Paul Dague, who had worked in the past with a guy named Charlie Garfield. Charlie had begun a bereavement counseling support group called the Shanti Project in the oncology program at Moffitt. By the time we saw AIDS patients, Charlie had moved to Berkeley and wasn't really active at UC anymore. But Paul was aware of what he had been doing.

Paul got the Shanti people, which was a tiny organization at that time, interested in doing something with AIDS. So really, at a very early stage, an organization formed in San Francisco.

Hughes: November '81; I looked at some of the Shanti newspapers yesterday.

Volberding: Yes, right from the very start. The credit for that goes to Paul Dague, who then himself died of AIDS later on. Shanti then hired Jim Geary, and I think he was hired very early on as well, another gay man who came into Shanti and really gave it much more of a gay spin. I don't think it had been particularly a gay organization before. But it became really for all intents and purposes a gay community organization focused on AIDS. I think it quickly stopped doing really

anything else, and its goal was a buddy system and practical nonprofessional support.

When we started an AIDS program here, because I knew Paul and Shanti, we sought them out as an ally in what we were doing here. They became involved in what we were doing, and when we opened up the AIDS unit and the AIDS Clinic, it was done in real collaboration with Shanti Project. So the connections with the community, the multidisciplinary nature of the care, really happened from the start. I think it's still what makes this a successful place.

Hughes: Did you feel from the start that you and your colleagues were accepted by the gay community?

Volberding: Yes, I think we were accepted. I was young and attractive, and I think some of them were hoping that I was gay myself. I think that helped. We were working closely with Conant, who was part of the [gay] community. So we had that; the doors were pretty much open. I think people appreciated that we were honest in what we were doing, that we were really trying to do our best to find some answers, and that the care that we were delivering here was sensitive to their social situation as well as their medical problems. So we achieved our credibility pretty early on.

We worked closely with a lot of the organizations, and Marcus Conant founded the [San Francisco] AIDS Foundation.[1] I was on the original board and got to know some of the gay community activists--not activists then, leaders. Before the activists. So I think by working out in the community a lot, we established that trust.

Hughes: What were some of the original goals of the AIDS Foundation?

Volberding: Well, the original name of it was the Kaposi's Sarcoma Research and Education Foundation; I think that pretty well summarizes it--it was research and education on Kaposi's sarcoma.

Hughes: Was some of the need for the foundation the fact that for whatever reason, money was not coming very readily in those early days from the federal or the state level?

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[1]Conant and two others founded the Kaposi's Sarcoma Research and Education Foundation, the predecessor of the San Francisco AIDS Foundation, in May, 1982. (See Conant's oral history in this series.)

Volberding: To some degree, yes. It's again hard to remember, separate out reality from memory, and I think part of it was that AIDS was an important problem. There were people dying. There was the need to mobilize the community, and I think part of the hope was that it would turn into a fundraising organization.

Hughes: Initially, were the funds mainly going to run the clinic?

Volberding: Well, the original funds were kind of on hand. We had a little grant--I think it was about $50,000--from the American Cancer Society.

Working with Mayor Dianne Feinstein

Volberding: I got in '82 our first support from [then-Mayor Dianne] Feinstein, with a total of ten patients at that time.

Hughes: How did you arrange support from Feinstein?

Volberding: Well, see her picture on my wall? I'm still a fan of hers. I think it was really kind of a remarkable moment when this happened. It happened at a time when there was extra space at this hospital. We could grow in empty space. When we moved to Ward 86, the only thing that was going on on the whole floor was a noon-hour exercise class in one of the rooms. It was empty. So there was space, and there was money. There was a budget surplus in the city. There was lots of money in the state.

So Feinstein, whose social inclinations are pretty conservative, or were especially then, wasn't naturally drawn to the AIDS problem, but recognized it as important. It got a fair amount of press early on. Any mayor recognizes the power of the gay vote in San Francisco, and she was able to put some resources into it without hurting anyone else, without anyone else squawking. So we were able by writing a letter to get money to run a clinic just by asking for it. There was no sense of resistance at all.

Hughes: Just from the letter?

Volberding: Just the letter. And the sum was modest; I think we got $70,000. But that was more than we had. It was important for me; it was the first independent money I brought into the hospital. And it established a linkage with the politicians, which has been very important ever since.

It's hard to separate out times exactly, but during that time or shortly after, the whole bathhouse issue arose [1983-1984], and that put us in really frequent contact with Feinstein, who needed to be educated about some of the issues of the disease and, to her enormous credit, was willing to sit and listen. That's much more than I can say for other mayors. She was really willing to sit down and listen and have a dialogue, and was rapidly educated by it. And when she was educated, then she was supportive of what we were doing.

Hughes: Were you mainly talking about the medical dangers of the situation?

Volberding: Well, it was necessary to make sure that she and other people were grounded in the medicine of the situation, so that when they formed policy, it was sensible policy. So it was impossible, I think, to separate out the medicine from the policy. I think the fact that San Francisco has always been a real leader in sensible policies around HIV is a testimony to her, and our willingness to go down and work with her as well. So we got some money.

The National Cancer Institute Grant

Volberding: In '82, we applied for a National Cancer Institute grant. I sort of lobbied for myself as the principal investigator on that, even though it was crazy.

Hughes: Why was it crazy?

Volberding: It showed how young and how green we all were, because at this point, if there's a big grant to be applied for, the junior person would never, ever be allowed to do it.

Hughes: But there weren't any senior--

Volberding: --weren't any senior people; that's what I mean. We were all junior. So here I was, a year out of my fellowship, and a peon on basically a large program project grant that I think was $700,000 a year or something--it was a sizeable grant. That was the first really large grant from the federal government. I think that came at the end of '82.[1]

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[1]The NCI grant was awarded to UCSF in April, 1983. (Conant to Julius R. Krevans, M.D., April 29, 1983. KSN Jan-June, 1983.)

Hughes: And who was that from?

Volberding: National Cancer Institute. It was a cooperative agreement with the NCI to kind of do everything--some epidemiology, some clinical trials, some basic science, especially by Jay Levy and Dan Stites. It was a good group of investigators who are still working together.

The Role of the Federal Government

Volberding: But we got that grant. It makes me less inclined to be totally negative in my memory about the federal government's response. I think this was at that point still a very small epidemic, and you can look in retrospect and say, "They should have known it was going to be an important problem." But at the time I'm not sure their response wasn't kind of appropriate, given the number of patients that were involved.

Hughes: Did it continue to be appropriate?

Volberding: Oh, it got more and more appropriate, I think. In '83, with the transfusion connections to HIV disease, with heterosexuals at risk, there was much more awareness and willingness of the politicians and the NIH to be involved.

I think early on, the NCI was not very eager to be involved. The director, Vince DeVita, didn't seem to be especially interested. Whether it's the gay disease aspect of it or not, I don't know. The AIDS problem was assigned to the National Institute of Allergy and Infectious Disease [NIAID], which at the time was a relatively minor institute at the NIH; NCI was totally dominant. The NCI was probably--I'm guessing --twice as big in terms of its clout as the rest of the NIH put together, because of the War on Cancer, which was in its last glory days then.

So it wasn't until a little bit later that [Anthony] Tony Fauci came on board as the director of the NIAID, and a deal was cut between NCI and NIAID that in fact AIDS would be NIAID's responsibility. But during the early part of the epidemic, it was NCI's responsibility.

Hughes: What was behind that deal?

Volberding: Oh, I don't really have any insight. It is an infectious disease, it's an immunodeficiency; so it makes sense. On the other hand, the NCI had always been involved in retroviruses.

Hughes: It also had the money.

Volberding: It had the money and [Robert] Bob Gallo and Sam Broder. So a lot of that money and talent and natural inclinations were at the NCI. But I guess my gut sense is that DeVita didn't really want this disease in his institute, that it was seen as something that wasn't up to the standards of the NCI, and that it could be tossed over to the weaker institute, NIAID. And then Fauci, who was a very ambitious person, took that and ran with it.

Hughes: In what sense?

Volberding: Well, with the visibility of AIDS, and with this now being an infectious disease field, he was able to get enormous support from the government for this work.

Hughes: So funding did go up after the switch.

Volberding: Oh, it skyrocketed.

Hughes: Do you remember what year that was?

Volberding: My guess would be '84, after the virus was identified. The deal was that the virology would still stay at the NCI; that Gallo would remain primarily the site of that. Then Broder's lab was mostly to have the responsibility for drug development, but that clinical management and the establishment of a system of clinical trials would be Fauci's responsibility.

Isolation of the AIDS Virus

Hughes: Now, with your background in retrovirology, were you following with particular interest what Gallo was doing to isolate the virus?

Volberding: Oh, sure. In fact--and these connections are all pretty interesting--Jay [Levy] had done part of his sabbatical in Paris, at the Institute Pasteur. When I was doing the fellowship in Jay's lab, a postdoc from France came over to spend some time--I think she spent about six months--in his

lab. Françoise Barré-Sinoussi, who in fact was the person who isolated HIV. I actually ran into her in Nice earlier this week.

Hughes: Did you get any insight into the Gallo-[Luc] Montagnier controversy?

Volberding: I didn't ask her about the politics at all. I stay away from that. Oh, but I followed the work on the isolation of HIV closely, absolutely.

It's impossible to convey the excitement of the field in those early days. Every patient we saw, there was something new. Whether it was up at Moffitt in the KS Clinic or down here in my clinic or on the wards, every patient we saw was absolutely fascinating. We'd say, "Can you believe I saw a patient with cryptococcal meningitis?" Or, "Amazing! I saw a rash on a patient getting Septra [an antibiotic]!" These things that are now just the absolute bread and butter of what we deal with, every one of them we saw with virgin eyes. It was this incredible excitement.

It was easy for a while for one person to really keep track of all the world's literature of this disease, from the virology to the epidemiology to the clinical management. In the first couple of years, there just wasn't much being done, so you could really follow it very closely. So yes, I followed the virology very closely.

I was at a meeting in Park City, Utah, in I guess it must have been '83. Gallo and Montagnier were both there and were both presenting their arguments for their virus. As I remember, it was still Gallo pushing HTLV-1 [human T-cell leukemia virus-1], but the data for LAV [lymphadenopathy-associated virus], later termed HIV, were really convincing. It became clear that we were on to something.

Hughes: Clear to you, or clear to the audience?

Volberding: Generally, I think the audience came away saying, "We're on to it." After that first paper of Montagnier's, which no one quite knew what to make of in early '83, it evolved pretty quickly.

I remember when a group of us went down to [California Assembly Speaker] Willie Brown's office in L.A. [in April, 1983], to write the first grant proposal to the state to request research money, which we were still highly dependent on. I was riding in the cab with Jay, and I said, "It looks

like this is going to be a retrovirus." He said, "No." I'm sure he would not remember this--but at that point he was still thinking hepatitis virus was causing it.

Hughes: Because of the transmission pattern?

Volberding: Transmission of the virus, yes.

Michael Gorman's and Andrew Moss's[1] Epidemiological Study of AIDS, 1983

[Interview 2: May 21, 1992] ##

Volberding: Andrew's study was organized before the virus was known. So as soon as the antibody test became available, then that study was used to tell us how common this disease was in the gay community. So it was the basis for a lot of other estimates of prevalence of the disease. The other important one was the city clinic cohort.

Hughes: Did the graphic results of those studies cause fear in the gay community?

Volberding: Oh, sure. The concentration of cases in the Castro [District]--horrible, horrible. I have to say it still colors my sense when I drive through the Castro. I live in the Haight[-Ashbury District], and I not uncommonly drive down Market Street. When I'm there, I look around--I can't really help it--and think, Every other person on the street is infected with this virus. And it's not a bad guess when you're at Castro and Market. Maybe more than 50 percent of gay men are infected.

Also, those studies were critical to tell us what fraction of people infected were going to develop the disease. So they have been important in a number of respects. Most recently, they've been used to go back and say, of those people that were in those cohort studies who got treatment with AZT or with prophylaxis for PCP, what effect did those drugs have? So they've remained very important.

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[1]See the oral history in this series with Dr. Moss.

Hughes: Did these various studies change the urgency of your counseling with patients?

Volberding: Well, yes. They made it possible for us to counsel our patients in a sense, because if you don't know something about the natural history of the disease, it's very hard to advise somebody on what to do and how to psychologically prepare him for the disease process that he's in. There was a lot of uncertainty about this data; there remains a lot of uncertainty. But it became possible to talk to our patients. I think that's good and that's bad. It's easy and then it's difficult. It's important and yet it results in a lot of stress for the patient. But the epidemiology studies have been really key.

Taking Patient Histories

Hughes: Did you feel any hesitation in what people might construe as interfering in the most private lives of individuals?

Volberding: Well, early on we didn't know anything. So we took very detailed questionnaires: how many times have you had sex, how many people have you had sex with, what kind of sex have you had, where have you put your organs in other people--down to excruciating detail. I think it was important to do that early on. I think increasingly as we worked with this disease, it felt more and more voyeuristic, because there was in truth nothing we as clinicians were going to do with that information. It didn't change my treatment of the patient to know that he was gay or not.

Hughes: But it could have changed his behavior, certainly in terms of the transmissibility.

Volberding: Sure. There are two things. First of all, I think for a real epidemiologist to ask those questions, it was important, and it still is important. We still are learning something about Kaposi's sarcoma, because it turns out that it might be related to fecal-oral contamination. And you're not going to learn that unless you ask those questions. For the clinicians, I think that it's not important to know specifically the details of somebody's sexual life as long as you're able to identify the fact that the person is having same-sex contacts, or is using intravenous drugs. I mean, I do think it's important to identify the risk factors to permit counseling on safer behavior. You're right.

Hughes: Was the questioning generally well received?

Volberding: Yes, absolutely. I can't recall a patient where asking was a problem, although the answers I received may or may not have been accurate. Again, the patients--especially the ones we saw early in the epidemic--were really stereotypically very sexually active gay men who were fully out about their homosexuality. There wasn't a lot of shame about their sexual orientation, so we felt comfortable asking questions and they seemed to feel comfortable answering them.

The Blood Bank Controversy

Hughes: Well, let's go on to the blood bank business, which we've touched a little on. I understand that it was the December 1982 baby [see page 121] that really precipitated events. Did you immediately begin to worry about the blood supply?

Volberding: Yes.

Hughes: Did you do anything?

Volberding: Well, again we should have been worrying before that. All of the information to conclude this was a blood-borne pathogen had been known for months before that baby became known to us --hemophiliacs, IV drug users.

Hughes: Well, in August of '81, the first heterosexuals with AIDS were reported by the CDC.[1] Most were drug abusers.

Volberding: Right. But what that says is we should have been thinking about a blood-borne pathogen right from the very start. We didn't want to. I'm not sure exactly what the dynamics there were, but we didn't believe that it was blood borne, or at least we didn't fully believe that it was, until the local blood transfusion case was clear.

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[1]Follow-up on Kaposi's sarcoma and *Pneumocystis* pneumonia. *Morbidity and Mortality Weekly Report* 1981, 30:409-410 (August 28, 1981).

Hughes: According to my notes, the first case of immune deficiency linked to blood products was reported in January of '82.[1]

Volberding: Right. So a full year before this case.

What did we do? Well, we talked about it a lot, because first of all, we were concerned about the blood supply, but second, we were concerned about our own health, and maybe that was what was really driving us. We talked about it a lot; we shared data; there were meetings. There was a meeting with blood bankers from around the country in January of '83 at the CDC to talk about what could be done.[2] I didn't go to that meeting, but it was talked about really right away.

In San Francisco, we sent a public letter urging that a surrogate marker test--hepatitis B core antibody test--be investigated by the blood bank to see if that could be used to decrease the risk of transmitting AIDS. There were calls to stop gay men from donating blood. We were sort of half-hearted in that at the time. Again, it became a political thing where on the one hand, you had data saying this was a blood-borne, sexually transmitted disease that could be transmitted in blood transfusions, and that gay men were affected by the disease; on the other hand, the gay community did not like the idea of saying that gay men couldn't donate blood. So we danced around that by saying that gay men who had multiple sexual partners were not allowed to donate blood. So it was really missing the point. But I think it was a response.

Hughes: Were you still seeing Herb Perkins regularly? You mentioned that he used to come to the Kaposi's Sarcoma Study Group.

Volberding: Oh, yes. Especially during that time.

Hughes: Was possible contamination of the blood supply a subject of discussion?

Volberding: Right.

Hughes: What was his attitude?

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[1]Randy Shilts. *And the Band Played On: Politics, People, and the AIDS Epidemic*. New York: Penguin Books, 1988, pp. 115-116. (Hereafter, Shilts.)

[2]For more on this meeting, see the oral history in this series with Donald Francis.

Volberding: Well, I think he was pretty well prepared to believe that it was a blood-borne pathogen. My sense was that he wanted to do things to improve the safety of the blood supply, but wasn't eager to go overboard on it. It became pretty clear that some blood bankers at least were really very conservative and driven to protect the blood supply--not as their only motivating factor but as a very important one.

Hughes: You mean protect in the sense of conserve the volume?

Volberding: Exactly. Maintain the donor supply. And if things would threaten the donation of blood, that was seen as a bad thing by the blood bankers to some degree. And I think it's probably true. There was a meeting in March of '83 at NYU where [Joseph] Joe Bove, who was the director of the blood bank at Yale, said he wasn't convinced that HIV could be transmitted in the blood.

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Volberding: Well, I think it perhaps wasn't proven in the strictest sense. You had an association between donation of blood and development of AIDS, and there was no test. So he could say that, but I have to say I don't think anyone believed him at the time. Again, we should have known even before December of '82. But once we had the case here in San Francisco, I think every reasonable person believed that AIDS could be transmitted in blood.

Hughes: Eventually a questionnaire for prospective blood donors was developed that was carefully worded.

Volberding: Not to offend people, yes.

Hughes: It asked about symptoms--night sweats, et cetera.

Volberding: Lymph-node swelling.

Hughes: Yes, that kind of thing. Was the hepatitis B core antibody test indeed instituted?

Volberding: Oh, it was tested by the blood bank here, and by other ones around the country. It was eventually instituted some time later. But by the time it was being instituted, the availability of HIV diagnostic tests [March 1985] obviously replaced the need for surrogate markers.

Hughes: Were names of blood donors checked against AIDS cases from the very beginning?

Volberding: No, not from the very beginning. I would assume not. I don't know the dates, but my understanding is that the blood bank was able to compare its list of donors with a list of AIDS diagnoses, and that's how the connection of Art Ammann's baby to a donor with AIDS was identified.[1]

Latency Period in AIDS

Hughes: Comment on the growing realization that there was a long latency period.

Volberding: Yes, that's interesting. With any disease, until you get to the point where most patients you're following have progressed past the median incubation period--we know that's eleven years now from HIV [infection] to diagnosis of AIDS--you never know what the median incubation period is, and it always gets longer. It's obvious. So early in the disease, with the information we had, we made guesses that the incubation period was two years, and then we said three, four, five. So if you go back and look at these old reports, it gets longer and longer.

Some have said, "Well, that proves that we didn't know what we were doing." And I would say yes, of course we didn't know what we were doing, but I think it also says that we were trying to communicate what we knew when we knew it, and that we were being as honest as we could even at the risk of seeming to change our minds. Which I think has been an important issue with this disease.

Hughes: Do you think it's been truer in regards to AIDS than for other diseases that people are willing to concede that misinterpretations have for natural reasons occurred?

Volberding: I think so; I hope so.

Hughes: Because of the urgency?

Volberding: I think the people working in AIDS really start out and end up feeling very committed to our work, and see this as a critically important problem. It would be immoral to be anything less than honest; the health of people with AIDS and the health of people yet uninfected are at stake. So the best

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[1]See the oral histories in this series with Ammann and Selma Dritz.

we can do is to educate people; that's our real calling. I think it's made the AIDS community much more receptive to working with the press as well. The press was asking us questions, and they don't often ask the GI [gastroenterology] doctors, "Tell us the latest about ulcers." But we were being asked questions, and it always felt important that we give as clear an answer as we could, knowing that that was going to be the way that people were going to hear about this disease.

Hughes: You spoke last time very poignantly about your attraction to AIDS patients, which was kind of an extension of your work with cancer patients. Do you think there was some self-selection in the physicians that were involved early in AIDS and remained involved?

Volberding: I guess I'd have to say absolutely, sure. I don't know exactly how you would define that selection process, though. People came at this from a number of different directions. Some, because it seemed an interesting academic exercise. Part of my attraction was that it was a fascinating new disease, as we talked about last time. A lot of other physicians came at it because they were gay men themselves, and saw it as something important for their own community. I guess I believe that even people who didn't come and search out AIDS experiences ended up getting drawn into it because it is so impressive. It's an impressive disease. I've seen it happen with residents who I don't think set out to spend their lives working with AIDS, but once they work with it and see the excitement, I think it's sometimes very hard for them not to get drawn in.

Hughes: Is this perhaps a partial explanation for what seems to have been a remarkable cooperation among physicians?

Volberding: Yes, I think that's true, not to say there aren't egos and there aren't tensions; there obviously are. But I do think there's a sense of higher calling.

Hughes: The issue of AIDS is larger than the individual?

Volberding: My religious background is going to emerge yet. But I think people do have a sense of calling with this disease that's probably not like most other diseases.

Ward 5B, San Francisco General Hospital: The AIDS Inpatient Unit

Hughes: Let's talk some more about Ward 5B. What went into actually setting up the ward? I know you'd been using the space, but it obviously took more than space; it also took personnel and money.

Volberding: Right. We'd been using the space. When we moved over here [Building 80], it became empty space, except for the housestaff sleeping there during the day. But they're easy to move around. The hospital was concerned with what was going on. They saw the numbers of AIDS patients increasing. They saw the visibility of the epidemic, the politics of it, I think. The patients that we were caring for were getting very spotty care around the hospital. Not every nursing unit was receptive to gay men. There was a lot of anxiety: what should we be doing?

Hughes: Was the lack of receptivity based on homophobia--

Volberding: Oh, I think so.

Hughes: --or the fear of AIDS?

Volberding: I'm not sure you can separate them. I think both. We heard horrible stories of patients who had to get up and change their own beds during the night, the night sweats, and would have to go beg for Tylenol from the nursing station. Not to say that that was common, but it happened often enough that we found ourselves doing a lot of work putting out those fliers. It just became clearer and clearer that this was a very complex disease, and we were going to see more of it. Merle Sande was immediately very supportive when Connie Wofsy and I approached him with the idea of an AIDS unit. Even though that flies in the face of his commitment otherwise to general medical units in the hospital, I think he saw it as the same problem.

There was also the fear of contagion early on, and we didn't make much of it, but I think there was some sense that maybe we needed an isolation area for this disease.

Hughes: AIDS patients had been on general wards?

Volberding: Yes. In large rooms, rooms with other people. So I would say that I don't think at any point fear or infection containment was ever really a strong part of establishing Ward 5B. It

really from the start was a way to centralize and improve the care of patients.

We went to Geoff Lang, who was the hospital administrator at the time, and he didn't bat an eye. He was willing to support it. I don't know why, but it was really very important. The hospital then took over much of the work and identified a nurse on psych, Cliff Morrison, who was recruited to be the head nurse.[1] He put together the nursing staff and the nursing plan, and it's remained to this day a unit that's highly prized by the nurses as their unit. I supply a doctor for the unit; there are doctors obviously doing the direct patient care, but it's still seen as a nursing unit, and a lot of the sense of pride comes from them.

Hughes: Much of that pride I understand stemmed from Cliff Morrison.

Volberding: Oh, he was very important in giving it a sense of its identity and pride in what it was doing.

Physical Setting and Operation

Hughes: Give me a feeling of the physical setting of the ward.

Volberding: Well, it's in the new [hospital] building. One corner of it, a corridor of it, was blocked off as a respiratory intensive care unit. So we had I think twelve rooms. All this was done between the nursing staff and the medical staff, with a lot of input from the gay community as well, from Shanti Project and others, whom we brought into the discussion early on.

We decided that we wanted private rooms for all of our patients, more for their own comfort than for fear of contagion. We decided that we would not erect any specific barriers between this unit and the rest of the hospital, again to avoid the sense that this was an isolation unit. Merle Sande was really instrumental in that. He said, "We won't do anything different. We'll put extra sinks in the hallway for washing hands, but we won't make people gown and glove to go into the ward. We're not going to succumb to panic."

Hughes: 1983 was the height of the panic.

Volberding: Yes, exactly.

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[1]See the oral history in the AIDS nurses series with Mr. Morrison.

I was at a meeting in New York in, I think, March of '83. I mentioned the concept of Ward 5B to some people in New York, and they just thought it was horrible. They thought it would be a leper colony, which was their term. And really from the moment we opened it, the exact opposite was the case. People preferred to be there; the nursing staff loved working there; the place was a must-see stop on the political tourist circuit. Politicians and other people would come to see what we were doing, and the patients' visitors increased.

Hughes: There were no hours?

Volberding: Right, no visiting hours. So it was a very popular thing, really almost from the very start.

Hughes: The whole "This World" section of the [San Francisco] *Chronicle* on January 15, 1984, was devoted to AIDS. There was mention of Sharon McKnight.

Volberding: Oh, yes. The torch singer from nightclubs who would come up and sing on Ward 5B.

Hughes: Was she the only one who performed?

Volberding: She was the main person, but there was another woman, Rita Rocket, who for years--I don't know if she still does--would bring meals by on Sundays. It's still a very viable and proud place where the [AIDS] care is still the best in the world.

Mayor Feinstein's Visit

Volberding: There's one funny story of 5B--it's now moved over to 5A, but the concept is the same. It's a little bit bigger. When 5B had been open a short time, Feinstein came for a tour. First she came over and saw the clinic. We walked over to show her 5B. Merv [Silverman][1] was the health director at the time. It was raining, so we decided to go through the tunnel. There are tunnels between all the buildings here. Feinstein was happy to do that because she used to play in the tunnels when she was a little girl, because her father was a surgeon here, and she remembered the tunnels.

We were going through the tunnels and we were about halfway over. She stopped, looked down, and there was a big

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[1]See the oral history in this series with Dr. Silverman.

pile of vomit on the floor, off in a corner. It had been there so long it was desiccated and had dust balls on top of it. She stood there, and right at that moment, Merv Silverman and Geoff Lang, the hospital administrator, heard that she was visiting. We had intentionally not told them. They came scurrying down the tunnel to meet the mayor. There she stood with the vomit on the floor and she said, "What's that?" [laughter]

So then we went over to the main building and went up the elevator, and there was graffiti on the elevator, and she said, "Why is that there?" So everyone was really totally tense at this point; it was not going well. And we literally no more than set foot on 5B when the wall underneath the sink, right in the main nursing station area, burst open and a hot water main pipe had burst. The place was instantly flooded. It was like a waterfall of scalding hot water. Here is the mayor standing there looking at this unit, and the housekeeping staff is trying to block it up with towels. [laughter] This is like a fire hydrant.

Hughes: Great timing.

Volberding: It was one of those days when you say, turn the tape back and start over.

Avoiding Burnout

Hughes: According to the same article in "This World," there were--maybe still are?--encounter groups for the staff on the ward.

Volberding: Oh, both in the inpatient and outpatient service, we worry intermittently about what we can do to make it a little bit more possible to keep doing our jobs. Burnout is a constant issue. I'm not sure what they're doing now, but we've done several things over the years here, from outside psychotherapy to spontaneous groups inside. It's seen as a very important thing. We have an ongoing grief therapy session now for our own staff.

Hughes: How do you deal with burnout?

Volberding: Oh, I think it's still very exciting stuff. It's still a challenging disease. The issues are changing. And those make it difficult, but they also really invigorate us, I think.

Hughes: Never boring.

Volberding: Never boring. The other obvious reality is that those of us that have been in this for a decade now are no longer seeing patients full-time. We do a lot more administrative and research work and travel, and I think all that helps us. I think it's much harder for the people on our staff who really do high-volume patient care and don't get the visibility that we do. There are a lot of people upstairs on Ward 86 seeing patients right now as we're talking here, not getting in the papers or anything like that. It's hard for them.

Hughes: Well, you spoke a few minutes ago of the perception of the ward as a potential "leper colony." It of course has turned out to be anything but that.

Volberding: I've had patients with leprosy complain about that term, so I don't use it any more publicly.

Model for Other AIDS Units

Hughes: Has the ward served as a model for other units?

Volberding: Well, it's interesting. I think the ward isn't so much a model, because it is modeled after oncology units. My experience, especially at Moffitt, was that cancer patients deserve an inpatient unit of their own. What we did here is exactly like an oncology unit, but with a different focus, AIDS, and with a little bit different energy because of that. You have people working there who are personally very committed to the work. And gay units have their own flavor. That is part of what 5A is like as well. But it really was modeled on oncology units, where you have complex medical diseases with a lot of psychosocial overlay, a lot of use of drugs that are complex and require a sophisticated nursing staff and psychosocial support staff. So really, it was modeled on oncology.

Now, it took a while after we opened 5B for other places in the country to start saying, "Well, I guess the experiment was a success." Now it's a model and it's used around the world. Many parts of Europe, Australia, have AIDS inpatient units that try to duplicate this. And I really do think it's a model. I think it is the AIDS inpatient nursing unit in the world. I'm a little bit proud of it. [laughs]

Outpatient AIDS Clinic, SFGH

Volberding: I have the same feelings about the clinic. People tend to notice the inpatient unit more, but my heart is really in the clinic, and the clinic has been a model in the same sense.

Hughes: Why is your heart particularly in the clinic?

Volberding: Well, it's two floors up instead of two blocks over [in the hospital], so the proximity helps. I think the most important thing we've done is build a system that really focuses on care at the community level. It's wonderful having an inpatient unit when you really need it, but it's much better to keep people from needing it, and there the clinic plays the critical role. We are able to use the clinic as a coordinating site for delivering care in the home, bringing patients into the clinic when they need it, and then as a last resort, bringing them into the hospital. So I think in terms of the model of care that San Francisco is known for, really to my mind the clinic is right at the heart of it.

I think it's harder working in the clinic, because you're dealing with so many patients. You don't ever have a chance to really sit down and get to know the patients that you have. Whereas on the inpatient service, patients typically stay a number of days, so at least there's less turnover. There's more death in the inpatient unit. But we see our share here as well.

Adapting to the Changing Demography of AIDS

Hughes: Is the system changing now that AIDS patients are becoming far more diverse?

Volberding: Well, there was some fear that maybe our model only would work for gay men. I think we're more and more comfortable that that's not true, that we've accommodated to an increasing fraction of intravenous drug users, we have a lot of African-American and Hispanic patients, more women, and our staff has accommodated to that. There's always a turnover on the staff. It is hard working in AIDS, especially if you're not getting all the visibility that some of us do. We try to make sure that we have the right staff for the current epidemic.

We really specifically brought people on board that have background in working with intravenous drug users. We've recruited people from the East Coast who have a lot of experience with that population. We've adapted over the years. I couldn't feel as proud about our model if it was only restricted to one type of patient with HIV. The strength of the model is really tested by its adaptability to new populations, and I think we're succeeding. It's hard, there's no doubt about it, but I think we're succeeding.

The group of people that were floating out as you were coming here are all working in the substance abuse program. We have medical staff that worked in the methadone maintenance clinic, dealing with HIV problems even before they were part of Ward 86. So it's a wonderfully integrated place, more than I'm sure any other AIDS clinic in the world.

Terminology: HIV Disease Rather Than AIDS

Hughes: I noticed that you refer to the disease as HIV disease, as opposed to AIDS. Why is that?

Volberding: Oh, for a lot of technical reasons. HIV is a progressive, fatal disease. HIV infection is in more than 90 percent of people a fatal disease. AIDS is an anachronistic term that we used before we knew what was going on.

Hughes: And it also only reflects a portion of the picture.

Volberding: It only reflects a portion of the picture. We can in fact prevent AIDS by using medical interventions, and yet we can't do anything to reverse the underlying HIV disease. So I think HIV disease is the true underlying problem. I try to avoid the terms ARC [AIDS-related complex] and AIDS altogether now. I give entire lectures where none of my slide material mentions AIDS. We're actually thinking about changing the name of the AIDS program to something that might more reflect HIV disease. I hate to do that, because--

Hughes: You've got name recognition.

Volberding: --it's in all the books and everything.

More on Kaposi's Sarcoma

Hughes: I want to go back to an early paper on therapy of Kaposi's sarcoma, which was published in *Seminars in Oncology*, 1984.[1]

Volberding: Right. There was actually an earlier version of it published in the *American Journal of Medicine* in 1983.[2]

Hughes: More or less the same work?

Volberding: Right.

Hughes: You mentioned that you and the people working on Kaposi's were suffering from a lack of knowledge about the natural history of the disease, and also lack of a staging system. Did you eventually work that out?

Volberding: Yes, I think we have. Kaposi's is a very fascinating part of this story. We just had a seminar two days ago at the new molecular biology center [Gladstone Institute of Virology and Immunology] here, talking about what we know right now about Kaposi's. We've made a fair amount of progress. We have a staging system that we more or less accept. We certainly know the clinical presentation of the disease extremely well. I don't think there's much new we're learning these days about that. But only now is the biology beginning to become a little clearer. It's not a traditional cancer; it's something that probably is triggered by HIV and perhaps another infection. So it's a very interesting disease epidemiologically, biologically, and yet our therapy hasn't progressed much since those days. We really still use the same approaches, but there's a lot of interesting cancer.

Hughes: Your focus in the early days was almost exclusively on Kaposi's. You didn't pay much attention to *Pneumocystis*, at least in your publications. Was that because the cases weren't there, or because you were interested in Kaposi's?

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[1]P. A. Volberding. Therapy of Kaposi's sarcoma in AIDS. *Seminars in Oncology* 1984, 11:60-66.

[2]P. A. Volberding, M. A. Conant, R. B. Stricker, B. J. Lewis. Chemotherapy in advanced Kaposi's sarcoma. Implications for current use in homosexual men. *American Journal of Medicine* 1983, 74:652-656.

Volberding: The cases were certainly here. But I was interested in KS, and it really was useful in working with a group of people for us to be able to say, "Your area is *Pneumocystis*; mine is Kaposi's sarcoma." We generally agreed that we could have our own areas within this disease without fighting with each other. I think that strategy has worked very well for us. It's less important now than it seemed then. When we were first starting out, we were all pretty insecure and needed our own identity with this disease. But now, I even give an occasional lecture about *Pneumocystis*, and some of our people in infectious disease are actually allowed to do HIV treatment, which has been my turf. So as we get more secure, the barriers fall. We all realize there's a lot to do. People are just more secure, I think.

Importance of Letters to the Editor

Volberding: I would like to do a serious research project on the role of letters to the editor in medical journals and the AIDS epidemic. When you really want to get something out quickly, you write a letter to the *New England Journal* or *Lancet*, and it gets published quickly. Especially at the start of the epidemic, people were more interested in getting the word out than in gaining academic credit. Letters actually played a very important role in dissemination.

One of the letters that I am proudest of was actually with me wearing an infectious disease hat. Jerry Groopman, Ron Mitsuyasu, and I--Jerry and Ron were both at UCLA--were talking and realized that we had seen a lot of rashes in people getting treated for PCP. So we wrote the first report in the medical literature as a letter to the *New England Journal*, "The incidence of side effects in the treatment of PCP." It's the most important problem in treating *Pneumocystis* pneumonia. We were the first to publish on the topic, but as a letter.

Hughes: Are the *Lancet* and the *New England Journal* the best places to publish letters?

Volberding: Probably. Less so the *Annals* [*of Internal Medicine*] or *JAMA* [*Journal of the American Medical Association*].

Hughes: Did you go to a very early workshop on Kaposi's, September 1981, at the NCI?

Volberding: I didn't go to that. John Ziegler did, who still was at the NCI then. I don't think even Conant went to that.[1] I think it was really very East Coast; drew in some of the people from New York--Bijan Safai, Alvin Friedman-Kien, Linda Laubenstein. We were aware of the workshop. They weren't aware enough of us at that point to invite us to it.

Hughes: Did they come up with any schema that you found useful?

Volberding: No. They reviewed some of the staging and therapy, especially drawing from Kaposi's in Africa.

Hughes: How was what came to be known as HIV disease defined in clinical terms?

Volberding: Well, it's less easy to point to a single meaning than it was early in the epidemic. We've tossed it around a lot. I actually wrote an article that I think we ended up publishing in the *Journal of AIDS*, where I tried to summarize why AIDS is not really the relevant term, why HIV disease is the relevant term.[2] I think it's been a really important concept, but it's not one that people have easily agreed on.

I remember at the Stockholm International AIDS Conference in '88, we had a Burroughs-Wellcome-sponsored post-conference symposium where a number of us got together, and I was advocating this idea of HIV disease. The term was still considered controversial then. But I think it's now pretty well accepted.

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[1]Conant went but had to request an invitation. See his oral history in this series.

[2]P. A. Volberding. HIV as a disease: The medical indications of early diagnosis. *Journal of AIDS* 1989, 2:421-425.

Defining AIDS

[Interview 3: June 1, 1992] ##

Clinical Definition

Hughes: Did the CDC's clinical definition of AIDS definition make much difference to your research?

Volberding: Well, sure, it made a lot of difference. First of all, it helped having a standardized term for what we were seeing. It struck us as a good term. It said what we thought was essential then about the disease that we were seeing. Also the classification system used diseases that I think without any real exception we tended to believe were really important.

There was some controversy right away about Kaposi's sarcoma, because people appreciated even early on that it was different in the sense that people in many cases could do better for a longer period of time with KS than with some of the other problems associated with HIV disease. I think there was pretty much agreement about the CDC definition.

Hughes: What role, if any, did the hepatitis B model play when you were tracking the disease?

Volberding: My sense in terms of analogies between hepatitis and what we saw as AIDS at that point was, we knew that hepatitis was sexually transmitted and transmitted in the blood, so it had that linkage. The same groups of people were at risk for both diseases, and we knew that many people infected with hepatitis virus didn't develop any serious disease. Until we had the AIDS virus identified and the test for it, we were still under the impression that probably most people infected with whatever it was that caused this disease wouldn't get it. I think it took a long time before it became accepted that essentially everyone with the infectious agent of AIDS was going to get AIDS. For a while there, though, we tried to use hepatitis as a more optimistic model.

Hughes: When did you realize that AIDS has a long incubation period?

Volberding: You can't establish that until you've followed groups of people for a long period of time. As I think we were saying last time, there was always the question of how long does it take to develop AIDS after you get infected. The longer you watch a population with an infection like this, the more

clearly you can establish the incubation period, and the more clearly you can establish the fraction of people that are going to be killed by a virus. We were able to establish after a number of years of observation that the incubation period was about eleven years, and that more than 90 percent of people appeared to be developing life-threatening disease.

Definition as a Disease of Gay Men

Hughes: In the beginning, I'm assuming--and correct me if I'm wrong--that you thought of HIV disease as a gay disease.

Volberding: In the very early period, in the very early parts of the epidemic. There were reports early on about hemophiliacs and drug users, and we saw occasional cases in those groups in San Francisco, but the vast bulk of our problem was in gay men. The vast bulk still is, although not quite as disproportionately.

Hughes: Did the cases that were not gay immediately make an impression?

Volberding: It's hard to remember exactly. I think to some degree. There was probably some suspicion that some people who said they didn't acquire this by homosexual contact really weren't being honest. On the other hand, I think there was plenty of evidence early on that parenteral routes of transmission--transmission by blood--were possible. Again, because hepatitis gives us a model of an infection that's both sexually and parenterally transmitted, it probably didn't take too much convincing for us to agree with that.

More on the Kaposi's Sarcoma Study Group

Hughes: Can you talk about your conversations with Herb Perkins [from Irwin Memorial Blood Bank], who was part of the Kaposi's--

Volberding: --study group. It's too bad we didn't give it an official name; it would make life easier now.

Well, the KS Study Group had been meeting in dermatology at UC in the ambulatory care center for some time. I would

think certainly for most of '82.[1] Typically, they were Thursday noon meetings, where we talked rather informally about common concerns about this new disease that we were seeing. Selma Dritz,[2] who was working for the health department, would always come and present updates on new cases of AIDS in San Francisco. Marcus Conant and I were seeing patients in the KS Clinic there at Moffitt [Hospital], and would present clinical updates. And other people from the labs would come.

I don't know at what time Herb started to come, but he was an occasional member of that informal group. Certainly his role became more prominent after Art Ammann's baby with AIDS became known to us, and that was in December of '82, as we discussed. Right at that time, the concern was that we were dealing with an infectious agent; we couldn't duck that fact any more. Again, we should have known that. The data that should have allowed us to reach that conclusion were already old. We knew that there were hemophiliacs who had become infected from blood products.

Hughes: Well, it's always easier in retrospect.

Volberding: So in retrospect, we should have known better, but we didn't. I don't think we knew better at least until that time [late 1982]. And then, our work got more serious. As I said, we became afraid that we were going to catch this disease. We still had no way of testing whether or not we were infected, and I think the energy that came about during those months was probably at a peak in a sense, even compared to later events. There was concern verging on panic. There were still no common, overt cases of discrimination against people with AIDS, but there was a lot of concern about that in San Francisco.

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[1]The Kaposi's Sarcoma Study Group began to meet in the fall of 1981, definitely by October 1, 1981, and perhaps as early as September 21, 1981, the first meeting of the KS Clinic. (Marcus Conant to Corrina Kaarlela, October 1, 1981. KSN 1981-2/1982.)

[2]See the oral history in this series with Dr. Dritz.

The Bathhouse Controversy, 1983-1984

Bathhouses as Sites of Infection

Volberding: The bathhouse events really were played against that backdrop of a lot of awareness, a lot of concern, and involved professionals working with this disease who were themselves rather frightened. It's not easy for me to know how that, or if that, changed our reactions, but I suspect it must have. As we knew that this was an infection that was sexually transmitted, at least in San Francisco mostly among the gay community, it seemed a logical enough thing to say that those businesses that were licensed to provide opportunities for sexual contacts be controlled or eliminated to remove the source of further transmission of this disease.

Hughes: Now, in your history-taking with patients, did you find that most encounters had happened in the bathhouses?

Volberding: To our credit, I would hope, I don't think we really focused clinically on how they got infected. It never really mattered very much. We did ask early in the epidemic when we were groping around in the dark trying to find what was going on.

I don't know numbers, but I'm sure a lot of our patients had visited bathhouses. They were popular social institutions in the gay community and tended to be used by gay men who were very "out," and those were the gay men who became the first infected with this agent. So yes, I'm sure the bathhouse was an important part of the vector of transmission of this disease.

At some point during the controversies that followed, we threatened not completely half-heartedly, although we never acted on it, to go out and picket the bathhouses ourselves, feeling so convinced that it was not appropriate to let business go on as usual. Now, there was an active debate, both behind the scenes and in front of the scenes, about what were the best methods to control transmission. We all agreed that obviously it wasn't having sex that did this; it was having sex in a way that transmitted this virus from one person to another. So there was a lot of concern about being too heavy-handed, being too intrusive into what other people said were their rights to do whatever they wanted.

So there was a debate. People would say, "Well, if people in bathhouses can be encouraged to behave in healthier manners, then perhaps they can be left open." Merv Silverman even argued that they should be turned into centers of learning about HIV, which didn't strike most of us as being very serious. But that was the debate.

A Meeting with Bathhouse Owners, Early 1984

Hughes: I know of one meeting, that's reported in Randy Shilts' book, where you met with the bathhouse owners.[1]

Volberding: Yes. That was pretty remarkable. Donald Abrams and Andrew Moss and I were especially involved in some of these discussions. We thought, It must just be that the bathhouse owners don't understand the nature of the problem. So we were going to be civic leaders and invited the bathhouse owners here to our clinic, so that we could talk with them and present them with a slide show about the disease.

We noticed several things: they arrived in business suits with lawyers at their sides, and here we were in our white lab coats. There was a feeling of hostility that I hadn't anticipated. We really went into this naively, thinking this would be a welcome educational forum. They came into it feeling, understandably so, that this was one of a series of attempts to shut their businesses down. That's really the way they approached the whole discussion. We weren't allowed to give a lecture about the disease.

Toward the end of the discussion one of the bathhouse owners turned to me and said--as I remember it, this is exactly the truth--"Look, we're both in it for the money. We make money from them having sex, and you make money when they get sick." It was as though, "No big deal. We understand each other." We [professors] kind of shook our heads--I did at least--and said, "I don't understand that at all." I think there was still denial, the belief that this was a disease like gonorrhea or syphilis. And it's not. It's a disease unlike any other we've seen. And these people weren't just getting sick; they were dying from the disease. Furthermore,

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[1]Shilts, pp. 421-422.

we weren't making any money from it, so the statement was wrong on all counts.

Mervyn Silverman's Role as Director of the Health Department

Hughes: Well, comment on Silverman's reluctance to close the bathhouses.[1] Do you have any insights?

Volberding: Probably no direct insight, except that he was reluctant. I'm certain he was under enormous pressure from the gay community not to close the bathhouses. The bathhouses were seen as something of a symbol of gay freedom that was obviously hard-fought. There were people who believed that giving in at all on this would be giving up on all of the advances that gays had accomplished. It was not unlike the present discussions with abortion, where if you're a radical pro-lifer, any compromise is seen as immoral. I think it was played on those same hard-edged discussions, so that it was hard to come up with a compromise position without finding some people very pissed off at you.

I think Merv found himself deciding which side he was willing to take the heat from, and I think ended up becoming convinced--I know him and like him and respect him--that it was less intrusive, and would accomplish the same end, to regulate the bathhouses instead of shutting them down. I think that an argument can be made for that. Certainly arguments were made for that. By opening up the doors and putting in lights and monitors and educational material, that bathhouses could be converted from unsafe sex places to safe sex places. It didn't convince many of the rest of us. It was like putting weight-reduction guidelines in a candy store, as Conant put it. There are places where you don't educate, and the bathhouses were not places for education.

The Medical Community Presses for Closure

Hughes: Were you involved in any concerted efforts by the medical community to try to convince Silverman to close the baths?

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[1]For Silverman's viewpoint, see his oral history in this series.

Volberding: Yes. We had a number of meetings into the late hours of the night and morning in Merv's conference room on the third floor of the health department building, where an assembled team of experts tried to make some sense out of this. It included local people--myself, Merle Sande, Donald Abrams, Andrew Moss --but also people from outside, from the CDC in particular--Jim Curran, Harold Jaffe--and also included people who were trying to walk that middle ground--gay doctors. We were looking for a compromise that wouldn't have to result in shutting down the bathhouses.

So it wasn't as though the room was unanimous against Merv. There was really a very hard-fought give and take. But clearly, it seemed to me, and I think to all of the people that were participating there, the arguments in favor of shutting down the bathhouses carried the day. And when Merv announced that he was having a press conference to make his decision known about the bathhouses, I certainly went--and I know Andrew did, because we drove down together--with the assumption that we were going to witness history in the making, i.e., Silverman shutting down the bathhouses because of AIDS.

We were just absolutely floored when he walked in front of the microphones, his room jammed with reporters, a series of doctors lined up beside him ready to help him take the heat, and he said, "I'm not going to make any decision." And we went, "Gee. This seems a little bit weak." And it obviously was.

Hughes: What do you think had happened to his thinking?

Volberding: I don't know. I assume he came under even more pressure from people who didn't want him to do what we wanted him to do [close the baths]. But it was really an uncomfortable moment. We lost some of our affection for that process.

Hughes: Well, about a month before closure in October, 1984, sixty physicians at what was then called Pacific Medical Center [now California Pacific Medical Center] signed a petition to Mayor Feinstein urging closure.[1] Do you remember?

Volberding: I remember vaguely. There were a <u>lot</u> of us that were calling on Merv to do more. The mayor was beside herself. She could not begin to understand why people would have sex in these places anyway, much less why the city should keep them open.

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[1]Shilts, p. 481.

It's no secret; I think that that was the major rift that resulted in Silverman losing his job.[1]

Hughes: Yet, from what I understand, Feinstein was very reluctant to close the bathhouses herself, because she wanted it to be a medical move, not a political move.

Volberding: Yes. Well, we had a lot of discussions with Feinstein about this too. I think she clearly is a social conservative, at least by San Francisco standards, and really couldn't understand the behavior that was at the back of this. But again, no political leader wants to take on the gay community head on, and I don't think she was any exception. If she could make it someone else's decision within her administration, well that person could take some of the flak and she could take some of the credit.

But she wasn't a passive member in this; she didn't just sit back and say, "Well, make up your mind whatever it is." It was clear that she wanted the bathhouses closed. That was no secret.

Hughes: Marcus Conant and a few other physicians actually made depositions in the legal action to close the baths.

Volberding: Oh, yes, I made one too.[2]

Hughes: Do you remember how that came about?

Volberding: I haven't remembered it until you said it this second. But yes, I remember a number of us gave signed depositions.

Hughes: Were you asked to do so?

Volberding: I remember doing it; I certainly don't think I started it myself. I'm not sure who did.

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[1]Silverman resigned as health director in December 1984. (Shilts, p. 503.)

[2]Declaration of Paul A. Volberding, M.D. October 8, 1984. In support of a temporary restraining order to close the bathhouses. October 10, 1984, Superior Court of the State of California in and for the City and County of San Francisco. Dean Echenberg papers, San Francisco Department of Public Health, Bureau of Epidemiology and Communicable Disease Control, drawer: Bathhouses, folder: 10-10-84 Declarations in Support, Volume I.

It was pretty much a foregone conclusion at that point that the bathhouses would be closed. No one was very happy with what happened after Silverman's first announcement, that in fact obviously things were still going on, business was dwindling, the bathhouses were slowly dying a financial death. And it really did seem time to bring this to a closure.

Closures Elsewhere

Hughes: Was there hope that the closure here would be seen as an example, and other cities would follow suit?

Volberding: Well, we were willing during that time, as we still are, to be leaders. I think that we're not so put off if we're the first people to do something in this epidemic, because I think usually we've been proven to be right. During that time, it surprised us that places like New York hadn't done anything, but on the other hand it didn't surprise us because we knew that decisions were not easily reached in New York City. Sort of nothing happened in New York, in contrast to San Francisco. So we were well aware that other places hadn't done it, but it didn't make us feel too anxious.

Hughes: Was the drive to close the bathhouses here somewhat for the symbolic value, so that other places would have a precedent for taking similar action?

Volberding: It might have been part of it; it's hard to sort out.

Hughes: Did other cities then close their baths?

Volberding: It never really became a major issue in most other cities. I think L.A. closed theirs eventually; I think San Jose did.

Hughes: But it wasn't a domino effect.

Volberding: It wasn't really, at least not a very obvious one. I think it took New York a long time to bring theirs under regulation. I'm not sure they ever really closed them. I think they tried, and then the courts wouldn't support it, in the way that that often happens.

Clinical Trials of Interferon and AZT

Hughes: Well, on another subject, we talked in the previous session about your trials of alpha-interferon. I saw an article of March of 1984 in the *Chronicle* reporting that you would soon be beginning trials of gamma-interferon.[1]

Volberding: [laughs] I just laughed because it was one of those magic treatments that was not exactly in the right direction. Alpha-interferon and beta-interferon do have activity against Kaposi's, and they do have antiviral activity. Gamma-interferon proved to have nothing much in the way of benefit, at least in the way we were using it then, so it proved not to be a big story. It's still around, and people are using it. It stimulates one of the cells in the body, the macrophage, that can be infected with HIV, and so people are trying to use it as an adjunct therapy for some infections where macrophages are an important part of the host response, like cryptococcal meningitis. So there are actually clinical trials still going on with gamma-interferon.

Hughes: Was the interferon genetically engineered?

Volberding: Yes.

Hughes: Do you care to comment on the FDA's [Food and Drug Administration] role in drug trials?

Volberding: Well, the FDA is very involved, and has been from the very start. I would say that I don't think our appreciation of the FDA's role was very dominant until probably '86 or '87, when we designed the first AZT trials. Until then, there wasn't really that much to use. My own involvement with the FDA had been more with the Bureau of Biologics, working with interferon. So I got a chance to see the FDA in action, such as that is, but it wasn't really until the antivirals were first developed that the FDA's role improved dramatically.

With the first AZT trial [1986], because I was an investigator on the trial, I went back to the meeting where we presented that information to the Anti-Infective Drug Advisory Committee. You could see the FDA saying, "Gee--." Suddenly hundreds of people were descending and fighting for space in their room, and there were TV cameras and stock analysts off

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[1]Charles Petit. "Drug Testing in S.F. on AIDS Victims." *San Francisco Chronicle*, March 8, 1984.

in the corner. They became very aware that this was a big issue. I think before that time, there weren't really many drugs that we needed the FDA very involved with.

Hughes: Did that response surprise you as well?

Volberding: That all those people came to that meeting?

Hughes: Yes.

Volberding: No. This was the first AIDS drug. This was hope for people with this disease for the first time. After everything else we had tried had failed, this was something that seemed to be working.

Hughes: You were in on the first trials of AZT?

Volberding: Yes, right.

Hughes: How were those decisions made?

Volberding: Well, the first trial was sponsored directly by Burroughs-Wellcome, and they came around to places with AIDS patients that they had heard about. Because we had done some work with interferon, we were more or less known in the pharmaceutical community as a reasonable research site. So they invited us to come to a meeting in 1986 in Bethesda, where we sat around a table and talked and designed the study. Then when the trial finished, we obviously then participated in the announcement of the results.

Hughes: Had you ever designed a trial before?

Volberding: Well, yes; I designed the alpha-interferon trials, and some trials when I was an oncology fellow, looking at liver cancer. It was a pretty amazing group of people--

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Volberding: --involved in that study; I think they picked good sites. The drug company went around and identified places that they might want to do the study in, and then they approached the investigators there and chose us to participate, one by one. And then we got together at a meeting to form a consensus on the design of the trial and what we were trying to prove in the study. So it was pretty typical of drug company-sponsored trials.

Hughes: Was there any attempt to speed up the trial of AZT?

Volberding: Oh, yes, it went amazingly fast. There was no problem speeding it up. I don't remember the dates, but it took only a matter of months from the first meetings until we had the trial started. It was in the good old days before the creeping bureaucracies that have descended on us. So it happened really quickly, and you remember, the trial was started in '86 and was completed in '86.

There was never anything like it, in any part of medicine, especially for a drug that's held up as well as it did. You might have guessed, as we would have guessed at the time, that this would just be the first of many similar drugs, and one which came later would prove to be better [than AZT]. Statistically, that would be a good guess. Here, the first drug tested proved to be--at least as we now talk--the most durable.

Unorthodox AIDS Therapies

Hughes: Were you aware that your patients were using unorthodox therapies?

Volberding: Sure, we were aware. I think we have--and especially then probably had--a really good relationship with our patients, where they felt free to tell us what they were doing and why. There weren't really that many therapies. There was high-dose vitamin C in that time frame; there was DNCB.

Hughes: What's DNCB?

Volberding: Dinitrochlorobenzene. It's a skin irritant, and the idea was that if you painted it on your skin, your skin would be irritated, which would cause your immune system to become activated, and you'd end up with more cells to fight HIV. Probably not a very safe approach when we know that activating the immune system was one of the triggers for HIV replication.

It just didn't make sense to us that with a virus in the DNA of the cells, that painting some irritant on your skin was going to help your disease. It struck me as pretty naive. On the other hand, people were trying those things. There was interest in unorthodox therapies, but it wasn't an industry the way it is now.

Hughes: How were patients getting that sort of information?

Volberding: Right from the very earliest days of this epidemic, most of the communication was through the gay press. So there would be articles talking about vitamin C, and debates back and forth about that. Many of the people advocating these treatments are very effective advocates, so it was easy for people to find the information, especially for gay men. It wasn't easy for people not in gay communities, which may be a continuing problem, namely, that we haven't really brought those people into the discussion.

Hughes: Did you feel it was your responsibility to your patients to comment about unorthodox therapies?

Volberding: No. The staff has talked about this from early in the epidemic, and I suspect that every one of our doctors and nurses upstairs has their own approach to it. Mine has been to say, "Who am I to be a judge? I don't know how to cure this disease." If I did, I'd cure it, and it would be out of here. So to me, the best approach in this is to admit what you know and what you don't know, and if you don't know, be willing to listen to what the patient's doing.

The only real concern that we've had over the years is that with a frightening epidemic disease, there's always a potential for exploitation. And there have been some examples. People in Berkeley advocated the use of extra-oral water. If you drank eight or ten glasses of water per day, you'd flush the virus from your system and detoxify yourself. It was ludicrous, obviously, especially because they were advertising it as a cure and charging $10,000 for the advice.

Hughes: [laughs] For water?

Volberding: For water.

There was a place in Saratoga that had little cabins out in the woods with electric mattresses in them, and this also was going to cure the disease. The idea was that you'd lie on the mattress for an entire day or more, and the mattress would be plugged into the wall, and the electricity flowing through the mattress would repolarize your immune system, whatever that means.

So those things were funny, but they were also--

Hughes: Yes, they were not funny really--

Volberding: Yes, not funny in the sense that they were potentially taking people away from therapy that they needed and involving them in something that was a total waste.

Hughes: Was that ever an actual problem with your patients?

Volberding: Not really. I mean, it's a problem individually; it's not a group problem. It's clear that some patients that we've followed, and still do, use unorthodox therapies either because they would rather call their own shots completely and not use regular medicine, or because they want to hedge their bets and do some of both--hard to know.

Our philosophy has been, who's to know what I would do if I were in that patient's shoes? Who's to know what I would think is most important? And who's to know that I wouldn't want to do this myself? So we've tended to be pretty relaxed about it, encouraging our patients to let us know what they're doing, rather than operating under the assumption that they're not doing anything. Which is not true.

Hughes: When would you date the rise of the black market in AIDS therapies?

Volberding: Well, I think it's been gradual. I think probably the biggest jump was--I'm not going to remember the dates--around a drug called AL721. AL721 is basically a mixture of three different kinds of fats in different concentrations, seven to two to one. The idea is that if you took in enough of these fats, in this ratio, that they would get into your bloodstream and that ratio would change the fluidity of your cells. Your cells have lipid-containing membranes, and if you took enough of this external lipid--fat--it would change the chemical nature of your cells. It would change the rigidity of your cells. Again, how likely is it that by taking foods--fats--in by mouth, you're going to get enough changes in the delicately balanced homeostasis of your blood to change how your cells work? I think it's rather predictably not going to work, and it didn't work.

But it was possible to make this drug. You could take egg yolks and extract the various fats from them using home chemical kits; basically gallons of acetone, this and that. So it was the first time that a therapy that was talked about in the medical literature was something that a dedicated person could make in his own home. Literally, it was one of these bathtub productions of AL721.

Well, it came out later that the combinations that were being sold in the health food stores had nothing approaching that ratio, if they even had all three components. There were reports of problems with infection following it, because of the *Salmonella* content in eggs. So there were a lot of reasons why that faded pretty quickly.

Those were the days when the underground market probably first really took off, because people felt they were doing it themselves.

Hughes: Do you remember the year?

Volberding: My guess is '85, but I don't remember.

Publishing on AIDS

Hughes: I was wondering about publication, the balance between wanting to get information out and the need to protect the information until it was published. Was that an issue?

Volberding: Oh, it's something that's been talked about a lot. There is an appreciation that a public health crisis demands immediate dissemination of anything important. If you know something, it's kind of your obligation to tell it, especially if you gained that information on a federal grant. It's really in a sense the government's property, although it's not quite worded that way. But I'd have to say that for the most part, the channels of communication have been great, at least locally in San Francisco, through the gay press and others, even the straight press as time went on.

In terms of research results, there is the Inglefinger rule in the *New England Journal [of Medicine]*, but for the most part I think results are both presented publicly and presented in writing in the journals.

Hughes: In what order?

Volberding: Well, in that order. For example, when the 019 study [of AZT] was completed, we immediately that day put out a notice on the electronic mail system, letting people doing the research know what we found. We sent out by regular mail a mailing to all treating physicians, pointing out to them the importance of getting people on AZT, keeping them on AZT. I'm not totally an apologist for the system; I think things can be improved

and should be, but for the most part, I think the system has worked pretty well in terms of getting information out speedily.

It can always be threatened by a drug company. I think the main problems that have come up are drug companies that really, for whatever internal reason, don't want to pursue the indication. Maybe they have something else that they're working on; they don't have the staff to do it; they know that if they just get the ball rolling, the activists are going to be looking over their backs making sure that they follow through.

Hughes: Was there any attempt to speed up the publication process?

Volberding: Well, what can help there is personal contacts. With our paper, 019, Tony Fauci called the *New England Journal* himself to let them know that this paper was coming and he considered it important. They gave him a green light to go ahead with a journal article. We interpreted that as prior acceptance of our research. It seemed to warrant it. The system isn't perfect, but I tend to be more in favor of it than not.

More on the Role of the Federal Government

Hughes: In April 1982, a congressional subcommittee on health held hearings in Los Angeles on AIDS. Did you attend?

Volberding: I can't remember.

Hughes: It was there that Congressman [Henry A.] Waxman accused the federal government of dragging its heels in terms of AIDS support.[1]

Volberding: It was becoming clearer and clearer to us in the trenches that this was an important new disease. The numbers [of patients] were so small, though. We could talk about icebergs, but you didn't know what was underneath the water. So the government responded quite slowly. Obviously it would have been much better had it responded more quickly.

On the other hand, how responsive do we want the government to be? We don't want it to overreact to anything

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[1]Shilts, pp. 143-145.

that comes along. So I think when history is written of this in the future, it will look like a reasonable response, considering what was known about the disease. It will obviously be seen as inadequate in retrospect, because it was, in retrospect.

Guidelines for Handling AIDS Patients in San Francisco Hospitals, 1983

Hughes: Well, in June of 1983, a twenty-four-person task force from San Francisco's hospitals completed the nation's first detailed guidelines on handling AIDS cases.[1] I presume that you were part of it.

Volberding: I don't remember anything, to be honest.

First, there was the issue of panic about transmission--isolation and all the rest. But as we got a little further along, we began to say, "Well, this disease is going to be with us for a while. How are we going to take care of it?" And there was one very important committee that was formed by the health department that started looking at an assessment of needs, but that's probably in '85.

Hughes: Assessment of needs?

Volberding: With respect to housing, patient care, psychological support.

Hughes: You and Merle Sande, chief of medicine, were reported to have said that all evidence indicates, "It takes intense contact with the secretions of AIDS patients--contact most often the result of sexual activity--for anyone whose immune system is normal to develop any of the AIDS diseases."[2] In other words, you were trying to downplay infectivity.

Volberding: Yes, right.

Hughes: The guidelines apparently were sent to CDC to serve as a national model for hospitals in every community touched by AIDS.

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[1] David Perlman. "UC Hospitals' Guidelines on AIDS Cases." *San Francisco Chronicle*, June 3, 1983.

[2] *Ibid.*

Volberding: I remember that, and the guidelines were published in the *New England Journal* a little bit later.[1] The only controversy was around my ego. I wanted my name more prominently displayed than it was.

Hughes: You couldn't convince the group?

Volberding: No. [laughter]

Hughes: There was also a debate centering around CPR [cardiopulmonary resuscitation].[2]

Volberding: We had a long discussions about did everyone have to participate in CPR training? We couldn't guarantee the sterility of the face of the dummy between users. Was it the obligation of the intern to do mouth-to-mouth resuscitation in a patient if the room didn't have any equipment in it to prevent mouth-to-mouth contact? I think the healthy thing that came out of that debate was the realization that CPR training is not all that important anyway. It's not as though it's an incredibly life-saving maneuver. People that arrest often stay arrested. But it was pretty heavily debated.

Hughes: The conclusion was that the health care giver should not be put at risk.

Volberding: Yes. It was at a time when there was concern about the risk to the health care worker.

The Obligation to Care for AIDS Patients

Hughes: What was and is your feeling about the obligation of physicians and other health care personnel to care for AIDS patients?

Volberding: Well, people should have access to high quality, comprehensive, expert, humane care for their diseases, whatever their diseases are. AIDS is no exception. You

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[1]John E. Conte, et al. Infection-control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). *New England Journal of Medicine* 1983, 309:740-744 (September 22, 1983).

[2]David Perlman. New Safeguards Urged in AIDS Emergencies. *San Francisco Chronicle*, September 22, 1983.

shouldn't have to be trundled off in a car to travel hundreds of miles to San Francisco General if you happen to have AIDS. It's the obligation of the hospital and physician to become knowledgeable if they aren't already.

Hughes: How much of the reluctance to care for AIDS patients is due to lack of education about AIDS, and how much of it is due to not wanting to deal with AIDS patients?

Volberding: Homophobia is the word. It's very real, and it drives most of the other problems. I think it's fear of working with gay patients, fear of "catching that disease" yourself, or being seen as too identified with gay men. It's ludicrous, obviously, and yet I think--

Hughes: It's a reality.

Volberding: It's a reality.

Hughes: Dr. Conant helped to establish an AIDS network among doctors.

Volberding: Well, he's done lots of things. The main network was really the KS Study Group, which was a loose but very effective network for physicians. He also helped to establish the AIDS Foundation, which itself is a network, although usually not for physicians so much as other personnel.

An Early Meeting on AIDS, UCSF, 1982

Volberding: I remember a meeting that Marcus and I organized that was the first big national meeting on AIDS; it was in 1982 at Toland Hall at the university [UCSF].[1]

Hughes: Well, tell me about that.

Volberding: Well, I don't remember a lot about it, but it was where I first met Bijan Safai and Alvin Friedman-Kien, who were both pioneer HIV dermatologists in New York City.

Hughes: What did you call it?

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[1]Acquired Immunodeficiency Syndrome and Kaposi's Sarcoma. Toland Hall, UCSF, October 29, 1982.

Volberding: I think it was a KS meeting on the face of it. We had people from the CDC; I believe Jim Curran came. It was a good meeting. It was well attended. It was I think the first big meeting in the country on AIDS.

Hughes: Did you learn at a symposium like that?

Volberding: All the time. I learned a lot. Earlier on in the epidemic, the learning curve was steeper than it is now. Although there are still things that come out of the blue to which I say, "That's how that works. I didn't know that."

More on Early Epidemiological Studies

Hughes: Could you tell me about the San Francisco Young Men's Health Study, and the San Francisco General Hospital Cohort?

Volberding: Several epidemiologists were interested in following groups of gay men to see if they became infected, and if they became infected, how long it would take them to get sick and die. Andrew Moss had one study that was randomly selected from households in the Castro. Another study that was already going on was a study of hepatitis B virus vaccine in the city clinic, and then another study was organized by Warren Winkelstein of UC Berkeley.[1] Warren participated in a Multicenter AIDS Cohort Study [MACS]. But because he wanted to do the recruitment in one way and [NIH] wanted to do it in another way, there was a quick falling apart, and so we ended up with three separate epidemiology groups studying gay men in San Francisco.

And really, they were remarkably consistent in what they've taught us. They've taught us that it takes about ten years to get the disease, and most everyone with the infection will get overt disease. They've also now given us some data that says AZT and prophylaxis for PCP can help slow down the disease process.

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[1]For more on this study, see the oral history in this series with Dr. Winkelstein.

Personal Contribution

Hughes: What would you say is your greatest contribution so far?

Volberding: Personally, or as an organization?

Hughes: Whichever you wish.

Volberding: I'd like to believe that the organization is more important than any of our personal activities within it, because I think the organization will unfortunately have to continue after we leave. What I've tried to do personally is model compassionate behavior, eagerness for new information, a lack of satisfaction with the way things are when it comes to treating the disease, and taking care of the people with the disease. What I've tried to be is flexible and creative when it comes to developing programs and taking on new challenges. I've tried to attract people who will be willing to similarly broaden their approach to this disease. To me, the disease is too important to get too focused on our approach. It seems to me that we have to be generalists with this disease.

Hughes: Very good.

More on the Kaposi's Sarcoma Clinic

Co-director

[Interview 4: April 10, 1995] ##

Hughes: Dr. Volberding, do you remember when you became co-director of the KS Clinic?

Volberding: No. It could have even been '81; I can't remember.[1] It was very early. I know that by the middle of '82, I had started

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[1]In July 1981, Marcus Conant proposed the formation of a KS clinic, which, according to Shilts, was established "within weeks." (Shilts. *And the Band Played On, p.76.)* In a memo dated September 2, 1981, Conant announced: "A combined Dermatology-Oncology Clinic will be established for the evaluation and treatment of patients with Kaposi's sarcoma. Dr. Paul Volberding has graciously consented to volunteer his time to serve in this clinic on Mondays from 12:00 until 1:00." The first clinic was scheduled for September 21, 1981. (Marcus Conant to William Epstein et al., September 2, 1981, KSN, 1981-2/82.)

talking to Schering-Plough about the [alpha-]interferon trial with Kaposi's, and I'm reasonably certain that we were already doing the KS Clinic before that.

Hughes: The KS Clinic first saw patients on September 21, 1981.

Volberding: Well, see, it could be that early, because when I started here at San Francisco General as the head of oncology, right from day one--and this is July 1, '81--my responsibilities included going to the melanoma clinic at Moffitt [Hospital at UCSF] to see patients there. And that's where I ran into Conant, and I don't think he ever had a coordinated KS Clinic without me. We decided that we should see patients together, and we decided that we'd see them in the derm clinic.

Hughes: Helen Schietinger became nurse-coordinator of the clinic in January of 1982.[1]

Volberding: Right. We hired Helen with money that John Ziegler got on an American Cancer Society grant that Marcus and I were both involved in writing.

Hughes: Did Dr. Ziegler see patients in the clinic?

Volberding: No, he never saw patients.

Hughes: Because his responsibility was the VA [Veterans Administration Hospital, Fort Miley, San Francisco].[2]

Volberding: Right.

Hughes: He was a senior investigator--

Volberding: With experience in Kaposi's from Africa. He had just come here from the NCI, so he had contacts there and knew whom to talk to.

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[1] See the oral history in the AIDS nurses series with Ms. Schietinger.

[2] See the oral history in this series with Dr. Ziegler.

Patient Evaluation

Hughes: Tell me what it was like in those very early days, starting with a patient presenting at the clinic. Do you remember step by step what happened?

Volberding: The real focus in the KS Clinic was doing a systematic evaluation of the patients. We thought that by carefully talking to the patient and examining the patient and doing consistent laboratory tests, that we might understand what was going on. The standardized evaluations focused on sexual activity, risk of acquisition of HIV, and recreational drug use--which was thought at the time to be a probable factor. And there was a careful physical exam documenting the presence of the Kaposi's sarcoma lesions.

Marcus and I didn't have any plan at first for therapy of the patients with KS, because neither of us saw patients regularly in the derm clinic.[1] He came to it from his office.[2] And dermatology typically doesn't do chemotherapy, except for local injections. So that lack of therapy was the weak link.

We let it be known through Marcus' contacts in the dermatologic community the awareness that we were there and interested in seeing patient referrals, so we got a lot of referrals, especially from dermatologists. We would typically evaluate a patient and then send the patient back to his dermatologist.

We were already seeing [AIDS] patients here at SFGH, but it wasn't until we got the [AIDS] clinic here up and running in terms of its research[3]--especially with the interferon, but even before that with the vinblastine therapy--that we made

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[1] The KS Clinic was held in dermatology space in the Ambulatory Care Unit at Moffitt Hospital.

[2] Conant has a private dermatology practice at 350 Parnassus Avenue, across the street from UCSF.

[3] The AIDS Clinic opened on Ward 86 in Building 80 at San Francisco General Hospital in January 1983, although AIDS patients had been seen on Ward 5B at the hospital (the site at that time of the outpatient oncology clinic) before the clinic was officially organized. (History of the AIDS Outpatient Clinic, Ward 86. [n.d.] AIDS Resource Program Archives, Ward 5A, SFGH, carton 4.)

the conscious decision to refer the patients here for chemotherapy, instead of developing the KS Clinic there at UCSF to treat patients.

Hughes: As of January 1983, the AIDS Clinic here at San Francisco General was off and running. Does that mark the beginning of the decline of the KS Clinic?

Volberding: I don't know about the timing. The AIDS Clinic here didn't materially change things, because it was just a change in location. Connie [Wofsy] and I were both seeing patients on 5B (while it was still the outpatient oncology clinic) through '81 and '82, and so we just moved the clinic over here to the sixth floor of Building 80, hence Ward 86. The decision to move the patients over here to SFGH for therapy was made before we moved into [Ward] 86, because I started the trial with interferon when I was still over in 5B. That was in '82.

My real interest was therapy much more than evaluation, so my energy more and more focused on the KS patients here.

Hughes: Did you stop going to the KS Clinic?

Volberding: No. It gradually ceased. I don't frankly remember when that was.[1]

We first had Helen [as nurse-coordinator], and then there was another nurse practitioner, Frank Baumgartner. Ernesto Hinojas [an administrative assistant] was one of the people who came and evaluated patients there. After a while, it almost got to be the nurse practitioner evaluating the patients under protocols that Marcus ran.

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[1] The exact date of the demise of the KS Clinic has not yet been pinpointed. It was still functioning at least as late as December 1984. (Kaposi's Sarcoma Clinic. Unsigned, undated report, probably written by Harry Hollander in December 1984 or January 1985. John S. Greenspan papers [hereafter JSG], 92-0123, carton 2-92, folder: AIDS Tissue Committee.) The KS Study Group continued to meet at least into June 1986. (Marcus A. Conant to Kaposi's Sarcoma Study Group, April 24, 1986. JSG, 92-0123, carton 2-92, folder: OAC-ASB Conant, Marcus A.)

Patient Referral Patterns

Volberding: I think the KS Clinic filled an immediate need of the epidemic in San Francisco when the patients being identified were mostly KS patients, or at least that was what was most visible about the epidemic early on. And a lot of the patients were being seen by dermatologists, because KS was a skin condition. It didn't take very long for people to realize, both in medicine and in the gay community, that KS was only one manifestation of a more complicated disease. Then the referrals weren't so much to dermatologists; patients were being seen by internists and family physicians, typically in the gay community.

Then the referral pattern didn't so logically go to dermatology; it would as likely go to an oncologist. And as the publicity in 1982 about our interferon trial hit the streets, it created a fair amount of attention. KQED did a story on their TV, which was the first TV coverage of AIDS work here at the General, I think. Patients ended up referring themselves here. So instead of a patient going to a dermatologist and then being referred to the KS Clinic, as often as not a patient would say, "Ah, there's a trial at the General. I'll go there." We'd get more and more calls directly from patients.

Hughes: Had you realized that attracting patients might be one of the effects of running a trial?

Volberding: I hadn't really thought about it. I mean, it made sense, and we knew pretty much right away that it was happening, as our patient numbers increased rapidly during that time.

Hughes: Was there any feeling of abandonment by the group that was left at the KS Clinic when you opened the AIDS Clinic at the General?

Volberding: I don't know, frankly, what the feeling was of the people that were left there. I haven't really talked with Helen about it. I would imagine that they felt a little floating in the breeze, because I think Marcus' attentions were not there any more, and mine certainly were more here.

Hughes: Was there ever any talk of Dr. Conant coming over to the General to practice?

Volberding: Marcus and I have talked about it in passing over the years, mostly as health care economies have changed, making private

practice financially difficult. We have discussed perhaps combining resources, but not in any serious way.

Hughes: And not at that initial stage when AIDS activities were being formalized at the General?

Volberding: No.

Clinical Research

Hughes: So the KS Clinic remained an evaluation and research unit?

Volberding: Right.

Hughes: It had a fair amount of connection with various basic and clinical science laboratories there.

Volberding: Right. We collected specimens--

Hughes: Which couldn't happen here at the General, right? Because there weren't basic science labs in the same sense.

Volberding: Not in the same sense then. The KS Clinic was a convenient place to collect clinical data and informal epidemiological data on the patients. The research wasn't really designed by epidemiologists, although they were certainly present for most of it, and it was a great place to collect specimens--blood specimens, tissue specimens--from patients.

Patient Confidentiality

Hughes: Well, since I talked with you last, I have talked with Helen.[1] One of the things that concerned her early on was the issue of patient confidentiality. You were collecting very intimate information which apparently went into the patients' charts, although there was some sort of code, as she told me. Was confidentiality a concern?

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[1] See the oral history with Helen Schietinger in the AIDS nurses series.

Volberding: Not in particular. I don't recall it being a concern. Naively perhaps in retrospect, we treated the medical record as a confidential document in its own right, and the sense of a real mission and purpose was so strong that I'm not sure we gave the same attention to confidentiality that we may have been forced to by law later on. I'm not sure which system is better, frankly.

I think in fact we have made many ludicrous mistakes in the name of confidentiality. I think HIV disease has been characterized by an excessive focus on confidentiality. I think it's added to the stigma of the disease. The idea that we're not meant to write down in a medical record that a person has HIV infection, but we can say he's a gay man with *Pneumocystis* pneumonia--seriously--is still the way the state law is interpreted by the university. You're not meant to write on an x-ray requisition that a patient has HIV infection, which is obviously a necessary bit of data for the radiologist to have when the films are being interpreted.

I think those are all political carry-overs from the early days of the epidemic when we allowed the epidemic to be stigmatized. We encouraged it by trying to hide some things away.

Hughes: Is there a tradition in the field of sexually transmitted diseases [STDs] of being careful about the information being collected?

Volberding: I don't think that there have been the same kind of rules as we have with HIV. I think the medical record has been viewed in STD work as, you talk about syphilis and gonorrhea, and you order tests, and you put the test results in the chart.

Hughes: And it's all right there in one chart.

Volberding: It's there, yes. You get a syphilis serology test and it's there with the rest of the medical information. Gonorrhea cultures are charted, and no one tries to hide them. So I think unique situations were constructed for HIV for political reasons. And it's not such a focus now. We've survived it, and I don't think it really hurt that much.

There was fear at first about creating special units for AIDS patients because of confidentiality. People objected on theoretical grounds to AIDS wards, because they said, "Well, then everyone will know that you have AIDS." Well, I'm sorry, maybe that is true, but I'm not aware of any problems having to do with confidentiality because of having an AIDS ward at

San Francisco General Hospital. People do know what they have, and they would rather get medical care for it than try to hide it.

Hughes: Was concern about confidentiality a stumbling block when you were trying to sell the idea of creating a ward?

Volberding: It was certainly an issue that was talked about. In the first years of 5B, when we put up the patient's name on the board out in the middle of the nursing station--the room number and the primary care nurse and the intern and resident and all that--only on the AIDS ward we'd use the first name and last initial. So it would be "Bobbi C." instead of "Campbell, B." And on every other ward in the hospital, it's the last name and first initial. Here it was the first name and last initial. And it was done in response to the concern about confidentiality.

But I think it was exactly the wrong thing to do. That says, Gee, there must be something to be embarrassed about. And now on the AIDS unit here, they put up the last name, and it's fine.

More on the AIDS Clinic and Ward at San Francisco General Hospital

Founding the Clinic and Ward

Hughes: Well, tell me more about what you had to go through to establish the AIDS Clinic and ward.

Volberding: The clinic was, in a sense, the most interesting, although the ward has maybe gotten more attention. We were seeing patients with AIDS on an outpatient basis on Ward 5B through '81 and '82, and the rooms were used by the interns and residents for their sleeping quarters at night.

Hughes: Yes, you told me that story.

Volberding: Right. It was a pregnant resident who said at the end of '82, "Gee, do you think it's safe for me to be sleeping in these beds?" I actually saw her just a couple months ago at an infectious disease conference at Snowmass, Colorado. We had dinner, and she remembered it exactly as I had. It was a

legitimate question. No one had raised it before, and the hospital immediately found space for the clinic. I'm not sure to what degree I had really beaten on doors before then, but they immediately found a space.

Hughes: Who's "they"?

Volberding: Geoff Lang, the hospital administrator, was the person I went to, and it was really his decision.

Hughes: Now, am I to read into this that perhaps the primary concern was not so much to take better care of AIDS patients but to protect the staff?

Volberding: [laughs] Yes, I think that's definitely true.

Hughes: If you had said, "We've got a bunch of patients with a strange disease. We need more service, more space," what would have happened?

Volberding: I don't think that would have made it, especially in '82. At some point, that argument probably would have worked, maybe even by the time that the AIDS ward opened up [July 1983]. And they are linked, because the AIDS ward was created in the space that I was in a sense vacating by moving the clinic to 86. But I think the initial reason we got space for the clinic so quickly was because of liability concerns.

AIDS Programs and Medical Subspecialty Orientation

Hughes: You of course were focused on Kaposi's, because your training is oncology. Why was there never a PCP clinic, or a clinic that was specialized in--?

Volberding: Infectious disease?

Hughes: --infectious disease. Is it an historically shaped thing?

Volberding: That's interesting. It's an historically shaped thing. An oncology focus happened here, and it happened in a couple of other places, but it didn't happen in most places. AIDS/oncology units were usually academic centers that were involved in HIV from the start and tended to have one clinical oncologist who was most interested and most committed and fought hardest for AIDS services, and that's where the services tended to be focused.

So at UCLA, Ron Mitsuyasu and Jerry Groopman, who were both in heme/onc [hematology/oncology], put the AIDS program together. Ron Mitsuyasu, who's an oncologist, still runs the program there. Margaret Fischl at Miami is not a fully trained oncologist, but was really doing general medicine and oncology, and she put the program together at the University of Miami. Jerry Groopman is now at New England Deaconess, and there it also has remained a heme/onc focus.

And that's probably about it, in terms of real oncology-focused [AIDS] programs. Mostly it was ID or general medicine. And in some places--the NIH, for example--the focus has been more on pulmonary medicine and critical care medicine. Henry Masur, who is really more or less the director of HIV services at the [NIH] clinical center, is a pulmonary and critical care person. So it depends on the leader's academic background.

Early in the epidemic, there wasn't exactly a lot of competition; not very many people were very interested. When I started the clinic here, John Mills, who was the head of ID, was on sabbatical. Connie Wofsy was acting head of infectious disease. Connie was seeing the patients with PCP; I was seeing the patients with KS. But I had my own space and she didn't. Part of the deal in bringing me here as head of oncology was that I'd have my own clinic. So it was much more possible for me to say to Connie, "Hey, drop on by and see this patient, because I think he's got a weird infection," than it was for her to have me come in to ID clinic as an oncologist.

Hughes: Was it ever an idea of hers to have an AIDS clinic that was focused on ID?

Volberding: Connie is not particularly--

Hughes: Territorial?

Volberding: --territorial, I think it's fair to say. She could have been, and that could have happened.

Hughes: I wonder too if it had something to do with the fact that she was both a fellow and acting head of ID?

Volberding: Yes, she was in transition herself.

Hughes: Perhaps that's not the strongest position in which to argue for a new program.

Volberding: Yes, right.

Hughes: Do you think that the oncology orientation made a difference in how the AIDS program developed?

Volberding: I think it helped us immensely and still does, and I think there is tacit agreement with that on the part of many ID people around the country. I think the issue here that really got us jump-started was the fact that we were building the AIDS program on an oncology model. The oncology model is primary care of patients with complicated terminal illnesses that require hospitalization and specialized care at the nursing and psychosocial level as well as the medical. This is the model. That's how oncology is done. It's been done that way for a few decades.

Hughes: So a multi-specialty approach.

Volberding: Multi-specialty, certainly including psychosocial, certainly expecting to be involved in primary care, is the way oncologists are trained. That's the way HIV medicine is.

ID people can certainly do that, but they usually required a period of retraining, because ID when the epidemic hit had evolved to the point where it was really almost exclusively a hospital-based consultant specialty. Most ID people didn't even have offices. They saw patients who were hospitalized by other physicians; they made recommendations as to the choice of antibiotics. And that was the real paradigm for academic infectious disease. So even in a lot of places where infectious disease has become very important in HIV management, it's really been almost more of a graft on general medicine than on the typical infectious disease program.

The Adult Immunodeficiencies Clinic at Moffitt is actually a good example. Harry Hollander, its director, came much more from a general medicine background, and only got his ID [medical] boards by experience as he was already doing the HIV clinic. And it's still not so clear that the AIDS clinic at Moffitt is part of infectious disease. It's very separate from infectious disease.

Hughes: Internal medicine doesn't have the multidisciplinary emphasis that oncology has?

Volberding: Well, general internal medicine is another pathway by which some places have come to doing AIDS care. The problem in general medicine from that point of view is that the patients with AIDS do require a lot of very specialized care, and most

generalists don't do oncology, for example; they don't do chemotherapy. So it certainly can be done and has been done in some places. Well, some examples. Harvey Makadon runs the program at Beth Israel in Boston. Harvey is a general internist and runs the HIV program; does a spectacular job. So I think that's another viable model.

A Unique Form of Multidisciplinarity

Volberding: It's my own conceit as much as anything else, but this is still a pretty unique place. We are really truly multidisciplinary in one division. In a lot of other places, there is a network that's been formed of oncology, infectious disease, pulmonary medicine--of people who see themselves as still primarily in their own divisions, but who come together and take care of AIDS patients.

Here, we have in one division oncology, infectious disease, pulmonary medicine, psychiatry, general medicine, family medicine--people who have that as their background and training, but who work full time in the AIDS program.

Hughes: Is that unique?

Volberding: I think it's unique. I haven't heard of any other place that's done that. If I had to pick one thing that really sets us apart and has been part of our success, it's the multidisciplinary nature of our program. The multispeciality medical care is really fully integrated.

Hughes: Why could that happen here, given the usual pattern of people being very protective of their turf?

Volberding: Well, I think the hospital was supportive; Merle Sande was supportive and didn't stand in our way. We never asked for much except space. We always were financially self-sufficient. As we had money, we were able to grow as needed. I think almost immediately we made the decision, without even really making a decision, to try to provide as many of our patients' needs in one place as possible.

And part of it perhaps was because we were over on Ward 86, from the early days.

Hughes: You mean isolated?

Volberding: Isolated from the rest of the hospital. So even if someone was inclined to put roadblocks in our way, they'd have to come over here to do it.

We were able to get money easily in those days, and it was easier for us to hire another ID person than to send the patients to the infectious disease clinic. It resulted in a really very amazing system where we can deliver comprehensive and cost-effective care. We've saved money doing it, because we don't have to refer patients all around the hospital.

Hughes: I would surmise, too, that you might have been helped by the fact that in the early days, AIDS was sometimes regarded as an oddball disease, so why would anybody want to interfere with individuals who were willing to take care of it?

Volberding: The rules don't apply. Yes, I think it's fair to say that a lot of people who became involved later on were not eager to be involved early on. The ethic in the community has changed a considerable degree, too. I heard many negative references to gay people early on from health care professionals who later on became very involved in AIDS work. So I think a lot of it was the stigma attached to the patient population.

A Specialized Nursing Staff

Hughes: Dr. Wofsy told me that staff was hired specifically to work in the AIDS Clinic, although I understand the usual pattern was that the nursing staff might work in several different clinics, and wasn't specialized.

Volberding: Right, another very important point. In the area of the hospital where the other clinics are, the setup is that one half day it's pulmonary clinic, next half day it's oncology, next half day it's GI clinic, and the nursing staff and the other clinic staff do all of them. So today it's onc[ology], tomorrow it's something else, and that's really the way it is most places.

It's horrible, because it was clear, especially early on, that not everybody wanted to work with these [AIDS] patients. We never had trouble getting staff that wanted to work, but it was clear that they were self-selecting heavily. We heard horror stories of other places where staff would refuse to

take care of the patients. So I think that's an important difference.

The Sixties Generation

Volberding: The other issue--and it wasn't just here, because I think there were innovative things done other places--is it's really true almost without exception, if you look at who is running AIDS programs around the country, they are people of almost exactly my vintage, people who had just gotten to the point of having some authority within medical centers but not so old that they had established their careers and already committed their time. So you had to be right there at the right moment and have time to say, "Well, gee, I think I'll get involved in this epidemic. No one else is. Let's go for it." Those of us who are running these programs are largely products of the sixties.

We were very young, and I think prepared to think outside of the usual channels, prepared to do things that weren't completely kosher, like multidisciplinary programs, because who cares, why not? I don't think it was just here.

Hughes: And the exceptions in terms of age in the San Francisco General/UCSF group, namely Drs. Conant and Ziegler, had other reasons for being involved.

Volberding: Obviously, yes.

Hughes: That's an interesting point, that your age group brought along a certain zeitgeist.

Volberding: Oh, yes--willingness to take on the establishment, right.

Basic and Clinical Research

Hughes: Was basic and clinical research on AIDS--not drug trials, because I know they were rooted here--a problem because you were geographically distanced from the Parnassus campus?

Volberding: I think it still is a problem, although what's happened is that basic research has fallen down considerably at Moffitt.

Some important people like Dan Littman have left; Dan Stites no longer really does AIDS investigations; Art Ammann left.

Hughes: Weren't these people doing clinical research?

Volberding: Not completely. So a number of the people who were very involved early on are either no longer there or not doing AIDS research. Jay Levy is almost the only person there from the early days who's really doing much basic research.

Meanwhile, basic investigations have increased here. Mike McGrath has done a tremendous job with the lymphomas. People in the [J. David] Gladstone [Institute of Virology and Immunology] have done important work.

Hughes: What was the impact on AIDS medicine when the Gladstone opened?[1]

Volberding: Well, not as much as we would have preferred, frankly. It was really meant to be a site for translational research that would be really synergistic with the clinical program. It accomplished more in the very basic research area, but hasn't really caught on with much clinical medicine, except for Mark Fineberg, who has been very integrated with clinical work. Mike McCune is another person joining the Gladstone who is really very interested in clinical work. So I think there still is a lot of potential there, but it hasn't been maximally explosive.

Hughes: The problem is that basic scientists at the Gladstone weren't particularly interested in making clinical correlations?

Volberding: I think it's fair to say that the investigators who came there were more strictly basic and not particularly interested in clinical specimens or clinical problems.

But the basic investigators at Moffitt in the early days were very interested in clinical pursuits, and it was a problem to maintain those collaborations with being out here--not extraordinarily a problem, because it's not that hard to get specimens back and forth. But there just isn't the same dialogue across town that there would be if we were all at the same location.

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[1] When the Gladstone Institute was formally dedicated in April 1993, five of its principal investigators had already begun their research. (David Perlman. New AIDS research center starts its work attacking virus. *San Francisco Chronicle*, March 2, 1993, p. A11.)

Hughes: The KS Study Group seems to have been the forum where different interests got together on a weekly basis. There's never been anything like that here at the General, has there?

Volberding: Right. Or there since. No, it happened at a time when there was tremendous excitement. The level of excitement, I have to say, has obviously faded somewhat. It's not a new disease any more. In the early days, everything we learned was fresh. Everything was startling. It doesn't take much to keep a group together as long as there's that feeling of excitement.

But I think as things got more predictable and people got their own grants and decided which aspect of this disease they wanted to focus on, interest in participating in a broadly based group decreased. It's arguable, but one point of view is that if you're a basic virologist, you'll be better off talking to other virologists about the latest findings than you will spending a couple of hours at a meeting, most of which is somebody talking about the number of KS cases or some other clinical aspect. And I think that declining interest in the study group inevitably happened over time.

Hughes: I wonder if there is a common personality trait that runs through this. Do you think willingness to break out of the mold and tackle something risky is a trait of early AIDS workers?

Volberding: I guess that's what I was trying to say before: willingness to take something on almost because it's unpopular; willingness to take something on because it's strange and who knows anything about it, instead of following a predictable career course. What I should have done is take care of colon cancer and breast cancer--

Hughes: Well, things certainly worked out for you! [laughing]

Volberding: I know, I know.

Hughes: But I know at that time colon and breast cancer--

Volberding: Right, that would have been the safe way to go about a career. Frankly, people that I trained with in oncology, we ended up in the same city in the same university, and some of them still can't figure out why anyone would want to work with AIDS.

Community Physicians

Patient Referrals

Hughes: You talked a little about patient referrals, but did community physicians fear that by sending a patient over here, they might lose control of their patient, or just simply not know enough about AIDS to keep up?

Volberding: Several reactions. I think it's fair to say that community physicians are not a monolith. There's obviously as wide a variety as one can imagine. So I'm not sure that there's one feeling out there.

In the very, very early days of the epidemic, hardly any community-based physicians were really thinking of AIDS as a focus for their time. No one had a lot of patients with AIDS. At first, I think there was a realization that the only place that had anything to offer in a coordinated way was the KS Clinic at Moffitt, and then gradually my clinic here. I was the only person that had anything to offer in terms of experimental treatments at a time when no one knew what else could be done.

Remember, in the earliest days, we didn't even know about Septra for the treatment of PCP. We thought that pentamidine was the only way it could be treated. That's how we could track the early cases of PCP, because pentamidine had to be obtained from the CDC by specific request.

So there weren't really very many community physicians clamoring to do AIDS work at first. Physicians would gladly refer patients here, I think without any sense of, Gee, I'm going to lose this paying patient. Instead, their motivation was, I don't know what's going on; maybe someone else does. Maybe somebody else has something to offer this person. My guess is that that was really the dominant feeling in the early days of the epidemic.

San Francisco County Community Consortium

Volberding: Now, as things stabilized and as the volume of cases increased, then maybe over the next few years, by '84 or '85, there came to be physicians who were seeing a high volume of

HIV themselves. That situation really gave rise to the Community Consortium.[1] I think there was a tension between SFGH and community physicians that led Dianne Feinstein to ask me to bring them together for a meeting. Even at that first meeting, people were willing to get together and talk about what we were all seeing.

Hughes: You are referring to the ACTG [AIDS Clinical Trial Group]?

Volberding: No, this is well before the ACTG. Dianne Feinstein, when she was mayor, asked me to bring together the community physicians. We had a meeting at the medical society on Masonic [Avenue], and shared information. At that very first meeting, it was clear that there was interest in keeping it going. Donald Abrams was elected or self-appointed or it just seemed obvious that he be the person to take that and run with it. And the County Community Consortium came from that.

Hughes: Do you remember when that first meeting was?

Volberding: Eighty-five, I think. I don't remember exactly, but Donald would know.[2]

Hughes: What was the impetus?

Volberding: Communication--the sense of sharing information and avoiding tension between university and community physicians. It was interesting: the impetus didn't come from the university; it came from the county; it came from Dianne Feinstein. It was not so much at first a matter of doing research together; it was sharing information about this disease. And that's good, because I think in the same way that our research program has been built on our clinical care, I think the consortium's research was a development of its interest in patient care.

Hughes: Had the tension between community and university physicians been brought to the mayor's attention?

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[1]See the oral history in this series with Donald Abrams for a history of the San Francisco County Community Consortium.

[2] According to his curriculum vitae, Abrams became chairman of the community consortium in 1985. The consortium first met in March 1985 after Mayor Feinstein suggested that a link be established between AIDS care providers at SFGH and those in the private practice community. (L. A. Simpson, D. I. Abrams. AIDS activism: The first decade. *San Francisco Medicine*, June 1992, pp. 22-23.)

Volberding: I can't recall. Donald might be a better person to go back to about this. I don't recall any major problems. This was around the time that there had been some cases of dumping patients from outside communities onto this one.

Hughes: Yes, that Florida case--

Volberding: Well, there was one from San Jose or Santa Clara. A patient was put in a car with an oxygen tank and sent here, and the oxygen tank was empty when he got here.

But actually, I don't recall the meeting between university and community physicians being in response to a perceived crisis so much as an appropriate thing to do in the middle of a growing epidemic.

Providing Primary AIDS Care

Hughes: In the early days, what happened to a patient when he was discharged?

Volberding: From this hospital?

Hughes: Well, start with the KS Clinic.

Volberding: Well, the KS Clinic never really took primary care of patients.

Hughes: So what happened to patients?

Volberding: They were already under the care of their other docs.

Hughes: Okay, so they would come to the clinic for one evaluation?

Volberding: One or two maybe.

Hughes: And that was it?

Volberding: Right. It wasn't a primary care clinic. The idea of doing primary care is what then led us to shift the patients over here for that part of it. They'd go there for evaluation and come here for their ongoing care. So in that sense, we competed with the physicians that the patients may have had already in the community.

Communication between University and Community Physicians

Hughes: Stepping back to that KS Clinic period, was there a system of communicating with a community physician about what indeed had been found out in the clinic?

Volberding: Yes, letters would go back. And we were pretty good about that, as I remember, because Conant's background was private practice, where that sort of courtesy was important.[1]

Hughes: It was rather new to you, was it not?

Volberding: Well, we paid lip service to it in fellowship here. We knew that we were supposed to do it, so it wasn't totally new.

Hughes: You probably didn't have the call to do it during your fellowship, because most of your referrals were probably in-house, weren't they?

Volberding: Right, exactly.

Hughes: What about educating physicians and other health care workers in those early days about patient care? You said previously that community physicians were pleased to refer patients to the university because they didn't know how to care for them.

Volberding: I'm not sure that we did anything in a very organized fashion at that point. There was a reasonably small circle of physicians in the community in the very early days who were seeing these patients. Again, from the KS Clinic's point of view, they tended to be dermatologists. And there was quite a bit of back-and-forth discussion among those physicians and the physicians at the university.

A number of those physicians would even come on a pretty regular basis to the KS Study Group. Jim Groundwater, Jim Campbell, Bob Bolan were some of the early docs involved in care of these patients. So I don't think there was anything very formal, but there was certainly an active informal dialogue going on. The consortium really helped that, but that was years later.

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[1] Helen Schietinger recalls problems in feedback to community physicians in the early days of the KS Clinic. See Schietinger's oral history in the AIDS nurses series.

Hughes: BAPHR [Bay Area Physicians for Human Rights] played a political role in the epidemic. Did they also play an educational role?

Volberding: I don't know precisely, but my sense is they saw themselves mostly as a political organization. A lot of BAPHR members, especially early on, were psychiatrists. Membership was much more slanted towards psychiatry, I think, than towards primary care docs.

Hughes: Why would that be?

Volberding: Oh, historically. I think there's a fairly large gay psychiatry community here which saw itself as more identified and interested in psychosocial/political problems. But BAPHR became quite involved in the epidemic, Bob Bolan especially.

Almost from the start, we gave lectures and community fora. Marcus organized a national conference that we had at Toland Hall [UCSF] in 1982, and brought a couple hundred people together for one of the first national conferences on AIDS.

Hughes: What followed?

Volberding: Well, we wrote our first NIH grant in '82; got it in '83. There was very little activity regarding AIDS between '81 and '83 at the level of the NCI. Obviously, [Robert] Gallo was starting to get interested during that time.

More on the AIDS Clinic

Accepting Clinic Patients

Hughes: Were there ever and are there now referral guidelines at the AIDS Clinic?

Volberding: With respect to?

Hughes: Who could come, and who could be referred.

Volberding: We would take anyone who came. [laughter] We were very interested in the disease, so I think from day one, we were very accommodating. I think later on, we became stricter about proving a person had HIV infection. We had some people

try to access our clinic who didn't even have HIV, which is a problem, because people with HIV do have access to additional social services and the like. So we now try to limit it to people who are actually infected.

Hughes: But in the early days, before the antibody test, it was difficult to tell.

Volberding: We didn't know. I'm not sure what our referral guidelines would have been, apart from somebody having some disease characteristic of AIDS.

Hughes: Were there any referral guidelines?

Volberding: No.

Hughes: Is it common for clinics to have an understanding but not a written protocol for patient referrals?

Volberding: I think so.

Hughes: So the informal referral system wasn't aberrant in any way.

Volberding: Right.

Developing Multiple Clinics

Hughes: I have the idea that what was called the AIDS Clinic was actually a series of clinics. There was an oncology clinic, a PCP clinic--I don't know what else.

Volberding: It was very organic; could be said still to be. We felt free to redefine ourselves at the drop of a hat. The initial clinic met, as I can best recall, one or maybe two half days per week, and was my oncology clinic. The patients with KS were seen in the regular oncology clinic with the rest of the patients. I know that's true, because I remember it even before we moved to 5B, when we were still seeing patients in the general medicine area when I very, very first came here in '81. So at first, it was really an oncology clinic with some patients with Kaposi's sarcoma.

As the number of patients with Kaposi's increased, the number of times a patient would come with an unusual infection increased, and so Connie more and more became a regular part of the clinic. And by the time we moved up to [Ward] 86 [the

AIDS Clinic], it was Connie and me running the place. We were the only docs.

Hughes: But the clinic was in one place? There was an entity that was the AIDS Clinic?

Volberding: Ward 86 is the clinic, and we started on January 1, 1983, and we rather quickly added some more staff. Tim Mess was a physician; Donald Abrams came over here in the middle of '83, and as we had more physicians, we then tended to establish focus clinics. Friday morning was an oncology clinic, mostly a Kaposi's sarcoma clinic, and that's when Donald and I and later on Lawrence Kaplan would see patients together. Mondays and Thursdays were more nonmalignancies, more opportunistic infections, especially PCP, just because that was so much the most common infection.

Hughes: Did you go to the opportunistic infections clinics?

Volberding: Oh, yes.

Hughes: You always went?

Volberding: Well, yes. But the focus was, this is ID day, this is oncology day, within the context of an AIDS clinic.

A Holistic, Multidisciplinary Perspective

Hughes: It is significant that, from the very start here, you couldn't be just an oncologist. Did you see that in order to treat AIDS patients, you had to have some knowledge of all the diseases associated with AIDS; you couldn't stick with just Kaposi's sarcoma?

Volberding: Well, it's certainly my sense, and I think every other physician's here, that if you're going to do a halfway decent job with this syndrome, you have to know the whole disease. Our oncologists know lots about cryptococcal meningitis, and they manage patients with it, and always have. Our ID people participate actively in managing patients with KS.

Now, I think right from the start, we would agree in most cases that if a patient had a very complex infectious disease, that it was best to talk to one of our infectious disease-trained colleagues. And mostly the ID-trained people wouldn't initiate chemotherapy on their own. If a patient needed a

bronchoscopy, we would need a pulmonary doc to do that. If a patient had cryptococcal meningitis, I would essentially always get an infectious disease colleague in the AIDS Clinic involved in that case. So it's not as though we've totally abandoned our subspecialties.

Hughes: No, I didn't really mean that.

Volberding: No, I know you didn't. I'm just saying that the structure of the place is that you retain what you were trained in, but you also know a lot about the rest of the disease. So you are a generalist in the treatment of AIDS.

Hughes: In other clinics you might pull in a colleague for a consult, but it would be a finite thing.

Volberding: Right.

Hughes: And wouldn't that specialist be less concerned with the full spectrum of the disease? He or she would be brought in to focus on that aspect for which she or he had particular training?

Volberding: Oh, yes. I think you sense the difference in our clinic, and I shouldn't say anything more, because I think you've got it. I'm still an oncologist, but I'm an AIDS doc first.

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Hughes: When did you realize you were becoming an "AIDS doc"?

Volberding: Oh, I think by the time we moved upstairs to Ward 86, by early '83, it was becoming clearer and clearer. The whole thing was fascinating. It was a small, graspable field; you could understand it, and it was interesting being involved in PCP. As I mentioned, I wrote, along with colleagues at UCLA, Jerry Groopman and Ronald Mitsuyasu, I think the first report of unusual toxicity in treating PCP. It was a letter to the *New England Journal* in '83.[1] None of us were ID people, but we were seeing these patients, thinking about it.

Hughes: Did that cause any tensions?

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[1] R. Mitsuyasu, J. Groopman, P. Volberding. Cutaneous reaction to trimethoprim-sulfamethoxazole in patients with AIDS and Kaposi's sarcoma. *New England Journal of Medicine* 1983, 308:1535-1536.

Volberding: Only in the sense that if you ask Connie what the first report of unusual toxicity is, she'll say the *Annals* article that she wrote a few months later.[1] [laughter] But no, not really.

Hughes: I was thinking more widely than that: why do these upstarts at San Francisco General feel that they can pronounce on aspects of medicine for which they aren't trained?

Volberding: I guess we got off to such a rapid start with this disease that as it became a field, we were the originators of it. So we've been given pretty much carte blanche to say whatever we want, not that everyone agrees with us.

We've really argued strongly from the start, Connie and I especially, that it is a multidisciplinary disease, and what we've modeled here is an honest, integrated approach to it that allows us to cross over those disciplinary barriers.

Hughes: Do you identify yourself as an AIDS physician?

Volberding: Yes.

Hughes: So you don't introduce yourself as Paul Volberding, oncologist?

Volberding: No. I would be hard pressed in most polite circles to consider myself an oncologist, if there are other oncologists in the room. They'll say, "Who are you? When have you last published in an oncology journal? Or, when is the last time you went to the national oncology meetings?" I would hang my head in shame.

At the same time, in giving lectures I often talk about being an oncologist, because I think the oncology community has shirked its responsibility to HIV. It could have done a lot more than it's done. But on a personal level, having been trained in oncology continues to inform my thinking about HIV. I see it as oncology care. I see the care structures as the kind that have proven to be useful in oncology.

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[1] F. M. Gordin, G. L. Simon, C. B. Wofsy, et al. Adverse reactions to trimethoprim sulfamethoxazole in patients with the acquired immunodeficiency syndrome. *Annals of Internal Medicine* 1984, 100:495-499.

Oncology's Neglect of AIDS

Hughes: Why do you see the oncologists as shirking their responsibilities to the epidemic?

Volberding: Well, an oncologist is somebody who does primary care of patients with fatal diseases. What is AIDS but a complex fatal disease? Patients with AIDS in many places have had a hard time finding appropriate places for primary care. At the same time, there are oncologists in those same communities who are not seeing AIDS patients because they don't have cancer. It just feels to me that the oncology establishment, led by the NCI, early on decided that this was a dirty disease that it didn't want anything to do with. And as soon as a virus could be found, they were happier than anything to put a bow on it and hand it to the NIAID. Well, this is an infectious disease. And I think the message was really clear to the practicing oncologist: This isn't your turf; you can safely avoid it; go on about your comfortable lives treating patients you know something about.

The problem is that oncologists could do an excellent job with this disease, even for the patients without oncologic problems. It just feels like oncology care. Yet it just hasn't happened. Still I hear to this day complaints from people who say, "Well, I can get surgery for my patients, but I can't really get the oncologists interested." I heard it last week. So it's still a problem. I think it was the national leadership of the field that gave permission to avoid this disease.

Clinic Volunteers

Hughes: What was the role of the community volunteer physician in the KS Clinic? There was one chap, whose name I've forgotten, who apparently came up on a regular basis from the peninsula.

Volberding: I can't remember his name either. Yes, older guy. For the history I better not remember his name, now that I've identified him as an older person! [laughter]

There weren't really the same roles here because it was a primary care clinic. Not that we don't have volunteer physicians now. Molly Cooke and Mark Smith come over here a

half day a week, and there are a few people who work part-time.

Hughes: But they're not coming from the community and volunteering in quite the same way as physicians did at the KS Clinic.

Volberding: Right, not in the same way.

Hughes: Nonphysician volunteers have been present in the AIDS Clinic from the beginning?

Volberding: Oh, yes.

Hughes: Was anything done to coordinate what the physicians were doing and what the volunteers were doing?

Volberding: We haven't had that many volunteers, frankly. The head nurse, Gayling Gee, then J. B. [Joseph Molaghan] later on, were in charge of the volunteer part of the program. We've had a number of volunteers that do things like run specimens back and forth to the lab. We've had a number of medical students that volunteer to work in the summers or even during the year. So they are integrated in and really supervised by wherever they most wind up. But there's not really an overall volunteer coordinator.

Social Workers

Hughes: Was there anything unique about the social workers and how they were integrated?

Volberding: Only that they weren't really integrated as well. Social work is obviously a central part of the management of this disease, but, historically, it's still not a resolved issue; we haven't really controlled the social services in our clinic. Social workers have been provided either by Shanti Project, or by the social work office here, or by AIDS Health Project. Well-meaning people send well-meaning people to work with us, but it's not ever been something that we actually hire and supervise and coordinate.

There have been times when it hasn't worked out very well at all, when people come with conflicting ideas and personalities. Not being able to supervise has been a real limitation, because there are many times when we would have said, "Well, if you guys can't get along, leave." But you

can't do that if they're being provided by somebody else. Lately, it's been fine; I don't want to imply that we're unhappy with the people that we have working here. But it's not been very well coordinated.

Patient Conferences

Hughes: Dr. Wofsy told me about a patient conference that you and she organized and alternately led.[1]

Volberding: Right.

Hughes: What was the orientation?

Volberding: Hard to say. I don't remember very many of the details of those meetings. But sharing information, mostly medical, at least when I did it--the latest information about the disease. This was probably before HIV was found. We met up in the waiting room on [Ward] 86, as I remember, at the end of the afternoon.

Hughes: Could anybody come?

Volberding: It was mostly for patients in our clinic. We didn't check.

Hughes: People couldn't wander in from the community?

Volberding: They could, but I don't think it ever was much of a community forum. A lot of times patients would bring in their friends or lovers, who also would prove to be patients.

Hughes: I attended a similar meeting that Dr. Conant, last I heard, was still running at UCSF.

Volberding: Yes, I think he occasionally does. More community-directed, I think.

Hughes: Yes, and anybody could come. It was medically oriented. In the session that I went to, he talked about the latest drugs

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[1] See the oral history in this series with Dr. Wofsy.

and what their problems were.[1] Was that the gist of what you presented?

Volberding: Yes, I think so.

Hughes: How long did those sessions last?

Volberding: Not very long. Maybe a year or so. I can't remember if we tried to do it monthly. But it was an important thing. What we found was that there are times when different things are required, when our staff is feeling burned out and we need to do group retreats and therapies for us. Other times, it doesn't seem as important. Over the years we've done big community fora, in Carr Auditorium [at SFGH], for some of our big clinical trials when the results come out. We've had meetings where people are invited to come and talk about the latest findings.

Clinic and Ward Interactions

Hughes: What about the interaction between the clinic and the ward?

Volberding: It's not a fully defined one, although it's gotten to be routine. When the ward opened up [July 1983], we obviously had a major role in how it was structured. Connie and I and Donald saw patients there all the time.

As we got busier seeing outpatients, it got harder and harder for us to be that involved in the ward. And there was a time--I'm going to guess maybe '86 or so--when the housestaff let it be known to us that they were really not very happy with the situation, that we were seen as dumping patients on them, admitting patients, and we were never around, and they couldn't find us. So they felt that they were taking care of patients with no input from us, sending them out of the hospital, back to us. I don't think, from our slightly defensive point of view, it was ever really that bad.

Hughes: But there was an element of truth to it.

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[1] *The New York Times* described Conant's monthly meetings, which are held in a UCSF lecture hall, as sessions on the status of AIDS treatment. He first gave them for his own patients but later opened them to everyone. (Jeffrey Schmalz. Riding AIDS roller coaster: Hope, horror, hope. *New York Times*, June 6, 1992.)

Volberding: There was an element of truth, and there was certainly a lot of, if not hostility, at least concern.

The inpatient ward is a hospital operation run by the nurses. The AIDS Clinic is mostly an outpatient, university-run operation, so there are administrative separations between us. But we thought, Gee, what are we going to do to decrease this tension? Because we were demanding a lot of the housestaff, especially at that point in the epidemic [1986 or 1987]. As many as a third of their patients had AIDS, sometimes more.

So I had the money and hired Mike Clement, a doc who had just finished his residency at University of Oregon, and a wonderful guy just out of residency, so really committed to housestaff. He knew a fair amount about AIDS; had come here and done a rotation during his residency, and we liked him. So we put him in charge of hanging out on the ward and doing informal teaching.

So we then provided, and we've done it ever since, at least one physician to be on 5A. The role is now pretty well defined, again never in writing. The inpatient doctor is available in the morning when the housestaff teams come on to the ward and see their patients, so there's daily teaching. Also, if issues arise on the inpatient side, then that doc is responsible for making sure the clinic knows about it. First it was Mike Clement, then it was John Stansell, and now it's Laura Worth. They also see patients in the clinic, so they're not just on the inpatient side.

It's been great, because we've got physicians doing that who are excellent teachers. They usually do it for a couple of years after residency or, in John's case, after his fellowship. What the housestaff wants is teaching. They want to learn. The amount of teaching they get on 5A is amazing, and I think it makes up for the work that they have to put out. For the most part, it's really eliminated any tension.

One title that we tossed around is medical director of 5A, but the nursing staff that runs the ward say, "Uh-uh. There's no medical director; this a nursing unit."

Hughes: They're very proud of that.

Volberding: Yes, and it's good.

Funding

Hughes: I'm sure that the issue of funding is very complicated. You mentioned previously that the mayor appropriated $70,000 to get the ward off the ground.

Volberding: Right.

Hughes: Can say something about the issue of sustained funding?

Volberding: Well, it's a broad question. We're a big program. Our annual budget is somewhere well in excess of $6 or $7 million a year. We've been here long enough to know that funding comes and funding goes; nothing is promised forever. To avoid unpleasant surprises, we've always tried to maintain as broad a base of funding as possible. No secrets. So we get city money; we get state money; we get federal money; we get drug company money; we once in a while even have a benefactor who gives us private money, which is pretty rare.

Our city money comes in the form of a contract from the city to the university. We use that for basic clinic operations, the secretaries, the nursing staff, the health care providers who are seeing patients.

Hughes: That's the continuation of the initial Feinstein appropriation in 1983?

Volberding: Exactly.

Hughes: The city appropriation has continued year after year?

Volberding: That's continued, absolutely.

Hughes: Almost as a given, or has that taken some lobbying?

Volberding: Oh, no, not as a given. I think it's always been seen as a given by the mayor's office, because they recognize the political fallout if it's threatened. But the hospital and the health department and the university often see it as a potential source of money for other purposes. We don't have to fight the mayor; we never have had to fight the mayor. We've often had to fight the rest of the people. So we've been able to keep it. But sometimes, we have to threaten to bring in the politicians to maintain our support in the hospital.

AIDS and the Patient-Physician Relationship

Hughes: How did having patients who were about your age and with whom you could identify affect your ideas about the physician-patient relationship?

Volberding: It's a sad commentary that they're no longer my same age. [laughs] It's not because they've gotten any different.

Well, that's obviously a big area, because on the one hand, as a physician taking care of dying patients, you want to be sensitive to who they are and what their life is, because you want to always keep their individuality in mind. On the other hand, there is a tendency when you're working with a large number of very sick patients to let them all blend, because it's a defense mechanism. It keeps yourself somewhat insulated from reality.

It's easier for me, and I think probably for most docs, to convince myself that the person in that bed is not me if it's a very old person, a woman as opposed to a man, somebody of a different ethnic or racial background than me. The more that person is different, the easier it is for me to deal with his death, or with his horrible disease, or with his pain, or with all the other stuff that is going on.

With this disease, I think there is a tendency to say, "Well, but they're gay and you're straight," and that's going to be how you defend yourself. But what I think happens--it certainly happened to me, and I think happens to most people in this disease--is that doesn't prove to be a very good barrier. Because it doesn't take working with more than maybe one or two gay men to realize that your sexual orientation is kind of, Who cares? Maybe some of the Republicans do, but I don't--it doesn't matter.

Once you get to the point of saying, "Gee, gay men aren't really that different than me," what you're then left with is, That really is me in that bed. And gee, they listen to the same music; they went to the same college; they eat at the same restaurants, and the similarities are much more than the dissimilarities. It is hard, I think, to distance yourself in that sense. So I think that is a real issue.

People have actually studied this, and they find that women physicians tend to be more comfortable dealing with gay men than men physicians, so there still is that thing about sexual orientation that I expect usually unconsciously can

come between the physician and the patient. But I think some of us feel that less strongly than others.

Hughes: Did you feel that in order to continue functioning optimally as a physician, you had to have some barriers, that you couldn't allow yourself to get intimately involved in the lives of your patients?

Volberding: I think the proper answer is, "Yes, of course." But certainly for me, and I would bet for every doc, it's an unconscious thing. You don't know what you're doing when you're doing it. There are things that I do. Why do I travel as much as I do? Maybe that's part of how I've kept myself away from the pure front lines. Maybe I find myself unable to deal with it, and so I gravitate to a more comfortable, less involved position. I don't go to funerals or memorial services. I tend not to think of patients as friends. It's not that I dislike my patients, but I maintain a social distance.

And I think we all do those things, and a million other things that we don't even know we're doing and can't articulate, that allow us to go on in this business. Exactly the same is true in oncology, and I think exactly the same is true in pediatric oncology, and any painful place in medicine where you see people going through pain and dying. You can't be totally open the way you would for your brother or your sister.

Hughes: You wouldn't survive.

Volberding: You wouldn't survive.

Hughes: Were you taught any of these coping mechanisms in your oncology training?

Volberding: No. Well, I shouldn't say no. During the oncology fellowship we had a couple of elective opportunities to sit and talk with somebody. I vaguely remember it, but I don't honestly think that's a weakness in oncology training. (Maybe it's the way I did it so I think it's the right way.) I think it has to be something that you yourself dig into and find out. I don't think anyone can easily help you decide that for yourself.

There's an immense self-selection process--who goes into oncology; who goes into AIDS. There are many people who know at some level that they can't deal with it and don't want to learn how to deal with it. And I think it's intuitive largely, and that some people find ways that work for them but don't work for other people.

I'm always especially amazed, frankly, at the nurse practitioners. Gary Carr has been a nurse practitioner on Ward 86 since 1983, more than ten years of front-line primary care day after day.[1] I talk to Gary about it, and he says well, there are times when it's hard, but he keeps going. I think obviously he is much more able than I, then, to stay right at that level.

Hughes: Well, I have to let you go. Thank you.

Transcribed and Final Typed by Shannon Page

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[1]See the oral history in the AIDS nurses series with Mr. Carr.

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University of California
Berkeley, California

The San Francisco AIDS Oral History Series

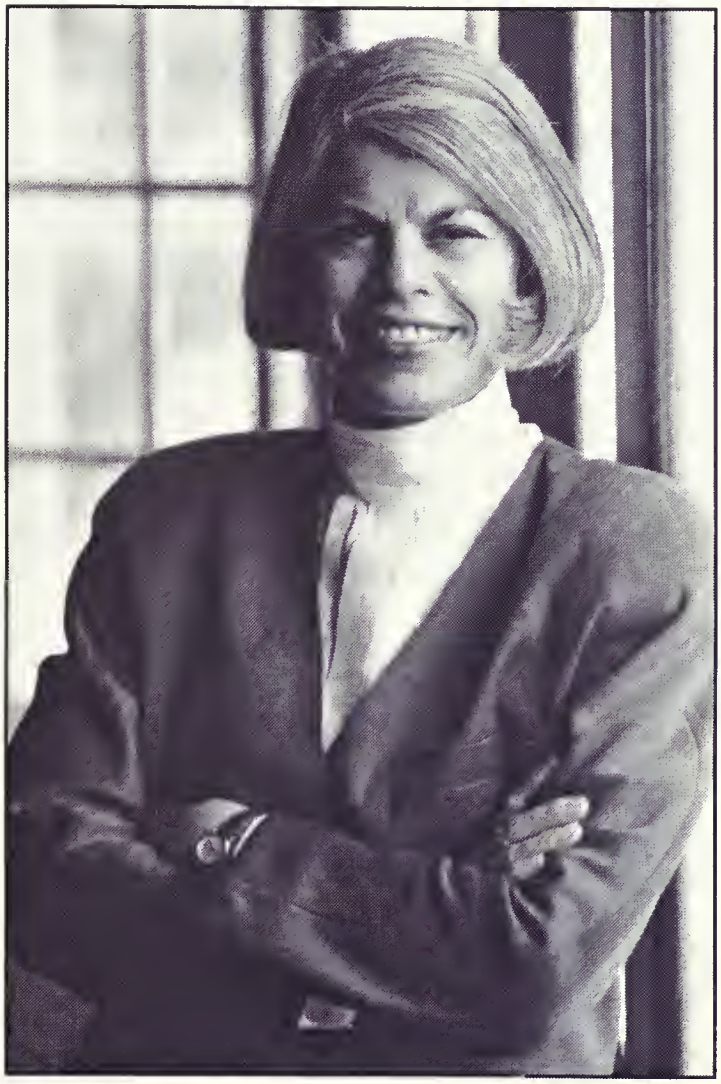
THE AIDS EPIDEMIC IN SAN FRANCISCO: THE MEDICAL RESPONSE, 1981-1984

Volume III

Constance B. Wofsy

INFECTIOUS DISEASE PHYSICIAN, AIDS EDUCATOR, AND WOMEN'S AIDS ADVOCATE

Interviews Conducted by
Sally Smith Hughes
in 1993, 1994



Constance B. Wofsy, M.D., 1989

photograph courtesy of David Powers

INTERVIEW HISTORY--by Sally Smith Hughes, Ph.D.

Constance Wofsy is an obvious choice for an oral history in a series on the early medical response to the San Francisco AIDS epidemic. As an infectious disease specialist at San Francisco General Hospital [SFGH], she in March of 1981 treated a patient only later recognized to have AIDS. The first official publication on the syndrome did not appear until three months later--the now famous Centers for Disease Control bulletin of June 5, 1981, on *Pneumocystis* pneumonia in five gay men.[1]

But there are more substantial reasons for conducting an oral history with Connie Wofsy. By 1982, she was seeing patients with *Pneumocystis* when they became hospitalized at SFGH. Realizing that after discharge these patients needed ongoing primary care, she suggested that they be seen along with Paul Volberding's Kaposi's sarcoma patients in his oncology clinic. When the clinic, because of an expanding patient load, moved out of the hospital and into Building 80 in January 1983, Wofsy went with it. In its new location the clinic came known as "the AIDS Clinic," and Wofsy, Volberding, and later Donald Abrams composed its original "AIDS physician team." Young, innovative, and near-obsessive about "solving AIDS," the team and a multidisciplinary force of nurses, social workers, psychologists, and community agencies developed a comprehensive system of AIDS care subsequently called "the San Francisco model." The oral history suggests the fascination, horror, and professional and personal camaraderie of these early years before AIDS medicine became an accepted--and monied--enterprise.

Wofsy went on to become an international expert on *Pneumocystis* and on AIDS in women. It is in the discussion of the later topic that her emotions are most evident. Accustomed in professional settings to speaking in her "male voice," as she put it, she was shaken by the intensity of the women activists she encountered in her women-and-AIDS work and by the conflict of her dual roles as physician and woman. The tension came to a head during the years she chaired the Woman's Health Committee of the AIDS Clinical Trials Group, the coordinating unit for national trials of promising AIDS drugs. As chairperson, was she physician or women's advocate? The oral history does not answer the question, perhaps ultimately unanswerable. But Wofsy's words suggest a time of professional and personal agony.

This disease from its inception has highlighted issues related to sexuality and socially marginal demographic groups. The AIDS literature, and other oral histories in this series, foreground the myriad problems which the epidemic raised for male homosexuals. This particular oral history indicates that issues concerning gender and personal and professional identity also troubled other "marginal" groups--in this case, heterosexual female physicians. Simplistically, the epidemic forced Wofsy

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[1]*Pneumocystis* pneumonia--Los Angeles. *Morbidity and Mortality Weekly Report* 1981, 30:250-252.

to ask: What am I first and foremost--a woman or a physician? Can the two identities be separated? And should they be? Read Wofsy and you will see the inner turmoil that such questions wrought.

The Oral History Process

Four interview sessions were held between November 1993 and February 1994 in Wofsy's office on Ward 84, the administrative floor of the AIDS Activities Division at SFGH. A striking presence, with steel grey hair and youthful visage, Wofsy began the interviews in her professional "male" voice, but sometimes lapsed into a musing, anecdotal style as memories of the epidemic's "early days" swept over her. "The history of AIDS," she told me in our first telephone conversation, "is more anthropology than medicine." And indeed her oral history could be seen in that light. Perhaps because we were two women of similar age and background, she spoke at times in the personal and confiding manner of "woman-to-woman." In emotional tone, the oral history is unique in this series.

The edited transcripts were mailed to Wofsy who delayed in reviewing them. After several promptings, she confessed surprise at her reluctance to go over the history of an emotionally charged episode in her life. Eventually she reviewed and returned the manuscripts, but left some editorial questions unanswered. Certain pages were then sent to her for a second review. She returned them with her approval.

The oral history provides unique insight into the early days of AIDS medicine in San Francisco. It also describes a time of unparalleled emotional toll and opportunity for professional and personal growth.

Connie Wofsy died on June 3, 1996.

Sally Smith Hughes, Ph.D.
Senior Interviewer

Regional Oral History Office
The Bancroft Library
October 1996

Regional Oral History Office
Room 486 The Bancroft Library

University of California
Berkeley, California 94720

BIOGRAPHICAL INFORMATION

(Please write clearly. Use black ink.)

Your full name Constance Bell Wofsy

Date of birth 10-6-42 Birthplace Cheltenham, PA

Father's full name Bernard Steinkuller

Occupation Sales Engineer Birthplace Washington, D.C.

Mother's full name Ruth Stevenson Blitman

Occupation Secretary Birthplace Cheltenham, PA

Your spouse David Wofsy

Occupation Professor of Medicine Birthplace New York, NY

Your children Kevin Wofsy (born 3-21-74)
Susan Wofsy (born 1-6-78)

Where did you grow up? Cheltenham, PA

Present community San Francisco, CA

Education University of California, Berkeley - B.S.
University of Southern California - M.D.

Occupation(s) Professor of Medicine - UC San Francisco
Co-Director AIDS Activities Program - SF General Hospital

Areas of expertise Infectious Diseases / HIV

Other interests or activities Literature, Art History
Needlepoint, Knitting
Travel

Organizations in which you are active University of California;
SF AIDS Foundation; California Academy of Sciences

Constance Wofsy, AIDS Researcher

Dr. Constance Wofsy, a pioneer AIDS researcher, teacher, clinician and activist whose work won international recognition, died Monday at her San Francisco home after a long battle with cancer. She was 53.

A professor of medicine at the University of California at San Francisco, Dr. Wofsy co-founded the AIDS program at San Francisco General Hospital with Dr. Paul Volberding in 1983 and continued her work there until recently.

Constance Wofsy

During the epidemic's early days, as she cared for growing numbers of primarily male patients at the hospital, Dr. Wofsy quickly recognized that women were at risk, too, and she moved rapidly to develop specialized types of treatment for the opportunistic infections that were striking them.

Known to her patients and her UCSF colleagues and to AIDS workers in many nations for her outgoing warmth, compassion and tireless work, she was praised for those qualities yesterday by Dr. Julie Gerberding of UCSF, who said:

"More than any other clinician, Connie was the leader in making this disease real, not only to those at risk, but also to the people who work with the people at risk. Her contributions to the education of health care providers had an enormous impact on the quality of care we give our patients, and to the dignity with which it is given and received."

1994. She also won awards in 1992 for her work on a documentary film for AIDS education called "HIV and the Health Care Worker," on which she collaborated with Gerberding.

Dr. Wofsy received her undergraduate degree with honors in bacteriology from the University of California at Berkeley in 1964 and her medical degree from the University of Southern California in 1971. She joined the UCSF faculty as an instructor of clinical medicine in 1975 and had been professor of clinical medicine there since 1989.

She is survived by her husband, Dr. David Wofsy, who is also a professor of medicine at UCSF; by a son, Kevin, and a daughter, Susan, and by her mother, Ruth Blitman, all of San Francisco.

— David Perlman

As a zealous advocate, Dr. Wofsy helped found the community-based organization called AWARE, for Women's AIDS Research and Education, which offered women confidential AIDS testing and counseling. She also founded and chaired the Women's Health Committee of the AIDS Clinical Trials Group sponsored by the National Institutes of Health. That national group of physicians has been a major factor in conducting clinical trials of new AIDS therapies quickly and thoroughly so they could win federal approval as soon as they proved both safe and effective.

Dr. Wofsy also created and directed an international AIDS training program called APEX, which has brought hundreds of AIDS caregivers to UCSF from around the world to learn the latest techniques of care so they could carry back that knowledge to their own countries.

Because of her profound understanding of the disease and the long lapse between infection by the AIDS virus HIV and the emergence of symptoms, Dr. Wofsy became deeply concerned about the issue of workplace discrimination against people with AIDS or HIV. She established close relations with major corporations such as the Bank of America, Pacific Gas and Electric Co. and Pacific Bell and helped provide them with teaching materials and videos to train their employees about the disease.

Her world-wide activities included chairing the communications committee for the Sixth International AIDS Conference in San Francisco in 1990; serving as the American chairperson for the first Sino-American AIDS Conference in Beijing in 1990; and acting as program director for the World Health Organization's Eastern European HIV Training Program in 1991.

Among her many awards, Dr. Wofsy was honored by Equal Rights Advocates in 1986, by the Harvey Milk Lesbian and Gay Democratic Club in 1987 and by the Women's Faculty Association and the UCSF Chancellor's Committee on the Status of Women in

San Francisco Chronicle
June 25, 1996

Dr. Constance Bell Wofsy

A memorial service for Dr. Constance Bell Wofsy, a noted AIDS researcher and clinician who died June 3 at her home in San Francisco will be held at 5:30 p.m. Saturday at the California Academy of Sciences in Golden Gate Park.

Dr. Wofsy, a professor of medicine at the University of California at San Francisco and co-director of the UCSF AIDS Program at San Francisco General Hospital, was a founder of the hospital's AIDS program in 1983, and was a leader in developing specialized treatment methods for women suffering from opportunistic infections caused by the AIDS virus.

She was also a founder of the community-based organization called AWARE, which offered women confidential AIDS testing and counseling and was a member of the AIDS Clinical Trials Group sponsored by the National Institutes of Health.

I FAMILY BACKGROUND, EDUCATION, AND EARLY CAREER

[Interview 1: November 17, 1993] ##[1]

Education

Hughes: Dr. Wofsy, would you give a brief overview of your family background and education?

Wofsy: I think probably what would be germane is that I went to the University of California at Berkeley [1960-1964] and was a microbiology major. I'm not quite sure why I chose microbiology, but I did. I was interested in looking at things through a microscope that went beyond medical school and the obvious of getting a medical degree. It really was a focus on little things that swim, unicellular organisms, and that's going to relate somehow to PCP [*Pneumocystis carinii* pneumonia].

I got a master's degree at Berkeley in 1966 in bacteriology and immunology after deciding not to get a Ph.D., but instead to go to medical school. I always wanted to be a doctor for a whole variety of reasons, including some personal illness. I gave up medicine for a while and thought I would get a Ph.D., and then realized that I wanted to go into medicine. I got my medical degree at USC [University of Southern California] Medical School. I did my infectious disease fellowship [1980-1982] after I had been on the faculty of internal medicine here at San Francisco General Hospital, six years after I completed my residency at the University of California, San Diego [1972-1974].

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[1]## This symbol indicates a tape or tape segment has begun or ended. A guide to the tapes follows the transcript.

Early Career

Wofsy: I realized that my initial choice of emergency medicine was too surgical and wasn't going to be a long-time career for me. Probably the most important and telling thing is that emergency medicine was much too political. I found myself, as I rose up the ladder in emergency medicine, getting involved in politics and negotiations. The staid and more predictable specialty of infectious disease would offer more of an intellectual field with a good generality of internal medicine and diversity of public health, but without so much controversy and brouhahas as in emergency medicine.

Hughes: Why is emergency medicine particularly politicized?

Wofsy: Oh, I think that among the issues at that time, which was 1979-80, was whether academic involvement in emergency rooms would be the purview of surgeons and internists, or turn into emergency medicine that was the emerging specialty. And the other big battle at that time was--[tape interruption]--the issue of whether paramedics could intubate in the field, and which ambulance went to what hospital, and a lot of departmental politics between the departments of medicine, surgery, family practice--those kinds of things were very active at that time.

I wanted a field that was already established, wasn't fighting for its place, and that I had a background in, sort of an academic hold. So infectious disease related not just to medical school, but to my earlier interest in microbiology, so it seemed a logical choice.

I arranged to do a fellowship with Dr. John Mills, who was then the chief of infectious diseases here and, interestingly, had been the medical chief of the emergency room. It was he who had hired me for my original job in the emergency room in 1974. So he was known to me and familiar, and he readily agreed that I could do a two-year fellowship, which I did as a faculty member, modifying my medical responsibilities for those two years, and going through the regular routine of a clinical fellowship, seeing patients, and just doing it like everyone else. So it was very interesting, going from six years of being an attending physician to presenting cases to an attending.

Hughes: This was '80 to '82?

Wofsy: Eighty to '82 was my fellowship.

Hughes: So the years that the AIDS epidemic was breaking.

II THE AIDS EPIDEMIC

Her First AIDS Patient

Wofsy: The reason this all ties together with the microscope is that the first year of my fellowship was very traditional, seeing patients and that kind of thing. In March of 1981, which would have been the end of my clinical year, as part of my everyday responsibilities, I saw a twenty-six-year-old gay man on the neurology service who had been admitted to neurology for a presumed astrocytoma, brain tumor. He had developed a pneumonia and they had done an extensive workup and figured out that the pneumonia was *Pneumocystis*. The hospital was actually not very well-equipped to do the specialized stains that were required to identify the organism, and I as the consultant infectious disease fellow was routinely called to see the case.

I became very intrigued with the case and very interested in *Pneumocystis*, which I had only heard of as a term, and followed this man's case in detail through about May. In April of that year, 1981, while I was a first-year ID [infectious disease] fellow, I went to a national meeting that crosses all specialties that happened to be held in San Francisco that year, the AFCR [American Federation for Clinical Research]. I don't normally go to that meeting, and I don't recall why I was there that year--perhaps I saw that there was a session I wanted to attend.

In a small side room, there was a poster on *Pneumocystis* in rats, and I fell into conversation with the person at the poster. It was really interesting. I hadn't previously known anything about *Pneumocystis*, PCP, but I had a patient with it, and it was very unusual because he wasn't a patient with a malignancy --just a man. I may have said gay man; maybe I didn't. But a person with a brain tumor had PCP.

The person I was speaking to, who did the rat research, said, "Well, that's funny you said that. There's a guy named Henry Masur in New York City who's had about three or four cases of PCP in gay men.[1] You ought to call him." So I did.

Henry Masur, who was then at one of the New York universities [Cornell University Medical School], did indeed have three or four cases of PCP in gay men, and had linked up with a fellow named Mike Gottlieb in Los Angeles, who also had several cases. Masur told me that he and Mike Gottlieb were going to write this up for publication in the *MMWR* [*Morbidity and Mortality Weekly Report*, Centers for Disease Control]. In fact they did, and it was the famous first report in the *MMWR* in June of 1981, about gay men in Los Angeles and New York with *Pneumocystis*.[2] My patient wasn't included. They had already started to write the article. But it made me realize that whatever I was seeing, something was happening. It was happening in New York and Los Angeles.

Hughes: Were you connecting *Pneumocystis* with gay men?

Wofsy: Their patients were gay, yes, so there obviously was a connection.

What then happened with my patient is that he ended up getting multiple brain biopsies, because they couldn't really find astro cancer tissue for the astrocytoma. I was involved in all of it, because I needed to get the specimens and be sure they were cultured properly. In one of the specimens, there was a single entity that stained and looked like it was *Pneumocystis*. We thought it was *Pneumocystis* of the brain, and wrote it up, in fact, in an article in the *Annals of Internal Medicine*, with the first author, Steve Follansbee.[3] In the *Annals of Internal Medicine*, as I recall, we stated that it was *Pneumocystis* in the brain.

Hughes: Which had never been reported before?

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[1] H. Masur, M. A. Michelis, J. Greene, et al. An outbreak of community-acquired Pneumocystis carinii pneumonia: Initial manifestations of cellular immune dysfunction. *New England Journal of Medicine* 1981, 305:1431-1438.

[2] *Pneumocystis* pneumonia--Los Angeles. *Morbidity and Mortality Weekly Report* 1981, 30:250-252 (June 5, 1981).

[3] S. E. Follansbee, D. F. Busch, C. B. Wofsy, et al. An outbreak of *Pneumocystis carinii* pneumonia in homosexual men. *Annals of Internal Medicine* 1982, 96:705-713.

Wofsy: Which had not been reported. We learned subsequently, and now it seems painfully naive and stupid, that of course what the man had was toxoplasmosis, and that what we saw was not *Pneumocystis* but in fact a cyst of toxoplasmosis. That can be difficult to interpret if you only have one cyst. He never did have an astrocytoma, or a malignancy of the brain.

On a CT [computerized tomography] scan, he had many lesions in the brain, which responded to the trimethoprim sulfa he was given for his *Pneumocystis*, and so we assumed it was *Pneumocystis* in the brain. We subsequently realized that of course toxoplasmosis is very likely to respond to trimethoprim sulfa, and so it all was in keeping with toxoplasmosis. He then left the hospital very well. He went to Hershey, Pennsylvania, as I recall, and somehow I kept track of him and discovered that some three or four months later he was readmitted to the hospital in Hershey with more lesions in his head. I think that it was over the course of the several months after he left the hospital that we became aware that this had to be toxoplasmosis.

We began to learn from a person named Gordon Dickenson that some of these unusual patients had toxoplasmosis. He was in Miami, and, over the course of the next year, he published a letter to the *New England Journal [of Medicine]* about several cases of toxoplasmosis in Haitians in Miami. Things were beginning to come together. We didn't know how, but somehow they were related.

Hughes: Was it unusual to find toxoplasmosis in the brain?

Wofsy: Yes. Toxoplasmosis was found almost exclusively in immunocompromised people and in pregnant women. The local expert was Jack Remington, so I called Jack Remington, and he told me a lot about toxoplasmosis, but we didn't really have a clue at that time why this gay man would have it.

Hughes: Did you suspect immune deficiency?

Wofsy: Well, yes, we suspected he had immune deficiency, because that's who gets these diseases. But there was no evidence of one. His complete blood count seemed to be fine. I suspect we must have done some special studies, but I can't remember what they were anymore. We certainly didn't do a helper T-cell or CD-4 count, because we didn't know anything about those. As I recall, this patient went unevaluated in terms of immune status, beyond skin tests and other very routine things one can do. There was no evaluation to be done.

I was in conversation with his doctors in Hershey. They started trimethoprim sulfa again, but by then we assumed it was toxoplasmosis and they probably treated him appropriately. I subsequently followed up, and he died not long thereafter. So that was all happening in the spring of 1981.

Establishing AIDS Services at San Francisco General Hospital

Wofsy: In 1981-82 I was to conduct my second year of fellowship. The chief of my division [infectious disease], John Mills, went on sabbatical. He asked if I would be the acting chief of the division while he was gone. And because I had been on the medical faculty for six years, it isn't as bizarre as it sounds--to be the acting chief of the division when you're still doing your fellowship. I had held an administrative position in the emergency room. I also did some work in the lab with herpes. I was completing my fellowship, acting chief of the division, and had taken this interest in PCP.

Paul Volberding

Wofsy: Paul Volberding that year [1981], as I recall, was newly minted from his [oncology] fellowship and was given the role of chief of oncology at San Francisco General Hospital [SFGH].[1] That wasn't our first encounter. I knew Paul because I had hired him to work part-time in the emergency room at night while he was a fellow. That wasn't technically allowed, but at any rate, he had worked in the emergency room part-time, and I had been the director of the ambulatory care emergency services. So I knew him from that relationship.

So sometime in 1981, Paul began to see patients with Kaposi's sarcoma, which didn't interest me particularly at all, and which had no association in my mind with PCP. But by late 1981, several

[1] See the oral history in this series with Paul A. Volberding, M.D.

papers had come out in the *New England Journal* by Mike Gottlieb,[1] who had seen the PCP cases in Los Angeles.

Hughes: He saw a connection between PCP and Kaposi's sarcoma?

Wofsy: Right. So it was clear that something was happening in gay men, and that PCP and Kaposi's were happening in the same population. It wasn't termed AIDS then, but there were words like immune deficiency syndrome in gay men.

So Paul set up a Kaposi's clinic here at San Francisco General Hospital, a very small one, and a much larger research clinic [the Kaposi's Sarcoma Clinic] over at UC, with Marcus Conant.[2] I began to go to the research clinics over at UC, because I had become really involved in this. Paul asked me to join him at that time, doing an infectious disease part of whatever this was that was happening.

The AIDS Clinic

Wofsy: So we joined forces to have a clinic once a week over on Ward 5B, which was the housestaff sleeping quarters in the hospital. We would take over several of the sleeping rooms then on that one-half day a week. Paul and I and Gayling Gee, the head nurse, would see patients for research purposes for Kaposi's, because they were using interferon, I think, and for clinical care purposes for other problems. There were no other cases of PCP.

I remember that a gay man who was forty-five who had blood in his urine was referred to our clinic. It turned out he had post-streptococcal glomerular nephritis, which has absolutely nothing whatsoever to do with anything related to HIV or being gay. But what evolved during that time is that gay men sometimes, when it wasn't clear what they had, got referred to our clinic. And in this case, it was a very traditional infectious disease. There was no HIV test, so we had no way of knowing whether he was one of these gay men with AIDS. But in retrospect, I now realize that I

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[1] M. S. Gottlieb, R. Schroff, H. M. Schanker, et al. Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: Evidence of a new acquired immunodeficiency. *New England Journal of Medicine* 1981, 305:1425-1431.

[2]For more on the KS Clinic at UCSF, see the oral history in this series with Dr. Conant.

am positive he wasn't infected. He got post-streptococcal glomerular nephritis, and he came to the clinic, and since I happen to be an ID specialist, we were able to take care of it.

I also remember that certain faculty in other departments began to be much less appropriate and referred gay men with bronchitis. In other words--how can I say it--gay men, just kind of--

Hughes: Getting rid of them.

Wofsy: Getting rid of them.

Hughes: So what did you do about that?

Wofsy: We began to re-educate, and I don't know how we tried to target people who really might have swollen lymph nodes, which were occurring at the time, and unexplained respiratory diseases. I probably made a courteous call to this particular faculty member.

The clinic didn't grow by leaps and bounds, but more patients began to know about it. At that time, both Paul and I knew every single person at SFGH and most at UCSF who had AIDS, because they were such a small number.

Hughes: So you didn't have rigid standards for patient referral? It was whoever was referred?

Wofsy: I have no recollection of the referral guidelines. Whoever was referred, came. And there weren't guidelines for primary care. Because I had been doing ID and had a long background in emergency medicine (and in San Francisco where there are a lot of gay men), I was very familiar with a lot of infectious diseases that are common in that population, a lot of bowel diseases, sexually transmitted diseases. I was very familiar with these disorders, and good at treating these, and we (the AIDS Clinic) didn't get those referrals, by and large. Patients self-referred themselves to the emergency room or the sexually transmitted disease clinic or the ID clinic or wherever they knew to go.

The Infectious Disease Clinic

Wofsy: Because I was in ID, I was also part of the infectious disease clinic. There, we were seeing a lot of gay men with swollen lymph nodes. And, at that time, the very beginning of the epidemic, there was the question mark, could these be associated with PCP

and KS? But not the assumption. They appeared to be three separate entities: gay men with swollen lymph nodes, this rare case of PCP, and Kaposi's sarcoma.

Lloyd Holly Smith

Wofsy: I have a funny PCP story that I love. It was probably in 1981 that I was attending on the medical service, so I was supervising a ward of patients with medical diseases. At that time, Holly Smith was the chief of medicine at UC, very revered, a remarkable man. It was the habit to do chief's rounds, so that once every few months, Holly Smith would come to San Francisco General Hospital and pick one of the admitting groups, and pick one day when he came on rounds. Usually we would select an interesting case and present it to him, rather than doing the more work-related activities, followed by a discussion.

We had on our service in the intensive care unit a gay man with a respiratory problem, and we were evaluating him. This man was in his forties. We presented him to Holly Smith, who gave an erudite differential diagnosis with all of the elegance and humor and magnificence that Holly Smith can give. He thought of things, simple things, that hadn't occurred to any of us, and he put it together in extremely elegant language.

Hughes: Can you remember any of those simple things?

Wofsy: Oh, he just drew on the wealth of his background in cases of chronic aspiration that have unusual presentations--cystic fibrosis in an adult, some of the immunologic diseases, Wegener's, something called Hamman-Rich syndrome. I think we had stopped using eponyms; but in his era you did. None seemed to fit, by his own definition.

And after it was all over, I said, "I wonder if it could be *Pneumocystis*?" And Holly Smith, who knows everything, even though he's not an infectious disease specialist, looked at me with his brow furrowed and said, "*Pneumocystis*?" I went on to mention that four or five or six months previously, I had had a gay man who had *Pneumocystis*, and that they had reported several cases in Los Angeles and New York, and then discussed a little bit about how the diagnosis had been made in that case.

On the basis of our discussion, we all agreed that it would be prudent to do a bronchoscopy, and see if it was *Pneumocystis*, which we did, ultimately. And again, the pathology lab didn't

have its staining techniques very well developed, so it would involve special calls to the lab. The lab was very interested, because by then there had been enough information on PCP that it was trying to get its staining techniques perfected. It did everything it could to look for *Pneumocystis*, and there was no evidence of it in this patient.

As I recall, he ultimately died of ARDS, adult respiratory distress syndrome. We treated with erythromycin for Legionnaire's, and used other antibiotics we could think of. But he was not treated for *Pneumocystis*, which is interesting in retrospect, because now you say, "Why didn't we treat him?" But in the U.S., there were six cases of PCP at that point. It really didn't seem like we were going to give--give what? Pentamidine? Pentamidine at that time was available for intramuscular injection. It was very toxic and hard to get. Trimethoprim sulfa was licensed for treatment and was used in pediatric malignancies. There was very little experience with the adult dose and very little experience with treatment. It certainly wasn't something that would be used empirically. And as I recall, he never was treated.

Hughes: Did you consider those treatments?

Wofsy: I don't recall. If we had considered them, we might well have rejected them, given that there was no evidence of *Pneumocystis*. I don't think we were politically savvy. No, I'm projecting today's mind-think. We would not have said, "Don't label every gay man as having *Pneumocystis*." I don't think we would have done that.

Interestingly, Holly Smith called back several weeks later to follow up on the case and had heard a little more about the syndrome in the meantime. I was very impressed at his sustained interest and follow-through.

Discussing Etiology

Wofsy: I remember sitting around over coffee having endless discussions: Could there be something genetic about being gay? Things in the water? Very early on, discussions of antigen stimulation syndrome. I remember political correctness, and slipping out the horrible allegations one would never have said before: Is there something biologic about gayness? Could gayness be linked to immune deficiency? People sat around the table saying things about gay men, speculating things, that wouldn't have been

thinkable to say in San Francisco, like maybe it's genetic, et cetera.

Hughes: There was also the idea that poppers might cause AIDS.

Wofsy: Yes, this was the time of the poppers, amyl nitrite.

Kaposi's Sarcoma Clinic and Study Group at UCSF

Participants and Research

Wofsy: The academic center for what was going on with this syndrome was over at UC, with the conference [Kaposi's Sarcoma Study Group] that Marcus Conant and Paul Volberding ran. It was a Wednesday morning, as I recall, and I would take the shuttle over--because everyone who was in the in crowd of this disease was there. There were thirty people routinely in the room. Donald Abrams was there, Selma Dritz, Judy Wilbur from the Public Health Department, Steve Follansbee. I remember gay physicians, some of whom are now deceased, and I'm blocking on their names. Who else was routinely there? Merv Silverman came sometimes.

Hughes: Jay Levy, I've heard.

Wofsy: Oh, yes, Jay Levy. Harry Hollander wasn't yet on board, so Harry Hollander wasn't there. I think he joined in in about 1983, but in these very early sessions, he wasn't there.

Format

Hughes: What was the format and tenor of those meetings?

Wofsy: The format was largely about Kaposi's sarcoma, though any time anything came up that might relate-- As I recall, we might have a discussion about possible etiologies, and some brought epidemiology data. It was the forum to discuss this entity. It was a speaker or speakers, always run by Paul and Marcus--probably Marcus ran it--and then people sitting theater-style in the audience.

Hughes: With patient presentations?

Wofsy: Patients were there in the audience. Patients were brought in to display the Kaposi's. A lot of going over Kaposi's sarcoma--slide presentations. I knew all about Kaposi's in gay men, and Hungarians, and Africans. I began to learn of names of people in New York City who were doing KS research. I learned the name of Susan Krown; I learned the name of Linda Laubenstein. She was in a wheelchair, which sets her apart from a lot of other doctors.

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Hughes: When did immune deficiency become a focus?

Wofsy: Dan Stites over at UC began doing immunology studies, and may well even have done T-cell subsets.

Attendees

Wofsy: So Dan Stites was the immunology; Jay Levy was the retrovirology; the infectious disease was Steve Follansbee, myself--I don't think John Conte got involved--no. John Mills, the chief of ID here, was on sabbatical. There wasn't a chief of ID. John Conte was chief of ID at UC, and was peripherally involved. The VA [Veteran's Administration Medical Center, Fort Miley, San Francisco] wasn't involved.

Hughes: John Ziegler wasn't involved early on?

Wofsy: I was going through the ID laundry list, and Ziegler is oncology. So the VA ID wasn't involved. Now, oncology at the VA: Ziegler got involved pretty early, because he had done a lot of work in Kaposi's in Africa.

Hughes: Was Larry Drew involved?

Wofsy: Larry Drew was involved in a parallel effort. He didn't come together with the UCSF KS Clinic. He was doing a study on whether people who newly acquired CMV [cytomegalovirus] developed immune deficiency. It was coincident in time that he was doing this study. He had been interested in CMV. He wanted to see if CMV was carried in the semen and urine, and he was interested in the research question whether acute CMV alters the immune system.

The parallel interests came together in the hypothesis that maybe CMV was causing the immune deficiency, that these very sexually active gay men had active or newly acquired CMV, which caused an immune deficiency, and they were now getting these other

diseases. So it was very much parallel. I remember watching when they converged.

John Mills, on his sabbatical, was at Stanford looking at the role of CMV in the immune system. Stanford is very isolated. This whole thing going on in gay men was [gestures]--what I'm doing is covering my eyes, my mouth, and my ears. Stanford doesn't tend to see these things.

Hughes: Because AIDS wasn't a respectable thing to see?

Wofsy: Not mainstream, not--who knows what. The techniques to look at immune deficiency that were being developed, at natural killer cells, at immune system subsets, to look at the CMV question, had a striking parallel with what ultimately turned out to be an area of investigation for HIV. But it was true that they were not related at the time.

Stigma

Wofsy: So there was the KS Clinic at UC; Larry Drew was interested in CMV; John Mills was at Stanford doing a sabbatical and interested in CMV and immune response. But the group of us that got involved in the KS Clinic were sort of our own little entity. We were an aberration. We were onto this crazy thing, and we were outside of traditional academics.

Hughes: You felt that at the time?

Wofsy: Yes. We were the upstarts.

Hughes: You were upstarts because AIDS was not a standard part of medicine?

Wofsy: Gay. Gay.

Hughes: Where was this feeling coming from?

Wofsy: The air. [laughter]

Hughes: Did you feel it here at San Francisco General as well?

Wofsy: No. San Francisco General has always taken care of its populations. We have a refugee clinic; we have a TB clinic; we look after the people we take care of; and we take interest in what they have. I don't say that to be politically correct--it's

just we are a hospital serving patients who aren't necessarily mainstream in society.

Now, of course, I was on the inside in terms of that population. Well, the group at San Francisco General got interested in it. Paul was chief of oncology, so that's mainstream. John Mills was on sabbatical and I was acting chief of ID, so that's mainstream. And the chief of medicine, Merle Sande, was not an uninterested party, is the way I would put it.

Hughes: Now, you're talking about 1981?

Wofsy: 1981-82. Merle, the chief of medicine, was intrigued by things--lots of things. He just is interested. So whether he used political clout, I can't recall, but AIDS was intellectually stimulating, and he is a person in general who picks up on things that are intellectually stimulating.

Hughes: He wouldn't be bothered by the fact that AIDS was concentrated in a fringe population?

Wofsy: No, I don't think that was a visible issue to him.

Hughes: Where did you get the feeling that AIDS was unacceptable because it was a gay disease?

Wofsy: I would say that was more a cross between gossip and conversation, that we realized that we were not taken very seriously, that it was becoming a problem, that the doctors who represented private hospitals, those hospitals did not want whatever this was in their hospital, thank you, please, that's it.

Hughes: What about UCSF? Moffitt Hospital?

Wofsy: UCSF didn't want anything to do with AIDS, other than its basic laboratory research. It was just hunky-dory that some upstart Paul Volberding was seeing these patients. And Marcus Conant, all right. Over at UC, that KS Clinic is off on a certain floor in a certain corner, and he can have that. And UC didn't want to be affiliated. The name San Francisco General got linked with this entity [AIDS] very early on, and whether they liked it or not, SFGH, at least as I recall, didn't try to really actively dissociate from AIDS. UC, again, eyes, mouth, ears [gestures]--covered.

Hughes: Was this upsetting to you from the standpoint of your career?

Wofsy: I think at that time, I wanted a job. I had a job in something that I was very interested in, this bizarre thing that was

happening. I knew I had a good situation in that I was part of this upstart group that was young Turks, active, aggressive, and that I had the support of my chief, John Mills, who came back from sabbatical, was thrilled that he had a faculty member dealing with AIDS, frankly, so he didn't have to. So he didn't take an interest in it, on the one hand; on the other hand, he's a person I hold in high regard. He recognized that someone in his division had to work with AIDS, and so it looked real good to him, I think, that someone was, and it wasn't him.

Hughes: You could read into that prejudice, but it wouldn't necessarily be so, because in what I presume was rather a small division, it wouldn't have made much sense to have two people working on the same problem.

Wofsy: Right. The other thing is the personality of John Mills. The gay issue was not an issue for him. That is, I think for many people, AIDS was "gay fringe." His issue was an intellectual one. His area of interest was herpes viruses. He had no reason to suddenly take up a new area of investigation; he was quite senior--youthfully senior, I should add--probably an associate professor. So his lack of interest was a lack of academic interest. Gay men, purple people--he could care less.

Hughes: In his research on herpes, presumably, he was used to working with gay men.

Wofsy: Right. So in his case, it was lack of academic interest, not that it was a fringe population.

[tape interruption]

AIDS Workers' Sense of Community

Wofsy: I remember some time in the very early years, Paul was invited to a hepatitis meeting. It was a meeting in which everybody who does hepatitis research was there. He said, "It didn't feel so much like a scientific meeting but like a family reunion." He didn't know anybody, but they all knew each other. It was clear he was talking beyond the old-boys professional network. You know: How's Sally? Glad Joe could come skiing with us--they knew each other. I remember at the time he said, "Do you think it's possible we [the UCSF/SFGH AIDS group] will get to be like that?"

Hughes: Do you remember what year that might have been?

Wofsy: Very early. I'm trying to picture the room in which we had the discussion. It was before 1983. He was so emotionally struck by how family they were. And it's so exactly what's happened to the AIDS group.

Hughes: When did you begin to feel a group identity, and why?

Wofsy: Well, I think very early in the epidemic. But family is the sense of watching generations grow, so even if you are renegades in this disease in 1983, you may be intensely bonded, like people were on Sproul Hall steps[1], but you don't have a history yet. You have a short history.

Meeting on Kaposi's Sarcoma and Opportunisitic Infections, New York City, July 1982

Wofsy: Keeping on this same theme of family, in 1982, a group of people at New York University and Mount Sinai Hospital, which included Linda Laubenstein and Donald Armstrong and Pearl Ma, decided to sponsor a conference on this entity.[2]

What was interesting about that is, it was the first time that an infectious disease department sponsored an AIDS symposium. Don Armstrong and Pearl Ma are in the infectious disease division at Sloan-Kettering. And it was the first AIDS conference of a national scope that brought together people from big cities who could fund their own travel. There was no funding organization to apply to. As I recall, there were talks like there always are, and people talked about what they were doing--it wasn't something you submitted abstracts for. It wasn't a selective process to get there. They set up a network and anticipated another conference.

But it also wasn't for continuing medical education credit. It was on ground-breaking research on AIDS people were doing, all from borrowed funds. There was no money. Pearl Ma worked in cryptosporidium; Don Armstrong probably worked with PCP at that

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[1] Sproul Hall at the University of California at Berkeley was a focus of student demonstrations in the mid-1960s.

[2] On July 13, 1982, New York University and Mount Sinai medical centers sponsored a symposium on Kaposi's sarcoma and opportunistic infections. (For more on this symposium, see the oral history in this series with Selma K. Dritz, M.D.)

time. Anything that got presented was presented by people who had been doing the work on their own.

I approached my chief, John Mills, and said, "Listen. I seem to be getting to be sort of the expert in this crazy thing [PCP], whatever it is, and they're holding this meeting. I'd like to be sponsored to go. I think somebody in our department should know about this, and I've already generated interest." And he provided the money for me to go. I think I'd not been able to go on some other trip two years earlier, and it was sort of like--

Hughes: "Now it's my turn."

Wofsy: My turn.

In retrospect, in a way, that was really the first national AIDS meeting. Everybody who knew about this got themselves there, so it was the beginning of the family. I remember talking at the cocktail break with Hunter Hansfield, who runs the STD clinic in Seattle, and they really weren't seeing any significant numbers, but he'd seen one or two PCP cases like I had, and he had gotten interested. I remember Linda Laubenstein was there. I don't think Larry Drew was there.

Hughes: It wasn't just on PCP, was it?

Wofsy: Oh, no. It was on other diseases--toxoplasmosis. Margaret Fischl appeared. Paul was there. Donald Abrams was not yet. Who were the rest of the early people? [pause]

Hughes: Marcus Conant?

Wofsy: Oh, of course he was there. He must have been. The meeting had a little different flavor, because it was ID-based. I know who else was there: [Alvin] Friedman-Kien. The name Friedman-Kien began to become very prominent.

Hughes: Why was he prominent?

Wofsy: As a private dermatologist, he saw a lot of patients with Kaposi's sarcoma, and he was describing them.

Hughes: He had a gay practice?

Wofsy: Yes. He's in New York.

Hughes: Selma Dritz was at that meeting.

Wofsy: She very likely was; I don't remember her.

I can picture myself at the punch bowl with Hunter Hansfield. I guess that was relevant, because I was a little nothing. I mean, I had just finished a fellowship. I had been on the faculty, which is very nice, but I wasn't any particular thing in any particular academic department. I didn't feel like I had a lot of credentials at that point; that someone else in my position might not have gotten funded to go to such a meeting. Whereas Hunter Hansfield was a very important person. I wouldn't have pictured someone with my relatively sparse credentials having a conversation with somebody who was respected, widely published, and on speaking tour. I remember being struck by, "I'm talking to Hunter Hansfield! Wow! He's a really nice guy. Golly gee."

Hughes: Did he seem to be interested in what you were saying?

Wofsy: Oh, yes. What characterized our conversations wasn't where we were academically, but the fervor of our interest in this disease.

Walt Stamm was at that meeting. Am I mixing up two New York meetings? Two consecutive years, there were meetings in New York, both sponsored by NYU, and they get mixed up in my mind. I think it's the second meeting that had a large Seattle contingent, so I think the first one had Hunter Hansfield and the second one had Walt Stamm and King Holmes. I remember that I had the same feeling about King Holmes and Walt Stamm, that these were gods. And there I was.

We ended up walking, oh, about three miles down the avenue that borders the Metropolitan Museum. We walked from the restaurant to the hotel, which was on Central Park South, and got one of those horse and buggies. I remember again thinking, How did life put me in the same aura as people so accomplished as Walt Stamm and King Holmes?

There were some industry people from Burroughs-Wellcome who did herpes research. Herpes was emerging in this population of patients, and so they were there largely as the herpes interest, not because they were going to become Burroughs-Wellcome with AZT interest yet. And Grey Davis was there, whom I knew from the herpes world. Grey Davis is relevant because she was in the very difficult position at the last ICAAC [International Congress of Antimicrobial Agents and Chemotherapy] of presenting a concept of acyclovir, a treatment for herpes, going over the counter.

The theme of what I'm saying is this family of AIDS workers. So these early couple of meetings were the first time I got to know some people whom I've always associated with another area of infectious disease. But in the context of this immune deficiency thing, we were all naive. So we were setting up a network in that

disease that put us more as equals, equals in the degree of knowledge we had, not in terms of our academic background.

Hughes: Did this family communicate on a somewhat regular basis, beyond meetings? Did you call each other on the phone?

Wofsy: Oh, there were phone calls; there were committees.

Reasons for Engaging in the Epidemic

Wofsy: What evolved over the next number of years was the ACTG [AIDS Clinical Trials Group]. For John Mills, my department chief who had not taken a particular interest in AIDS, I think that really crystallized his interest. Under some pressure or encouragement from Merle Sande, the chief of medicine [at SFGH], John Mills in some sort of all-night marathon submitted the application for the first ACTG for this institution. And it was awarded, and my memory may or may not serve me--I'm not so sure just how enthusiastic he was. That is, I think he did it because there was money and you were foolish not to apply, but I'm not sure that he did it with a lot of fervor.

Hughes: Why?

Wofsy: I think he was driven by logic: money, new disease, should get involved in this. But I think that he would much prefer to have continued on the line of research of his greater, larger interest, which was herpes. So in a sense, the epidemic was something that he didn't expect at that time to get into.

Hughes: Could it also be that it wasn't yet apparent that this disease was going to be important?

Wofsy: A, it wasn't apparent that it was going to be important, and B, very few people with academic credentials were taking it on. That may be why it was particularly noteable that Don Armstrong, King Holmes, Walt Stamm, became interested. You were beginning to see very traditional academic clinicians, as opposed to bench researchers, beginning to take an interest. A lot of the others were upstarts or rebels or people who were in private practice and hadn't previously done clinical research. I think Alvin Friedman-Kien had done some research, but that wasn't his principal interest. Marcus Conant was well respected, but I don't think you would say he was an academic leader at UC. Paul [Volberding] was just a kid out of fellowship. So a few academicians were coming in, and I think John Mills was in that situation.

Hughes: Because this was a new and undefined field, did you have a latitude that you wouldn't have had if you'd gone into a more established area?

Wofsy: Anything went. If you could do it, fine. There was no money. We didn't know what we were doing. I had a feel of what it must have been like in history when unexpected things happen. I relate it to flood times. I'm not sure that it's always the environmental flood control district that figures out the organization of how to keep roofs on houses. I think people just get together and do it. And I think I was very aware that that's what was happening with AIDS. The public health department was kicking in and doing some things, but in general, it was just upstarts who got together and did it.

So there were no guidelines, because nobody wanted it [AIDS]; nobody cared about it. If we had money, it was fine. And we were mostly too inexperienced to set guidelines. Another of Paul's quotes is, "There was no grey hair" in this disease, anywhere. None. In fact, there was a lot of green behind a lot of ears.

Hughes: Which is significant, isn't it?

Wofsy: Very.

Hughes: Your example of John Mills probably carried for a lot of people: older, established people would have had older, established fields, and why switch into this bizarre disease?

Wofsy: Exactly. For some it was gay homophobia, but for many, I think you can't point fingers in that direction at all. I think what happened, though, has really influenced the way HIV has gone, because the upstarts eventually became directors and department chairs--and they were from outside the tradition. They might be internal medicine, they might be pulmonary, they might be oncology, so it ended up whoever picked AIDS up ran it. So very multidisciplinary, not because it is multidisciplinary, but because that was the rebel who took it on, number one; and number two, infectious disease departments didn't want it. So it is only now, a decade later, that the ID society [Infectious Disease Society of America] is dealing with the issue of, Do we claim AIDS? Is it our disease?

You think of some of the most visible people--Paul in oncology; Mike Gottlieb, who left under difficult circumstances, was immunology; Margaret Fischl is general internal medicine. Her situation is an example of--

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Wofsy: --parallel departments.

Dr. Fischl, an internist, developed the entire AIDS program at Miami, totally outside of the ID division. At any institution, there may be a chief of ID, and then another now rather respected and senior ID person who does the AIDS. So the parallel track concept--[internal] medicine and ID, or ID-AIDS, or ID-ID--and that's definitely what happened. AIDS in many institutions has become its own department.

John Mills got the grant to do the ACTG; it began to be its own separate thing from the regular ID division; it took on a life of its own. He became a collaborator with Paul, but he and Paul basically had very little association in those early years. In fact, either by personality or as a woman, and I don't know which, I remember conniving ways to get them in the room together--I can't believe I'm saying this on tape--but almost artificially setting up situations that would require that the two of them would have to be in the same room together, to begin talking with one another. Because they each had their separate pathways within this crazy epidemic. They hadn't started out as part of that bonded nucleus of early AIDS researchers, and so it was evolving in several different channels. In a way, there was an ID person as a buffer, but it was clear that traditional ID had to wake up to oncology, as far as I was concerned.

Hughes: You were the one that saw the necessity for that link?

Wofsy: That's only from my point of view, [laughter] but yes, I saw that it was imperative.

AIDS Clinics at San Francisco General

Hughes: At first, patients with KS and patients with PCP were seen in separate clinics, and you thought that both groups should be seen together.

Wofsy: When we first set up clinics, and expanded from one clinic to two clinics to three clinics--oh, there's so much history! It's like opening flood gates--we decided that we had a PCP clinic, a KS clinic, and a something else clinic, and then it was clear that this was naive. PCP [patients] got KS, KS [patients] got PCP, and we had to come to a decision pathway of whether we just should have an AIDS clinic, or whether we should continue these targeted clinics.

I remember long discussions, and then we realized, you couldn't fractionate physicians any more. We're all going to have to learn to do primary KS management, primary PCP management. And then for the more difficult cases, it sort of re-evolved to PCP specialist, KS specialist. But it melded so that initial and routine disease, everyone could manage. There are six or seven national experts on individual OI's [opportunistic infections] or malignancies in the department; everyone has a specialty.

Hughes: A paper that describes the history of the outpatient clinic includes a weekly schedule of the clinics seeing AIDS patients.[1] There were something like five different clinics.

Wofsy: Right, and they all had separate names.

Hughes: Would a patient present first at the general AIDS Clinic?

Wofsy: I don't know how we screened them. I think we gave a little questionnaire to the telephone intake person, and callers were asked certain questions. Then the intake person would have to make a decision: if callers have PCP, they go here; if they have KS, they go here. If the answer is, they have AIDS--because at that time we weren't so specific and politically correct about HIV versus AIDS--then they go into this pool, and we distributed the doctors based on that, too.

More on Etiology

Hughes: Well, go back to the evolution of your thinking about etiology. You mentioned the various theories.

Wofsy: Oh, the theories! God, the discussions! Hours given over to them, with slides and intricate graphs, and arrows going here and arrows going there, and poppers in the right-hand corner of the slide. Oh, multiple antigen stimulation, and syphilis, and chlamydia down there in the corner, and arrows going right and left and up and down. Then sometime in the late 1983 or what have you, you'd see one of these mixmaster slides where everything happened, and if you were just in the wrong place and the arrows all converged, your immune system went to pot.

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[1] Gayling Gee. Information Manual, Ward 86 AIDS/Oncology Outpatient Clinics, San Francisco General Hospital, September 1985. (AIDS Resource Program Archives, SFGH, Carton 4, folder: Ward 86.)

And then you'd see slide B, unifying infectious agent. Which would explain that rather than the mixmaster causing immune deficiency, something caused immune deficiency, and then the immune deficiency could take different pathways: opportunistic infection, Kaposi's sarcoma, yabba yabba. Then we'd debate those back and forth, back and forth, back and forth. There were strong opponents of either model, and it was very slow to come to the inevitable realization that it was a single agent and a new agent.

Hughes: What was the mixmaster model?

Wofsy: Multiple agents causing immune deficiency. If you had herpes and hepatitis and CMV, they all slashed away at the immune system and left you susceptible, either to an agent or they triggered some sort of immune disorder cascade that then made you susceptible to *Pneumocystis*.

I can see the headline, 1984, so I know that that's when Gallo discovered the AIDS virus. So it must have been by '83 that we--by we, I mean just most of us around here--were pretty sure that there must be a single entity of some kind.

Hughes: Was that single causal entity in your mind a virus?

Wofsy: Yes. Nothing else could have caused this disease.

The CDC's Role

Wofsy: A very, very, very important point in the history is that somewhere in this came Legionnaire's disease. So we had another epidemic that killed people--white veterans--at the Bellevue Stratford Hotel in Philadelphia. CDC went in, they took their army, they dusted the air conditioning system, and within no time, they had the organism identified and serologic tests. The allegation was that if these AIDS patients were white veterans, they would have found the answer to this epidemic sooner, and that the Legionnaire's episode just goes to show what the CDC is capable of, and yet what they're not doing here [in AIDS]. So lots of allegations.

Hughes: How legitimate do you think that criticism was?

Wofsy: I think it was and it wasn't. I think it was naive, because Legionnaire's was a great big bacterium. It stemmed from my comment that we thought it was a virus, because we knew that

something bigger would be identified quickly. The CDC wasn't rushing, I have to agree.

I have a feeling if you talked to somebody in the CDC, it would be almost a parallel evolution. There were the young upstarts, the people who were between jobs, the people who had credentials but had just finished a project--they all came together for AIDS. I bet the CDC was similar. I've seen it in *And The Band Played On*, and I've lived the history. I don't know if Don Francis really played whatever role was described in the book, but certainly Mary Guinan did--they were just there. I think the development was probably very parallel, and they made things happen, and I don't think they were getting orders to make things happen. They were allowed to do some things. Jim Curran was painted very badly; myself, I've always thought Jim Curran was pretty terrific.

Hughes: Did you pay attention to the studies that CDC was doing?

Wofsy: Oh, of course!

Hughes: Were they coming to the KS Clinic? Was there personal contact?

Wofsy: Yes.

Hughes: Some of their studies, of course, were right here in San Francisco.

The Hepatitis B Study Cohort

Wofsy: Yes. They visited, and we have the famous hepatitis vaccine study that was so instrumental.

Hughes: Well, talk about that.

Wofsy: In 1979, since San Francisco has a large population of gay men and they're very organized, and the hepatitis vaccine was at an investigational stage, CDC gathered together a cohort of a large number of gay men, collected blood, and gave some the investigational hepatitis vaccine, and to others they didn't. They followed them over time to see if the vaccine was protective, and how many who were vaccinated got hepatitis. Because CDC is organized, because we have a very good STD [sexually transmitted disease] clinic, there was very good follow-up with a lot of gay men in San Francisco. There was blood drawn every six months.

So when 1983 or so came around, and somebody--and it may well have been Don Francis, which may be why he's eulogized--said, "Excuse me, we have sera from gay men in San Francisco starting in 1978." So when the HIV test became available anywhere in the world, it was the best organized batched blood with a lot of demographic information on gay men. So the famous quote, that it's an average of ten years from infection until AIDS, comes from that hepatitis vaccine study.

The study was ongoing over a decade, and it was very well run and managed, and the people who were involved in it, by coincidence or design, became part of the "in" group of the San Francisco consortium of UC, San Francisco General, health department, et cetera. So the vaccine study really was the country's prima epidemiology study of HIV that was coincidentally there just by the grace of--who knows.

Hepatitis B as a Model for AIDS

Hughes: I notice time and again, hepatitis B comes into this story as a model. For example, the infection control guidelines that had already been established for hepatitis B are the ones that were recommended for AIDS. Does this tie in with what you're saying?

Wofsy: It ties in only coincidentally. The hepatitis B study I mentioned here was remarkable because it had blood on a particular population at incredible risk for HIV. The hepatitis B model that keeps coming up in infection control has relevance because the transmission of the two agents is presumed to happen the same way, by blood and semen. So, at least to my mind, they are very related. But if the hepatitis B study of gay men had never happened on the face of the earth, if there were no hepatitis B vaccine, it wouldn't change the dominance of hepatitis B as the model of transmission and prevention of AIDS.

It was truly an extra that this cohort of men was being studied for this vaccination. And gay men and drug users get both; both diseases are blood-borne. And because hepatitis B was something we knew a lot about, and felt secure about, it gave us something we could use as a model, including some of the early ethical issues. There was nothing else to go by; hepatitis was the closest there was. There was one little article in about 1985 of a nurse who had hepatitis B and infected some other people, and the ethics of what do you do about telling patients about hepatitis B. We'd never dealt with these issues. We just glossed them over.

So I think the hepatitis B model comes up for two reasons: that cohort that had so much blood drawn, and then the similarity of transmission.

Transfusion AIDS

Hughes: Well, thinking still of the etiology, what about the case of the UCSF baby which by December of 1982 indicates that the AIDS agent is transmissible by blood? Do you remember that being influential in the way you were thinking about etiology?

Wofsy: Yes. I wish I could think of the timing of the second NYU meeting.

Hughes: Which would have been 1983, right?

Wofsy: I guess it was 1983. Probably '82 was the first, that was Armstrong-Ma. Eighty-three was larger, and now I can't remember all the people that were at that meeting, because it was getting too big. But it had people from various blood banks.

Hughes: Because of this baby, which alerted the blood industry to the potential dangers of transfused blood?

Wofsy: I can't even remember that first reported case of transfusion AIDS.

Hughes: Well, that case was publicized in December of 1982, and then on January 4, 1983, the CDC called a meeting to which all the national blood agencies came--a big meeting, with representatives from many different institutions.[1] The fear was that the nation's blood supply was at risk.

Wofsy: Right. I was never more than peripherally involved in that aspect of things, so I have a very limited view, but maybe that's good, because I have sort of an overview. I remember the following: that it was the hot topic of the second NYU meeting. I can see whoever was next to me, it was probably a stranger listening to

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[1] Possible transfusion-associated acquired immune deficiency syndrome (AIDS)--California. *MMWR* 1982, 31:652-654 (December 10, 1982); Agenda: Workgroup to Identify Opportunities for Prevention of Acquired Immune Deficiency Syndrome, Centers for Disease Control, Atlanta, Georgia, January 4, 1983. (Irwin Memorial Blood Bank, CBBL, binder 2, January-May, 1983.)

the speaker from a blood bank. I mean, I can feel the bodies just where you have to make eye contact with somebody, because you can't believe what you're hearing: there's no evidence that AIDS is transmitted in blood.

I remember that I always thought Herb Perkins was right up there and honest and thinking and trying and testing for hepatitis B, and deciding whether you could do a surrogate marker of hepatitis core antibody to test blood for HIV. I always read him as having concern, and I didn't at that time know him personally at all. I remember I didn't know where other blood bankers were coming from, but they were living on some other planet than the one we were living on.

I remember somebody telling a story about designated blood donors. It was maybe an office blood drive or a family reunion or something, and of the fifteen units of blood that were from designated donors, one had active syphilis and one had some other terrible transmissible disease. I was really struck by the creativity of that simple little investigation. And the point was made, maybe the last person you want to donate is a designated donor, because he can't tell you what risky behavior he's just done. I always thought San Francisco was way ahead of the game in screening donated blood, and that it was hours and hours and hours and hours of discussion. That's about all I remember.

Fear and Self Protection

Hughes: Well, another dimension is fear. This is obviously a fatal disease for which it becomes clearer and clearer that the cause is a virus. And you're using hepatitis B as a model, which you know to be terrifically infectious. What are you thinking about your own personal safety?

Wofsy: We didn't. I think I can accurately say "we". I think we were naive. I think we were so into it that we felt invulnerable. Most people I know had nightmares. I don't think I did. I heard what I wanted to hear from what the CDC said, and I believed it. They were like mantras.

Hughes: That it wasn't terribly infectious?

Wofsy: If it was infectious, why wouldn't there be more infected people? Stuff that's just bullshit scientifically.

Hughes: That's what you wanted to hear.

Wofsy: That's what I wanted to hear.

Hughes: What sort of precautions were you taking? I'm talking now about pre-Gallo/Montagnier.

Wofsy: What did I do about needles? I was careful with needles. I used the hepatitis B model and wanted to do whatever you do for hepatitis B. So it wasn't so much blood precautions that were unclear. I think I was more careful than some of my colleagues who I felt were very cavalier. People almost bragged, I think, about the number of needlesticks they'd gotten. I mean, really almost that cowboy-like approach.

I remember the big deal for me was, we went the other way: You don't wear gloves; you don't wear masks. Each person remembers his own role. I remember an infection control meeting in about 1984--and I wish I had the documents--where the infection control guidelines might have read something like this: "Don't wear gloves unless you are touching the patient's blood. Don't wear a mask unless you are doing bronchoscopy."

I remember at an infection control meeting making the statement, which was heartily endorsed: "It's time to reword this, and say, `Wear a mask if you are doing bronchoscopy or da or da. Wear gloves when you're exposed to blood.'" In other words, we were so focused on the belief, "Don't make gay men feel like they're lepers," that you were almost intimidated if you wore protection. You were intimidated. And the guidelines said, "Don't wear protection, unless..." There was a turning point where we said, "Stop this. It's time to protect. Wear gloves."

Hughes: Did the turning point come after the isolation of the virus?

Wofsy: Probably.

What I remember in early exams before the virus was isolated was that I had to make a decision personally about wearing gloves, because you're always looking for axillary lymph nodes. I have never been real keen on people's armpits; it's just not where I prefer to have my fingers. I decided that I wanted to wear gloves when I had my fingers high up in people's armpits. But I remember that doing that was a real breach of etiquette. I would do all the exam: I would look at their nose and their eyes with my bare fingers. I would be very sure that I would put on gloves, examine the axillary area, then dramatically take the gloves off, throw them away, examine the chest and the abdomen with my bare hands, so that I could still be making the statement, "I'm not afraid to touch you." But I remember it was a big deal.

Hughes: Was the big deal made by the patients, or by your colleagues?

Wofsy: By certain colleagues there in infection control. The patients thought it made real good sense to wear gloves for examination of most areas. Frankly, I could have worn gloves for the whole exam, and the patients wouldn't have given a damn, because the way in which I touch isn't a separatist touch. That's what people feel. It has very little to do with latex.

But it came from certain members of the infection control committee: "We do not discriminate against our patients." The nurses on what was then Ward 5B, the inpatient AIDS service, were incredibly lax. And you wouldn't dare have said, "Take more safety for yourself." That would have been interpreted as, "Be afraid of those patients."

Hughes: So this was a cause, in a way.

Wofsy: It was a cause. We were rebels with a cause. Some of us were more rebellious than others.

The Division of AIDS Activities at San Francisco General[1]

Formation

Hughes: In 1983, the Division of AIDS Activities was formally instituted. Did that have any real meaning?

Wofsy: Yes. I think it had tremendous meaning to me, because in my prior life, I had been the associate director of the emergency room. So I came from an area in which a department appeared to be an academic unit--ER medicine--but wasn't. Although there is a specialty of ER medicine here at San Francisco General, the emergency room was a meld of the Department of Surgery and the Department of Medicine. But it functioned almost autonomously as if it were its own department. So that model was very familiar to me.

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[1]For better continuity, this section was moved from its original position in the last interview session.

The AIDS Activities Division is the only other place within the university system within San Francisco General that I can think of in which an apparent department isn't also an academic department. So the AIDS program, or AIDS Activities Division, as it is called, is an administrative division, whereas the word "division" in academics usually implies a division with a specialty and boards that go with it. So the cardiology division is cardiologists who get board-certified and become cardiologists. Pulmonary board-certified individuals become pulmonologists. The AIDS division is an administrative division. You can't be board-certified in AIDS; there is no training program per se. And by definition, it's multidisciplinary.

So in setting up the AIDS division, it felt like the ER. In fact, the model persevered in that it does form its own unit, but its faculty then either reflects back to their academic home units of oncology, general internal medicine, infectious disease in my case, or family practice in one person's case. But we function as if we are an entity. We have our own staff meetings and journal clubs and research meetings in which the multidisciplinary people spend as much or more time with each other than we do with our home departments.

Co-directors

Hughes: You became co-director, with Paul Volberding, of the AIDS Activities Division.

Wofsy: It happened very early. That was circumstantial, probably for both Paul and me. Paul speaks for himself, but as I recall it, he had completed his oncology training; he was hired to be chief of oncology, and AIDS happened.

I had left the emergency room and done a two-year fellowship [1980-1982] in infectious diseases and got involved with taking care of the first few AIDS patients. I didn't know where my path would take me thereafter, what I would do after the ID fellowship, because when I started the fellowship, lymphadenopathy--none of that existed. So I hadn't a clue what was going to happen at the end of the two years. My husband [David Wofsy] is on the faculty here, and we have children.

Somehow it all just came together that in this multidisciplinary disease, it would be good to have an infectious disease person and an oncologist. So I joined Paul. Then very shortly thereafter, Donald Abrams, for reasons that he can

describe to you far better than I,[1] came to join the group and brought expertise in lymphadenopathy, which at that point seemed like a whole separate entity. It was two physicians, and then within six months, a third came, and we were sort of like a triangle. We were the key faculty [for AIDS] for quite a period of time.

Hughes: Was it deliberate that you and Dr. Volberding represented the two specialties that had the most connection with AIDS, or was it because you two were here doing it?

Wofsy: Well, I was here doing it. I think if I had been a pulmonary doctor, the same evolution wouldn't have happened. So I think that it was circumstantial, but it also was that infectious diseases were emerging as the biggest thing in AIDS.

AIDS Clinical Research Center

Hughes: What was the relationship between the Division of AIDS Activities here and the AIDS Clinical Research Center [ACRC] at UCSF, which was formed in 1983, with Marcus Conant as head and later John Ziegler?

Wofsy: The ACRC is largely an administrative body to determine the dispensing of funds administered by the state of California for research in California. The funding initially was largely targeted, and I was indirectly involved, for research done within the University of California system. Over the course of time, it evolved to a more typical pattern of grant applications, review committees, granting of awards, and administration of them. I was really only indirectly involved.

I've become more directly involved in the last few years, because my husband has chaired for the last three years the grant review committee that decides which grant applications to accept and goes through the whole grant process. I think when John Ziegler left the country, perhaps on sabbatical, my husband--coincidentally--was asked if he would chair that committee, and still does chair it.

Hughes: What was happening at the AIDS Clinical Research Center was administrative, and what you here were doing in the AIDS Activities Division was hands-on medicine?

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[1]See the oral history in this series with Dr. Abrams.

Wofsy: It was hands-on medicine. Right. Now, people from our clinic put grant applications to the ACRC, got money, and conducted trials on our patients here.

Hughes: Because the AIDS Clinical Research Center was at UCSF, because the AIDS Activities Division was at San Francisco General--a part of UCSF--and because Merle Sande for years [1983-1988] was head of the Universitywide Task Force on AIDS, did UCSF have an advantage over other campuses applying for state funds?

Wofsy: That's a very loaded question. [laughter] If I were at another campus, I would certainly see it that way. This campus broke a lot of ground to get monies available [for AIDS research] and to set up the infrastructure of clinical research, et cetera. While the ground was being broken, it was not so visible. I think people who are conversant with the system may well have a leg up. And I don't think I can really say much beyond that, because I really was quite peripheral. I have not at any time sat on that committee, and so whatever my vision is, is hearsay and very episodic.

Expansion

Hughes: What about the effect of the expansion of AIDS activities at San Francisco General? You've said that people had to give up space. But was there also resentment, as the epidemic progressed, that the hospital had to put more and more resources into fighting it?

Wofsy: I think that it's gone through stages and generations. The first was, "I don't want to touch it. Let somebody else do it." I think there was sort of an acceptance that "they" were doing something. The space we took over was not used for other academic activities; it was used for very important activities and programs that were taking care of people who had horrible things happen in their lives. It seems to me rape crisis has probably moved two or three times to accommodate us. There was a program that had to do with children, playrooms and toys, and we took over space that they were displaced from.

My recollection is that they weren't very large programs, but rather two or three offices for this and an office for that. It was a miscellany. All of that miscellany was very important, and there are always fights about space, but it probably related more to, "We're both serving people who have significant difficulties," than displacing other academics.

Then there was huge jealousy generically: "AIDS gets too much money. AIDS gets too much space. AIDS gets too much attention." Sort of the yin and the yang of it, at the same time, though: "They" take care of it. "They" all go over to the clinic. "They" do this. "They" do that. So there have been phases of admiration and respect from people. It just goes all over the map, I think. And now it feels sort of like an equilibrium.

Infection Control Guidelines

Infection Control Committees

Hughes: It seems to me that there are two different groups that are involved with the formulation of guidelines--

Wofsy: I'll give you my interpretation. Each hospital has an infection control committee, which is a long-standing committee dealing with toxic waste since forever. It's so boring. It's the committee you least want to be on, and that you basically bring No-Doz to. Every hospital has it. And at all hospitals, it got involved routinely with AIDS because it's the infection control committee.

The University of California, San Francisco, Task Force on AIDS

Wofsy: Then, there was another committee, the UC Task Force on AIDS. Committee members were the ones that grappled with the issues and had an academic focus to publish. So infection control committees enlisted people supposedly with nothing else to do. That's not true: I'm on the committee, and I have things to do.

The task force was composed of people from all three UC-affiliated hospitals, as opposed to each hospital's individual infection control committee. It had Merv Silverman; it had some other people from the public health department, and it sure had John Conte.

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Wofsy: So the three hospitals--VA, UC, and San Francisco General--all have their infection control committees. John Conte chaired the one at UC and sort of based his career on infection control. He took a very big leadership role in this oversight committee. Whereas these infection control committees [at each hospital] are appointed by hospital guidelines and have to meet requirements for JCAH [Joint Committee on Accreditation of Hospitals] accreditation of hospitals. That's why these infection control committees exist. This university task force was appointed by a chancellor or somebody at UC, and then people were invited to be on it.[1]

Hughes: So it was big deal.

Wofsy: It was. This is prestige; this is punishment. [laughter] And so this prestigious committee, of which I was a member, which goes to show that I was one of the early ones in the group, met in the afternoon when the members had time, so it met at five o'clock. Merle Sande was always there. And somehow we came up with guidelines, which we felt was important to do, and that they were so universal that we had to go beyond any one hospital's particular opinion.

Contentious Issues

Wofsy: But there were one or two items in which we had disagreement, and it got heated. What I remember is that John Conte eventually said, "Sometimes you have to write a guideline that says, `There are dissenting opinions, and these two points of view are offered.'" And that's what we did.

Hughes: Which is unusual, isn't it?

Wofsy: It is unusual. We couldn't resolve our differences.

Hughes: I believe there were at least three areas of particular contention.

Wofsy: I wouldn't be able to remember them any more.

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[1] In March 1983 Acting UCSF School of Medicine Dean Robert Crede created the UCSF Task Force on AIDS, a campuswide committee charged with developing AIDS-related infection control procedures. (Dianne Leiker. Historical Report: UCSF Coordinating Council. [n.d.] Binder: "AIDS Coordinating Council: Historical Report", UCSF Alumni House.)

Hughes: One of them was the double versus single room for hospitalized AIDS patients.

Wofsy: Ah, yes.

Hughes: And another was--I suppose this was the thorniest--the obligation to care for AIDS patients. And then there was also an issue of CPR [cardiopulmonary resuscitation].

Wofsy: Oh, yes, CPR.

Hughes: Can you re-create any of the contention?

Wofsy: Without seeing the document--

Hughes: I have it.[1] [tape interruption]

Wofsy: It was the patient-care issue where the controversy really rang out. I remember John Conte's voice was a dissenting opinion, but I can't remember which dissent. [laughter] As I recall, there were two dissenting voices.

Hughes: Was he one of the two?

Wofsy: Yes.

Hughes: Was he reluctant to say it was the absolute obligation of every physician to care for AIDS patients?

Wofsy: Yes.

Hughes: Do you remember his argument?

Wofsy: Let me just read that. [pause] I just cannot bring it back. Isn't that amazing! It was so argumentative that it seemed like it was etched in stone, but I can't remember. God, talk about memory lane!

Hughes: It's probably hard for you to isolate the meetings that led up to this particular paper.

Wofsy: I remember where people were sitting. I remember it all.

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[1] J. L. Conte, W. K. Hadley, M. Sande, and the University of California, San Francisco, Task Force on the Acquired Immunodeficiency Syndrome. Infection-control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). *New England Journal of Medicine* 1983, 309, No.12:740-744.

Hughes: Did people get steamed up?

Wofsy: Hurt easily. Chairs began to straggle at quite an angle as people adjusted themselves to talk to one another. John Conte was in the front of the room, angled sort of at 45 degrees to see the board that was at the very front and the rest of the room, which he was trying to persuade to his point of view. Wow. To be clear, John Conte's views were earnestly felt and he was not lacking in sensitivity.

Hughes: Similar issues must have presented themselves with other infectious diseases?

Wofsy: Hepatitis B was killing more people then, and nobody ever talked about it.

Hughes: Why?

Wofsy: I have no idea. It was even in gay men. I mean, it was gay men and drug users who got hepatitis B, so it was even the same populations.

Later Developments

Hughes: Do you remember what was the reception of those guidelines here and at a wider level?

Wofsy: We were given credibility. We were making decisions, and that's the way it was going to be. People either overdid or underdid, but that by itself says guidelines were there. They ignored them, or overly adhered to their own internal standard of masks and what have you. And then somewhere along the line, universal blood and body substance precautions fit into a whole CDC channel that I was not part of.

That's the other thing that happened at about that time ('83-'84): the key players were at every meeting, whatever the topic--always the same people. It was a clique that no one wanted to join. We had to do it--all of it--or it wasn't going to get done. And the first one that split off was blood bank. Which hospitals are going to take care of AIDS patients? Go to that meeting. Infection control? Go to that meeting. How are we going to treat PCP? Go to that meeting. Everybody went to everything. There was both the left-out and the lack-of-control feeling, I think, about the meetings you didn't go to. Blood bank meetings were the

first that I realized, okay, neither of us wanted each other. I didn't want to be part of that; they didn't need me.

The second, third, and fourth generation of infection control, when it began to move nationally and get involved with CDC, I was at fewer and fewer of those meetings. I was moving into my own sphere. So another group took that on. Then there were studies of how actively people actually adhered to the guidelines.

Through our infection control committee and Grace Lusby,[1] the infection control nurse, we set up many classes. I remember the classes and the discussion about whether we should hire somebody to teach them, and who that somebody should be. We hired a special employee, Keith Hadley, to educate for a period every department. And then there was a time at which we realized that employee education was no longer needed. Every employee had had classes, so you could now give classes for employees every month--maintenance. And it was now becoming routine; it was becoming part of the system. AIDS and infection control were inseparable.

Hughes: Was there an enforcement procedure?

Wofsy: No. What I remember as the big subjects of discussion here were opening the AIDS ward, and the endless discussion about whether we really were putting patients in one place because they would get better care, better infection control, or whether we were ghettoizing them. That word didn't come up, but "leper colony" came up. And the very people who felt you should touch all patients, never wear gloves, got torn in realizing patients would get better care, but creating an AIDS ward also ran the risk of segregating them.

The conversations that I remember because of sheer volume were not the private-room-versus-double-room debate, but segregating patients from the hospital in an AIDS unit, and endless discussions of what the doorway should be like.

For years, only the patient's first name and last initial were on the locator board in the inpatient unit. And only sometime last year did I start to see last names of people on the public locator board.

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[1]See the oral history with Lusby in the San Francisco Bay Area AIDS Oral History Project: Contributions of the Nursing Profession, 1981-1984. A project of the Department of the History of Health Sciences, University of California, San Francisco, and the Regional Oral History Office, University of California, Berkeley. Hereafter, AIDS nurses series.

The San Francisco Model of AIDS Care

Hughes: Does the 1983 paper on AIDS infection control in the *New England Journal* provide a model that is duplicated elsewhere?

Wofsy: Yes, it was a model. There are probably statistics on how frequently an article is cited. You can't tell how frequently it's Xeroxed, but I bet that one's high.

Hughes: So people looked to San Francisco more than New York, more than Los Angeles, for infection control guidelines?

Wofsy: Absolutely. I never thought of it before, but that paper may well have been the start of the San Francisco model. We now think of the San Francisco model as being a system of care. The San Francisco model was when San Francisco was saying it like it should be [comprehensive care of people with AIDS], and I think that may well have been the start of it.

The Epidemic and Personal Lives

Wofsy: This is off the topic, but it is so palpable. For years, at whatever meeting it was, I think we felt AIDS was solvable. Not curable, but solvable. And if we stayed late enough and had enough meetings, we'd get all the business done. Not cure the disease, but get the business done. And so in those early years, it never felt legitimate for anything else to have a higher priority, and I think that my colleagues would say something similar. It was not acceptable to say, "My kid has soccer practice." "My kid has a piano recital." "I promised I'd take my mother to the doctor." "Maybe we're going back East to a family reunion. I can't be there [at an AIDS activity]."

But it never felt like it was legitimate for an intermediate-level personal thing to interfere with doing whatever the thing was concerning the epidemic. It felt like the same imperative as that after the flood along the Mississippi [summer 1993], only that lasted for a few weeks. Or the fire in the Oakland hills, where for a week it was, stop everything. You wouldn't dream of going to the dentist. But the AIDS crisis went on for years. And of course, people did have their own lives, and they did go to soccer practice and the dentist.

Hughes: Now, what you're saying is that the disease was given much greater priority than events in your personal lives.

Wofsy: By that group. And none by anyone else. I felt like I/we had to do it, because no one else was. And if we just worked at it enough, we'd get all the policies--we were not going to cure all the patients--but we'd get the way we were going to do it all lined up in a row.

Hughes: You would manage the disease.

Wofsy: Right.

Physician/Patient Relationships

Wofsy: I definitely remember the day I went on rounds on 5B and gave up knowing all the patients. I made a decision one day that I didn't, I couldn't, and that it was okay to not know everybody.

Hughes: Do you remember the year?

Wofsy: Early. The ward opened in 1983. It seems like it was a couple of years into it. And by know everybody, I didn't mean know them personally or even recognize them. In other words, if I saw that Greensmith was on the ward, I knew that Greensmith was one of our patients, and that I'd at least have some little list that would say, "Greensmith, okay, he's PCP." I actually felt, for reasons that I have no understanding of, that it was my obligation to know of them all. It's bizarre when I think back. It's scary.

Hughes: Do you think it has anything to do with the fact that many of these patients were likeable, generally well educated, and cooperative, so you might have felt a kinship that you wouldn't have felt with a random population?

Wofsy: Definitely. But I think it was also the sense of this emergency group of physicians who was doing it. But I agree with you, there was an element of bonding.

The other thing that relates to that is, this was a private patient population suddenly put down in the middle of a world [at SFGH] that had never had that population. So there were private patient expectations, and I think it elicited a certain kind of relationship that doesn't exist with most of the patients [at SFGH]. It's just the way it is. For many patients at SFGH, you care about them very much, but they don't send questions back at you as you're doing with me and as educated AIDS patients do with their doctors. So it's all one-sided.

Hughes: It's an acknowledgement, I suppose, of social distance, which you can't avoid.

Wofsy: Right.

Hughes: Well, it seems to me that you're talking about bonding at two levels: the bonding that you felt with patients with HIV who were different than the ones you generally found at San Francisco General; and secondly, this bonding not only with your group here, but with the "family" of AIDS researchers developing across the country. Were those bonds ingredients for this urgency that you were experiencing?

Wofsy: Yes. The first international AIDS meeting was in Atlanta [1985]. At that meeting I knew most everybody. At the next international AIDS meeting, wherever that was [Paris, 1986], I went into the main conference hall and said, "Who are all these people? I don't know them. How could that have happened?"

Hughes: Within a year.

Wofsy: And rather than initially seeing it as, "More troops!", there was a piece that said, "This is fragmenting our group. I can't sit down next to somebody I know here. What's going on?"

The AIDS Clinic at SFGH

[Interview 2: November 22, 1993] ##

Foundation

Hughes: Dr. Wofsy, let's start with the AIDS Clinic. Were you involved with its foundation?[1]

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[1] In July 1981, Paul Volberding was appointed chief of Medical Oncology at SFGH. The oncology service consisted of an inpatient consultation service and an oncology clinic which met one half-day a week. In September 1981, Gayling Gee was hired as a nurse for the service as part of a plan to establish a faculty practice unit similar to that of UCSF's Hematology-Oncology Clinic. Anticipating growth, the Oncology Clinic was moved out of General Medical Clinic and established on Ward 5B, an inpatient unit of the hospital. (Gayling Gee. "Information Manual: Ward 86 AIDS/Oncology Outpatient Clinics, San Francisco General Hospital,

Wofsy: I think that the negotiations and a lot of the hard part, frankly, are attributed to Paul. He really worked. I and a whole lot of other people were involved in a zillion ways in getting it up and running, but in terms of the energy and the push, the locomotive, the tribute is Paul's. Having done that, we then worked together a lot in how to actually set up the clinic: What we would do, how we would function, who we would see, when we would meet, what the guidelines would be.

It started with Paul and me and Gayling Gee, followed by an administrative person named Bobbie Wilson.[1] We had one-half of the top floor of this building, 86, and in that half we had our offices and the clinic rooms, and we started out with one half-day, maybe three half-days a week. We talked last time about who was referred. We did not have appointment books in the emergency room. We didn't have an appointment book in the medical clinic.

Link with the Kaposi's Sarcoma Clinic at UCSF

Wofsy: We had our own direct number, and from the very beginning, as I recall, were linked up with UC and had a University of California phone line. Which seems like a very small point, but it isn't, because all the other clinics here are hooked up to lines that are part of San Francisco General Hospital, so you only have to dial four digits if you're anywhere else within the hospital. Whereas, the UC lines are largely reserved for research, where you have to dial 476 [the UCSF prefix]-blah blah, and are not a standard part of a clinic. So it creates sort of a separatism, in a certain way.

Hughes: Why was it set up that way?

Wofsy: Probably because we were so closely linked with the KS Clinic at UC, rather than being an extension of clinical services at San Francisco General Hospital. We were a parallel to the AIDS services through the KS Clinic at UC.

September 1985. AIDS Resource Program Archives, Ward 5A, SFGH, Carton 4, folder: Ward 86.)

[1] Roberta Gonzales-Wilson transferred from UCSF in January, 1983 as administrative assistant to "further develop" oncology and AIDS services for the clinic. (Gayling Gee. "Information Manual.")

Hughes: Well, talk about the relationship between the KS Clinic and AIDS activites at the General.

Wofsy: I don't know that I can give the insight. That's probably Paul's to give. Certainly the visible location [for early AIDS activities] was UC. That's where the faculty gathered. We never were a faculty-gathering point; we were a patient-care operation here at San Francisco General. There wasn't a conference where everybody came.

Hughes: But the KS Clinic was also seeing patients.

Wofsy: Over at UC, right.

Hughes: The patient-care aspect of each clinic was totally separate?

Wofsy: Totally separate. I suppose patients went back and forth, but I can't remember. But ours was patient care. That was the design. And there were a couple of research protocols that were being done here as well as at UC.

Patient Conferences

Wofsy: I remember some of the innovative aspects--they seemed innovative at the time. I remember well that on Wednesday afternoons, Paul and I alternated and had a conference for patients. That sounds so unimaginative now. It was unheard of then. So any patient who wanted could come from whatever it was, three-thirty to four-thirty, not for discussion of anything about their care, but we would pick a topic--Kaposi's, *Pneumocystis*, testing--I don't think we got social service in. But we, the doctors, addressed some of the social issues at the time. We might have taken on the issue of paperwork, like wills and disability, because there wasn't anybody else trained to do it. Those conferences went on probably for about a year and a half.

Hughes: From the very outset of the clinic?

Wofsy: Close to it. It was one of our early things to do.

The other thing that I remember is that, because the clinic and the offices were all scrunched together, you had to walk past all the exam rooms to get to your office. That gave us some pause, because we realized it got inconvenient to be marching right through the patients every time you were going back and forth to your office, when in fact you maybe weren't responsible

for the clinic that day. That happens in lots of places, so there was nothing unique to that, I guess. But I remember that issue.

One of my favorite stories is that when the clinic really was inaugurated, let's say maybe it was four or five months after the clinic opened, and we had all of our equipment--we held an open house. It was Christmas, because I have photographs with Christmas decorations. We had a huge buffet, a lot of it donated, because a lot of the men were affiliated with catering services. So a magnificent spread of food. A catering service, I think, even donated their services, so there were attractive men, as I recall without shirts, wearing bow ties and collars, going around and servicing the food areas.

The line I love was overheard in the elevator: "I'm going up to the AIDS Clinic. They have great food there!" And it was juxtaposed at a time when that *New England Journal* article[1] was coming out, when there was a lot of anxiety about AIDS patients. We didn't know it was a virus. And the people were pouring up the elevator to eat the food that was laid out in the halls of the AIDS Clinic, and being served by these waiters who it wouldn't have been unreasonable to suppose came from the risk groups associated with HIV.

Expansion

Wofsy: Then the clinic expanded, and Donald Abrams came over [from UCSF][2], and then it's an absolute blur about the next group of doctors. I know we hired Gary Carr,[3] our first nurse practitioner, and we all interviewed him. This was sometime in the early eighties. We didn't know the role of a nurse practitioner in what were fairly complicated diseases, and whether

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[1] J. E. Conte et al. and the University of California, San Francisco, Task Force on the Acquired Immunodeficiency Syndrome. Infection-control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). *New England Journal of Medicine* 1983, 309, no.12:740-744.

[2] Donald I. Abrams began to work on Ward 86, the AIDS clinic, in July 1983, bringing with him from UCSF a caseload of more than 200 lymphadenopathy patients. (Gayling Gee. "Information Manual".) Also see the oral history with Abrams in this series.

[3] See the oral history in the AIDS nurses series with Carr.

we physicians would supervise every case, how independent he could be.

Hughes: And what evolved?

Wofsy: What evolved is that it was our good fortune to meet just a wonderful, mature, balanced person, who is independent and thoughtful and responsible, but is so aware of his limits that we didn't have to police or think about would questions be asked [of Carr's physician colleagues] at the right time. Gary turns out to have a marvelous internal mechanism of knowing when he needs to ask. Perhaps that set a tone subsequently for nurse practitioners in the program.

Social Services

Hughes: When was the Shanti Project involved?

Wofsy: Shanti came on very early[1] and had counselors in the clinic.

The thing I remember the most is, I used to carry a little book, like we all do, with relevant phone numbers, et cetera. I remember over the course of the first few years that my book used to have all the phone numbers for everything--where you called to pick up a disability form, the number you called to get [San Francisco] Food Bank--all those kinds of things. You get too many phone numbers; I would lop off phone numbers that no longer were mine to be concerned with. So I stopped carrying the Food Bank number.

A time came when we had a resource person, and if Food Bank was the issue, I would tell the patient to go see her about Food Bank and a disability form. It was a huge relief to me, not to feel like I had all of this responsibility, that there were other resources. I remember the onset of social services from my own perspective as, "Ah." It's so hard to keep up with the pathogenesis of KS. I was really having problems with keeping up with exactly who was eligible for Food Bank, too. And now I could give someone else that responsibility and spend a little bit more time on PCP. And then gradually, more and more social service pieces were added.

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[1] According to Gayling Gee's history in "Information Manual", Ward 86 and 5B had "a full complement" of Shanti counselors and practical support staff since March 1983.

Hughes: Had you ever had "nonmedical" responsibilities with other types of patients?

Wofsy: Well, it's hard to say, because my professional career had been from residency to emergency room, which is episodic care. The emergency room had a social worker. I had been out of residency for six years before I did my ID fellowship, and I hadn't been in a practice setting. However, it's my opinion, based on what my colleagues were doing, that someone seeing a similar volume of patients in the medical clinic or the endocrine clinic or the family practice clinic in 1983 would not have been carrying the number for the Food Bank--I just use that as an example. There would have been information about social services posted on walls. There would have been a social worker. There would have been a head nurse who had a lot of that information at hand. Our initial head nurse [Gayling Gee] was wonderful and provided much of this, but she came as a research nurse and was working beyond her limits.[1]

Hughes: She came to do research exclusively?

Wofsy: That's why she came initially, because the clinic didn't yet exist. So she was hired to do research.

Clinical Trials

Early Drug Trials

Hughes: Now, when you say research, do you mean drug trials?

Wofsy: Well, I think it was the first trial in Kaposi's. I think it was an interferon trial.

Hughes: Yes, it was.[2]

Wofsy: So Gayling was hired to do the interferon trial. And then all three of us [Gee, Volberding, and Wofsy] did a trial on

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[1]For more on Gee and her perspective on the AIDS Clinic, see her oral history in the AIDS nurses series.

[2] A phase II trial of alpha-2 interferon in Kaposi's sarcoma began on August 1, 1982. (Gee. "Information Manual.")

interleukin-2 [IL-2].[1] I remember that we gasped when, in 1984, the virus was identified, because interleukin-2 stimulates the proliferation of cells that produce the virus. I mean, oh god, it was the dark ages [in AIDS therapy].

Hughes: What was the rationale for trying interleukin-2?

Wofsy: The thought was that Kaposi's sarcoma was probably immunologically mediated, so if you could alter the immune response in sort of a cellular down-regulation, you might decrease the severity of Kaposi's sarcoma. Really the whole thing was in its infancy at the time.

Hughes: So this was a proposed therapy for Kaposi's, not for opportunistic infections.

Wofsy: That's right.

Initiating a Trial

Hughes: Tell me how a drug actually comes to trial at a given institution. Who approached whom in this case?

Wofsy: I wasn't even part of the alpha-interferon trial. The IL-2, I was. It was a pharmaceutical company in this case.

Hughes: Which approached you?

Wofsy: Yes.

Hughes: Knowing that you were dealing with a lot of AIDS patients?

Wofsy: Right. And I think they were becoming interested in the role interleukin-2 would have in modifying, probably actually increasing, the immune response, which was probably the goal at the time, because that's what IL-2 stimulates.

I think the pharmaceutical company probably approached Paul initially. Paul was very aggressive at seeking these kind of arrangements.

Hughes: Why?

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[1] On April 27, 1984, a phase I trial of recombinant interleukin-2 began in patients with AIDS. (Gee. "Information Manual.")

Wofsy: He wanted to study IL-2, and that was the level of clinical research. It wasn't at the time for drug company money, although certainly the money that supports a trial also supports activities in general. But there was a general interest in altering the immune system.

And then other companies approached, or were approached, whatever direction it went. There was IL-2, then there was--oh, my god--suramin. And then Donald [Abrams] came, and he got involved with--oh, god, this is like calling up names of people in your high school class--

Hughes: Was that ribavirin?

Wofsy: Oh, there was a big ribavirin trial. And then there was one--dextrose, dextran--

Hughes: Dextran sulfate, was it?

Wofsy: Yes. Oh, my god, this is just memories--.

Hughes: Do you have memories of specific trials?

Wofsy: Yes. My memory of the trials is that the rage at the lack of involvement of whoever--the NIH, government--started very early. And very early there was this buzz amongst a very active network primarily of gay men--it was a gay disease at that time in San Francisco--not of a conspiracy, but everything not being as open as it should.

A Difficult Patient

Wofsy: I remember one particularly difficult patient who was particularly demanding of getting onto clinical trials, felt that we were overly cautious, that we weren't realizing people were dying, that we needed to be more aggressive, get out there, study, study, study, study things. He ultimately got on a trial, suramin, that taxed our ethics about whether to embark on it, because it had known toxicity in other populations. But it also had laboratory benefit, which was the story of immunomodulators for about five years: Something that would work in the lab, you'd put it into humans, and it would be toxic.

This individual got onto that study, signed the consent form, and was handled with kid gloves, because he was a challenging personality. He was one of the people that got a totally

unexpected and very severe toxic reaction. I remember--this is all filtered through the sands of time--how loudly he shouted about the lack of proper concern for patient safety, and taking care and time before rushing into these trials. It was hard to believe that the words were coming from the same mouth.

What it really underscored was how emotional a disease it is. Difficult personality that he was, he was totally in control of his faculties--it was the degree of the emotion, not that he wasn't thinking clearly. He died early on.

Hughes: For every trial, did you have very specific criteria about who could be entered?

Wofsy: Very. And the institutional review board has been an active and very careful organization here, of course, for years. But over the course of the decade of AIDS trials, I think that there have been even more stringent internal regulations for the institutional review board.

Consent Forms

Wofsy: When we first started clinical trials, we didn't necessarily know who ran the institutional review board. It was sort of one of those committees that was out there. Now institutional review boards and clinical research just go hand in hand. They're so much more sophisticated about patients' rights.

I remember doing some studies, not on AIDS, but on herpes, at the time. I was working with Dr. John Mills, whose name I mentioned, on clinical trials of herpes. There was kind of a boilerplate for a consent form. There was certain language that you could modify. There was one particular paragraph you had to put in, something like, "In the event of an adverse outcome, the university will be responsible within certain limits." A three-sentence thing that the university had worked out with its lawyers. The rest of it was more just suggestions. "These are typical ways you might write a consent form."

And now, writing consent forms is very stylized. There's an order in which you do things; certain sentences that have to be in the consent form. It's really changed over that decade.

Hughes: Do you attribute those changes largely to the epidemic?

Wofsy: They were coincident with the epidemic. They might have happened as a result of other clinical trials and patient rights. But I think AIDS has sort of pushed certain things along.

Hughes: Is it more than just having articulate and demanding patients who attract attention? What factors influence this heightened sensitivity to the consent process?

Wofsy: From the patient's point of view, I think there's the sense that research is the opportunity for access to drugs that wouldn't otherwise be available, and that sense is very new. Research previously was usually something the scientist wanted to do. Obviously there were potential benefits, but largely the scientist knew of the potential benefits, not the patient.

In this instance, the patient knows that out there, there's nothing much that's manufactured for AIDS treatment, so clinical trials are what there is. So there is an avid wish to be part of them, and probably then a corollary wish to control one's choices. The liability issues became very, very important.

Clinical research was really a bastard research. It didn't have the academic respect of basic research. And I think the level of statistical analysis and respect for the scientific integrity of the investigators has gone way up because of or coincident with AIDS.

Alternative Therapies and Buyers' Clubs

Hughes: What did you do about unorthodox or alternative therapies?

Wofsy: That was a whole other world, with buyers' clubs. I can't remember when they sprang up. They were already there in 1985 or '86. Buyers' clubs are run by people in the risk groups. In San Francisco, they were pretty much within the gay community. Buyers' clubs would find ways to get certain products and at a reasonable grade of purity, that is, so that there wasn't risk of toxicity. The buyers' club was down on Market Street. Some of the drugs they would get through underground networks; some through underground manufacturing; some they'd import from overseas, and some would be medication of people who had died, whose lovers or others would donate their medication. So it was not a pharmacy.

Meds were so hard to get that we sometimes indirectly referred people to buyers' clubs. We may have even directly

referred them. Buyers' clubs could negotiate quite a good price. They had to maintain their overhead, et cetera, but the goal wasn't money-making; it was to serve the community.

Hughes: You would refer a patient to a buyers' club to buy a drug that you would have prescribed if you had had it?

Wofsy: Might have prescribed. When ddC first was available, there was a period when it couldn't be gotten by any legitimate route, but the buyers' clubs had it.

Coming along in this was parallel track where a drug that wasn't yet licensed could be prescribed by a doctor if the doctor would fill out all the paperwork. It was de facto a large simple research trial. So you had to record lab work and adverse effects every month, and then you'd get a shipment of the drug for the month, and you could take care of the patient and provide that drug.

But even with that program, we had patients who didn't meet the criteria for ddC, let's say, who didn't want to take AZT, so that you couldn't use AZT failure as a reason for eligibility, and there was no way you could lay your hands on ddC. But you knew enough about the drug to think this was the match for this patient, so he'd go to the buyers' club. Early on, even AZT was through the buyers' club.

Hughes: How did it get there?

Wofsy: I can't recall.

I had run this educational program, APEX [AIDS Provider Education and Experience]. This too is old hat by now, but it was very innovative then. We took these doctors down to the buyers' club--doctors from Des Moines and god knows where. Eyes big as saucers. Including a woman who came to take the course who had a very high position in the FDA [Food and Drug Administration]. When we took her down there, she reassured people, "It's been agreed, I'm taking this course as a doctor to upgrade my information. I'm not taking it as a representative of the FDA. I'm learning as a human being, not in a professional capacity." So she did it very, very nicely, and it was a very big relief to everybody. I think that course was a highlight of her life! [laughing] I think when you work for the government, you never get to see the real world.

Hughes: What about therapies you knew did not have any scientific merit?

Wofsy: Oh, people were on everything--vitamin C, heavy drugs, DNCB [dinitrochlorobenzene]. The biggest challenge was that since the drugs weren't prescribed--they were being gotten from buyers' clubs or god knows where--there was nobody to monitor the blood tests. So you had to deal with the ethics of monitoring bloodwork for a patient who was on a substance you might not personally agree with. What I got in the habit of doing was saying, "I'm looking out for your total health." And if I was neutral to the drug: "I know you're on this. You understand that I can't tell you all the things this drug might do to you, but I'll keep track of the usual kinds of things that often happen with drugs," like by doing liver tests and blood counts. "And if I become aware of something about the drug, I'll tell you, but you can't hold me responsible for knowing about this drug." We didn't sign consents, but I would note on their chart that we had that conversation, so it was very clear. And then I would monitor their bloodwork.

There was one particular study done by a physician who was for-profit. Most of us didn't agree with the study design and didn't feel his motivations were scientific advancement.

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Wofsy: I had a lot of trouble with patients of that particular doctor. That's not uncommon if the doctor is rather charismatic, and the patients think he is doing work that other doctors don't do, and they think nobody cares, and he cares. The patients didn't realize that any medical consequences of this research compound were being, in my opinion, ignored. It could get a little contentious.

I remember in at least one patient's case, I said, "You have to make a decision. I can't manage you clinically with all the ups and downs and things you're taking that really are a consequence of this research drug that's being administered by the other doctor. You call me on a weekend"--people couldn't get directly through on the weekend; we had another system--"and at odd times about side effects and how you're not feeling good. I'm not actually prescribing anything for you. All of your symptoms are from this other investigational drug. Yet you explain that this other research doctor is too busy; you can't reach him; he won't take calls...this isn't working." On one occasion, I remember I had to say, "Fish or cut bait." But usually we worked with alternative therapy, and it worked very well.

Hughes: If a patient were part of a trial, was it possible to control what the patient might be taking outside the trial?

Wofsy: Well, that's a problem of all research studies, and that probably became more of an issue in the last five or six years. There are some exclusions for most patients on a research protocol for, let's say, ddI. They're asked not to take certain categories of drugs. And so if they are, they usually don't tell you. But then of course, people are taking a wide variety of other drugs. As the years went on, we recognized that we had to be more and more lenient about what other drugs they were taking.

So the goal is to record the other drugs the patient takes. Let's say you're studying ddI. If everybody with ddI had a low white blood cell count, maybe they were all taking an antifungal drug, so that had to be written down.

Following a Patient through the AIDS Clinic

Hughes: Well, I pulled you away from a discussion of the clinic. What happened to a patient when he--probably he--

Wofsy: Yes, it was he.

Hughes: --presented himself for the first time?

Eligibility

Wofsy: When he presented himself for the first time, he would come off the elevator right into an eligibility area where he would talk to someone at the front desk who initially probably did the intake eligibility as well as make the appointment. A chart would then be initiated that would--

Hughes: What made a patient eligible?

Wofsy: Just being there. In other words, whatever eligibility applies to patients at San Francisco General now applies to patients in the AIDS Clinic. I think eligibility requirements were less stringent in the early to mid-eighties, and probably less also in the AIDS Clinic. So in terms of reimbursement, someone who lives in Contra Costa County shouldn't come here unless he has some sort of insurance. We will take care of indigent people from San Francisco, but not Contra Costa County. Patients got around this by having multiple residences. So people gave San Francisco

addresses. It's not clear they always spent all their nights at the address that was listed.

Hughes: But you didn't worry about that.

Wofsy: We didn't worry about that; we didn't try to police. In fact, the physician probably hadn't a clue what address the patient put down. I knew from my work in the ER [emergency room], because we would send letters to people with abnormal lab tests, how routine it was for the patient to give a fictitious address. They weren't bills that were going out. We'd send them out because they needed to know results of a lab test.

The billing operated through the UC system here at San Francisco General. And then some time in the late eighties, we got an eligibility clerk, which is a position through the county [of San Francisco]. All the other clinics--the medical clinic, the surgical clinic--had eligibility workers to determine your eligibility for Medi-Cal, for services here. And we began having those workers in the clinic. That was the first employee who wasn't a UC employee. She was a city employee.

Links with UCSF

Wofsy: The clinic is a city clinic, but it's staffed by personnel who are all hired through University of California because they've arranged a contract. So the city monies are handled by the University of California.

Hughes: Is that true of every clinic here?

Wofsy: No, all the other clinics are county. All of that seems like, "Why is this a deal?" But all the other clinics--medicine, surgery, family practice, obstetrics, diabetes--are part of a county system and have telephone lines that link with all the other telephone lines in the county hospital. We have UC phone lines, we are UC employees, and our clinic follows UC holidays, when the clinic one floor down follows county holidays. So the clinic downstairs may be open on Washington's birthday, and we're closed. And they may be closed Christmas Eve, and we're open because we follow a different set of holidays. It's bizarre.

Hughes: But it also has broader implications, does it not? If AIDS is the only university clinic, the approach is going to be different?

Wofsy: I don't think that's true, because the academicians are in the other clinics. They're UC faculty.

Hughes: I see.

Wofsy: The unusual part is that the clerks, nurses, and phlebotomist in our clinic are all hired off of the UC contract. So they're UC employees. Whereas in the medical clinic, the phlebotomist, the nurse, they're all city employees.

Hughes: All right. Our hypothetical patient was in the eligibility stage. When you mentioned eligibility, I thought you meant in terms of AIDS symptoms?

Wofsy: No.

Hughes: But that must have come along at some point.

Wofsy: It did, but that was largely for screening to see if there was a particular clinic that was most suited to that person's requirements. That wasn't eligibility so much as triage.

Hughes: How did the patient first get to the AIDS Clinic?

Wofsy: There are probably some early data of whether they were self-referred, whether they were referred by the [SFGH] medical clinic, whether they were referred by the AIDS Health Project or the San Francisco AIDS Foundation. Many different ways.

Hughes: And did the word get out--

Wofsy: Very fast. We didn't have data; we weren't computerized.

Expansion

Wofsy: The clinic outgrew our half-floor, and again largely Paul negotiated and got the other half of the floor, kicking other people out. It was a bad scene, and we were told never ever again would we ever get one ounce more space. Then we outgrew that; and again, there were negotiations, and we got this second floor, Ward 84. So Ward 84, administrative; Ward 86, patient care. And then we were told, "That's it." That's pretty much been it.

Hughes: Who was involved in the negotiations?

Wofsy: The negotiations were principally Paul.

Hughes: With whom?

Wofsy: The chief of medicine, Merle Sande, the people who were using the space, and space committees. Since Paul was doing most of it, I don't know who all he met with. But there were a lot of negotiations.

Hughes: What accounts for his success?

Wofsy: Partly I think it's his personal characteristics and negotiating skills, and partly it is an epidemic runaway disease. So that if you could frame your needs in a reasonably articulate way--this isn't to diminish Paul's skills, because I think his skills are extraordinary--but it wasn't as if he got space for a disease that wasn't expanding. There was a very important secondary motivation, which was that patients were going to other clinics.

Hughes: What was wrong with that?

Wofsy: They didn't have the staff. So there were a lot of reasons to ensure that there was adequate space for patients to be seen here.

Hughes: Can you remember when the first expansion came?

Wofsy: It happened fast, so within the first couple of years, eighteen months even. And then we moved to [Ward] 84. I was initially in Donald's office. I was there for a couple of years, then I was upstairs in [Ward] 95. Seven or eight years ago, we moved down here, probably in '86, something like that.

Hughes: Would you say that with each expansion the administration acknowledged the importance of what you're doing?

Wofsy: Which administration?

Hughes: The administration of San Francisco General.

Wofsy: I don't think so. I think the fact is, the turf battles for space are legendary everywhere, and they're no different here than anywhere else. Some of the expansion was due to obvious need. I don't think that there was really any quarrel with expanding from half a floor to a floor. I mean, there was, but I think by the time it was said and done, it didn't feel like a space war; it felt like an epidemic.

When we wanted this whole floor [Ward 84] for administration, I think there was a space battle. The issue was not empty space and you're competing for who's going to occupy it, but the fact that people have to get kicked out.

Hughes: That wasn't the case in the very beginning, was it?

Wofsy: People were always kicked out. Ward 5B was the housestaff sleeping quarters. So other locations had to be found for them, and they were, and they were very unattractive.

Hughes: Well, let's go back to our abandoned patient. [laughing]

Wofsy: Right. He's gotten through eligibility. And then he would go to a room right next to the front desk where he'd get vital signs, blood pressure and that kind of stuff. Then a nurse would take the chart and put it wherever the doctors were, indicating, Ready to be seen. And over the years, we got more sophisticated at assigning patients to individual doctors. I think in the very beginning, there was a pile of charts, and just like the ER, you took one, saw a patient, took another.

And then we pretty quickly went into a system of at least having your own lists of patients, which is the way a lot of the clinics do it here. You don't have an appointment time, but you know you have this stack of patients that's going to be yours. And then we moved to appointments, and now that's what we have--appointments for your own patients and new patients.

Hughes: How quickly did the staffing of the clinic increase, and where did it come from?

Wofsy: It came early on [1983] from a city contract providing money to take care of AIDS patients. But the city contracted with the University of California, so that the paychecks for the nurse, the social worker, come from the University of California. So it's city money. Then some is research grants. Then there's something called CFAR, Center For AIDS Research, an NIH grant, to provide infrastructure for places seeing a lot of AIDS patients and doing a lot of AIDS research.

And then doctors began to affiliate, applying for money and getting their own grants. So like topsy, it grew. It was me and Paul and Donald and Gayling and Bobbie Wilson. And then who came? Probably very early on a social worker. We've had a number of social workers who've died of AIDS, so probably a social worker got added in about there. And some of those social workers came through a social workers pool, were hired by the city and then told to spend half of their time here or some such, and some of them had come from other contracts.

Hughes: Does that system work well in a very specialized area?

Wofsy: There are problems. It works okay. It's not unlike what happens elsewhere in hospitals, so that's not unique.

Hughes: In the AIDS inpatient ward, I understand that the staff was self-selected. They were there because they wanted to be; they chose to be.

Wofsy: Oh, they chose. By assigned, I was thinking of pay source. Nobody's ever been here who didn't want to be here, by and large.

Patient Examination

Hughes: Where is the patient now?

Wofsy: The patient is now being examined. Then we designed a couple of things along the way in the early eighties. We designed a nurse screening form, because we were getting so many patients.[1] They were usually relatively well, but the nurse could do an initial assessment: a history, a physical enough to identify needed blood tests. The nurses can't officially make [diagnostic] pronouncements on the physical examination. In other words, Kaposi's can be staring them in the face. They can say, "That looks like Kaposi's to me." By a technicality, the nurses can't be the final diagnosticians because of licensing rules.

So there would be a nurse screening clinic where the patients would see a nurse. We devised a form specific to AIDS. All of this is so ordinary at this point! But it was a big deal then.

Like other diseases where there's a routine--eyes, nose, ears--there are certain things that are so routine for AIDS. In the oral exam, there was a checklist for hairy leukoplakia, which you never see anywhere else but in AIDS.[2] So we focused on those conditions you see with HIV, and we didn't focus on the psychosocial history. We did get a history of allergies, but not all this other information.

Hughes: Were you periodically having to update this form?

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[1]For more on the nurse screening clinic, see the oral history with Gayling Gee in the AIDS nurses series.

[2]For more on the association between hairy leukoplakia and AIDS, see the oral histories with Deborah and John Greenspan in this series.

Wofsy: No, we actually used it for a number of years. We did a very good job. We initially had nurses do that. Then we gradually hired two or three nurse practitioners, who are licensed to do a physical exam, and gradually the nurses phased out of doing this screening, and the nurse practitioners began to do it.[1]

Hughes: Was this fine with the physicians involved?

Wofsy: Oh, yes.

Hughes: You were glad to get rid of the work.

Wofsy: Oh, yes. It was Paul and me and Donald calling the shots, and then additional people were hired. So oh, it was great adding nurse practitioners.

Hughes: Nobody ever felt, These nurse practitioners are moving into our territory?

Wofsy: Oh, no, not at all.

So the patient's been examined. If it's a nurse visit, they have recorded this [nurse screening] form; if it's a doctor visit, they have recorded as they would. Then there's a piece of paper that has the blood tests that are needed and when to come back to clinic and ultimately a billing code. Those all sound so straightforward, like every clinic in the world must have something like this. But they didn't. So they got developed phase by phase.

What was different about our clinic than the other clinics that go on in the County[2] is that it was a little more like private practice in that the doctor made a checklist of what was needed, and somebody else stamped the forms and wrote the lab slips. So you'd see the patient and say, "You need this, this, this, this, and this," and send the patient up to the front desk. They would have a stack of forms. They would pull out the right ones, stamp them up, record what was needed.

At the same time I was seeing the clinic patients here, I would go over to the infectious disease clinic and see rather similar patients. But there, I had to collect all the lab slips, get the patients' cards, write them, stamp them, check them, give

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[1]See the oral history with Gary Carr, a nurse practitioner in the AIDS Clinic, in the AIDS nurses series.

[2]"The County" is a nickname for San Francisco General Hospital.

the patients directions on how to get to the laboratory, how to get to x-ray, how to get back from x-ray, and tell the patients the location of the bus stops in front of the hospital. So the two clinics operated quite differently.

Hughes: Why was AIDS run more efficiently?

Wofsy: Dedicated staff. Because we have enough patients, and the staff were hired to do just AIDS, we are in control of the staff. The staff belongs to the AIDS Clinic. In other clinics, a nurse will do endocrine clinic in the morning, ID the next morning, diabetes the next morning. So individual nurses may develop particular areas of expertise, but they're not on one unit exclusively. Here, there's the doctors, the nurses, the social workers: we are familiar with each other at our staff meetings.

And so the patient's been seen, he gets his x-rays, he does whatever, and then he comes back two weeks, four weeks, eight weeks later.

Hughes: How does the set of clinics in the AIDS Activities Division fit in?

Wofsy: There was a set of clinics, so patients would come to the OI [opportunistic infection] clinic or the Kaposi's clinic, and then within a year, the clinics all looked the same because Kaposi's patients got PCP; the PCP patients got Kaposi's. We initially had ID people in the ID clinic, and oncologists in the KS clinic, but then the oncologists were managing cryptococcus, and the ID people were managing Kaposi's sarcoma. So the term "AIDS specialist" was coined. But it's a descriptive phrase, because there is no board certification. There's no reason why I shouldn't help take care of Kaposi's sarcoma, or Paul shouldn't help take care of cryptococcal meningitis. Those conditions are way outside our specialties--one's an oncologist; one's an ID specialist.

Gayling Gee really developed the clinic in terms of its structure and when the social worker came in and how we all related. She put the form to it, at a real administrative nursing level. Her title was head nurse, but she ran it--not the doctor practice, but how we did things here.

The AIDS Inpatient Unit at SFGH

A Unit of the Nursing Service

Hughes: Please comment on the interrelationship between the clinic and the ward.

Wofsy: In the clinic, the head nurse functions as the senior administrative decision maker, is hired as part of AIDS, and so reports to Paul or me or later a clinic director--all of us over here in this brick building [Building 80]. In the [AIDS] inpatient unit, the head nurse is part of the inpatient nursing service and reports not to a doctor, but to the head nursing administrator. She or he is expected to run a nursing unit by certain guidelines and expectations, just as in the orthopedic ward or the pediatric ward; that's the line of responsibility. So there isn't a doctor who's head of the inpatient unit, and never was.

Paul and Merle [Sande], and I to some degree, and many others, were responsible for developing a fixed site in the hospital where AIDS patients were seen and for setting up the guidelines for a head nurse. But the first head nurse, Cliff Morrison,[1] really developed the unit, just as Gayling did the clinic.

Hughes: And you knew it was going to be that way.

Wofsy: Well, we didn't know what would evolve. Cliff was the one that took the ward where it got.

Hughes: Yes. But it was intended that he was to develop it.

Wofsy: Right. Paul and I were very present on the ward. We were resources, but not the directors of the ward in the way we directed the clinic. The clinic was really its own administrative unit.

Hughes: Is this typical of other wards at San Francisco General?

Wofsy: Yes, except that other wards don't really have any associated doctor.

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[1]See the oral history in the AIDS nurses series with Morrison.

Hughes: So they're strictly nursing units.

Wofsy: Yes.

The 5B Conference

Wofsy: There were a couple of years where I was the liaison, and I would meet with the nurses and head nurse periodically, and we would go over decisions. I guess for two or three years, I ran with the head nurse a conference, the 5B conference, that took place on Tuesday afternoons. We either reviewed the cases on the ward or sometimes had a topic for discussion. They were very widely attended; thirty or forty people would come, as many nurses as could get away.

After a couple of years, a conference sort of runs its limit. Attendance dropped off, and it became more of a nursing discussion. Then after a few more years, it turned into a discharge planning meeting. Nurses would review all the patients being discharged and plans that were made for home therapy, et cetera. A nurse from our clinic would be a liaison for the discharge, but the physicians largely were no longer part of it. I would say that conference had its heyday from about 1984 to 1986 or '87.

Medical Directors of the AIDS Inpatient Unit and Clinic

Wofsy: So sometime in the mid to late eighties, Dr. Michael Clement, who had recently completed his residency at the University of Oregon, was hired to be the director of the AIDS inpatient service, to actually give it medical direction, working with the head nurse. The overwhelming majority of his time was spent in the inpatient unit, though he came often and saw patients in the clinic. So he was very familiar with both units, but he served the inpatient unit. He did consultations on the patients and he met with the nurses so that they had a sense of direction.

Then the inpatient unit took on a structure that was much more like a ward: a head nurse reporting to nursing administration, but working in a team approach with the new doctor-director. Michael was very green. He was wonderful, but he had just finished his residency.

Hughes: Was that an easy transition since the nurses had been running the show, so to speak?

Wofsy: Oh, yes, I think it worked very smoothly, largely because of Michael's personality.

Paul was technically the clinic director. I was the co-director. The AIDS Clinic was such a big operation; it now had clinics every day of the week. Paul and I had taken on so many other responsibilities that we couldn't really keep up with the day-to-day management of the clinic, do all the research studies, the education, and the, and the, and the. We decided to have a clinic director, and Michael Clement, who had been in the inpatient unit, was asked if he wanted to come over to the clinic, which he did. That left the inpatient unit high and dry.

So another doctor was hired, Dr. John Stansell, and he did a magnificent job of running the inpatient unit. Then Michael Clement left to go to Kaiser, so John Stansell took over as clinic director. By that time, there were two doctors working with the inpatient service, so they worked it out so that both units were covered.

Friction

Hughes: Were there ever frictions between the clinic and the ward?

Wofsy: Absolutely. It's always been a friendly squabble--just like siblings. So much in common, and when the chips are down, it's a bond. When the chips aren't down, there's--not rivalry--just a little suspicion that the other side is getting more attention, more acknowledgement, more something. And it's not generated by either side. It's just there.

Hughes: Does it sometimes revolve around coordination, such as referring patients from the clinic to the ward?

Wofsy: No. For that kind of thing, there are very smooth pathways. That doesn't happen at all. It has to do more with who's in charge of research studies, approaches and philosophies to patient care, and certain things which are ambiguous about the patient. For example, suppose a patient is sent over to the transfusion center to have a transfusion, so he's wandering around the hospital, looking for where he's supposed to go. He has a stomachache. Well, he knows the people up on the inpatient unit really well, so he stops up and he mentions the stomachache. But they're not

really supposed to take care of stomachaches of people in the outpatient clinic. So they say, "Go over to the outpatient," but that's two blocks away.

The other thing that happens is that the research in this clinic is directed almost exclusively by the doctors who are here in the clinic. The research that goes on in the inpatient unit comes from a lot of different sources and different doctors. So it's a different group of people conducting a lot of the research, and that has its own area of tension. I will put a balance on tension, not a capital T, a little t.

Dedicated AIDS Inpatient Unit versus Integrated Medical Ward

Hughes: You mentioned last time the debate before the ward had even been established about whether it was a good idea to create what might be construed as a "leper colony."

Wofsy: Right. I was asked to give a talk after the ward had opened [1983] on "Dedicated AIDS Unit versus Integrated Medical Ward." It was a topic I hadn't thought about at all. But to give the talk, I had to give it considerable thought, so I interviewed nurses, and I really put a lot of effort into it. There were a lot of people in the audience. I'd been asked to talk about the topic because it was very germane, and people were giving it a lot of thought. I subsequently saw almost a transcript of the talk appear in every possible kind of nursing and throwaway journal.

I think the bottom line is that the ward was initially set up with the belief that we could monitor infection control, that there would be a dedicated group of nurses with clinical expertise, and that the nursing-to-patient ratio would be different than the other units, and that certain kinds of things would go on in terms of patient education. Shanti services, certain kinds of counseling, were truly unique for this patient population, and it would be best for everybody to have AIDS patients together in one unit.

So we developed a philosophy when it was opened that although another person could construe this as isolation, we were isolating based on what we thought was truly the best interests of the patient and the staff. We also established a philosophy that only staff would be hired who wanted to be on the ward. There wouldn't be any staff assignments to the unit. Then there was a big ceremony when the ward opened [July 1983]; the mayor [Dianne Feinstein] was there, and everybody was there. It was a big deal.

The other thing we debated when the ward was opened was because the beds wouldn't be full [of AIDS patients], what other patients would go up there? At the time we began initiating the planning of the ward, there were two AIDS patients in the hospital. But by the time the ward opened, every bed was full. Initially it had twelve beds. As far as I know, there has never been a person up there without AIDS. Maybe there has been because of unique bed-control problems, but for all intents and purposes none.

The flip side was the concern that the existence of an AIDS ward would allow other nursing units to lose their skills in AIDS medicine or say, "I don't take care of AIDS." But not only was the ward full from the first day it opened, but also it was clear that we couldn't house all the AIDS patients there. Because we initially said AIDS patients had to have a private room, that meant the overflow couldn't all go to one other ward, because it didn't have enough private rooms. Patients had to go to private rooms on each of the floors, so all nursing units maintained their skill at taking care of AIDS patients. I mentioned last time a very aggressive infection-control program in terms of educating people. So all nursing units were highly educated.

Hughes: Educated also in the unique problems of caring for AIDS patients? Infection control is about safety issues.

Wofsy: I think that was a little bit more lax. It did turn out that there was a cluster of AIDS patients that occurred on another medical ward, so that if the beds on 5B, which was then the AIDS unit, were full, and there happened to be beds available in this other ward, they would go to the other ward, where there was a group of nurses who took considerable interest in AIDS.

Obligation to Care for AIDS Patients

Hughes: Was there a problem with staff who didn't want to care for AIDS patients?

Wofsy: There was. We made a policy decision, which I think was in that article,[1] that San Francisco General is a hospital with a lot of AIDS patients, and that everybody must take care of patients with AIDS. There probably were individual situations where a person

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[1] Conte et al. Infection-control guidelines..., 1983.

had such a horrible attitude that there were silent nursing reassignments, but if so, that was not a major visible issue.

The next thing we had to deal with was pregnant nurses and doctors, and people who had other reasons why they shouldn't care for AIDS patients, such as they were on some immunosuppressant medication. What we ultimately concluded was that if a person was immunocompromised because of medication or a disease, that they could of course get a note from the doctor exempting them from AIDS care. It would be reviewed by a subcommittee of the infectious disease committee, but you couldn't specify exemption from care of just AIDS patients. The risk of tuberculosis, the risk of a lot of other diseases around here was high, and we would certainly be sensitive to employees who had special immunologic problems or whatever. But that policy had to be applied across the board.

Hughes: What was the decision about the obligation to treat AIDS patients based on?

Wofsy: We based it on the existing evidence of no AIDS in health care workers, that the modes of transmission by infected people were so clearly that of hepatitis B, and that there were guidelines for protection. It evolved that you couldn't have one group of people who did and one who didn't care for AIDS patients, just by their preference. You had to say, "I'm employed at a hospital that at all times has a dozen or more patients with this condition. I have to decide whether I can work at a hospital that has that character."

I don't know if we ever made the analogy, but it might be the same as, "I don't work with criminals. I think people who are in jail are terrible people." You couldn't work at this hospital, because we are the designated place where people from the jails come for their medical care.

Hughes: Did the policy work?

Wofsy: Eventually, yes. [tape interruption] It's important to remember that this hospital had highly visible incidences of dieticians leaving trays to get cold outside of AIDS patients' doors, and people gearing up in all kinds of protective costumes that weren't necessary. You could write legends about those kinds of things. But they probably were nipped in the bud here more quickly than at most any other institution. It was those things that prompted us to hire somebody that just gave classes in infection control every day until everybody had had two or three of them. So it was by no means simple, and we had all the problems all the other hospitals did.

Hughes: Those classes nipped problems in the bud?

Wofsy: I think the classes contributed, but it was more the attitude of the supervising level of nursing medicine that said, "It is a priority that we will get people into the classes," not policied to death, but educated to death. The philosophy of, We will teach you what you need to know so that you can be comfortable, permeated in many different ways. The other thing is that it became clear that in the units where there were problems, it was almost invariably because a particular supervisor had an attitude. We would then target that supervisor, because if the supervisor got it [the obligation to care for AIDS patients], the staff would be okay.

Fear

Hughes: Why was some staff reluctant to deal with AIDS patients?

Wofsy: Just ordinary raw human fear. Nothing malicious. Homosexuality is so acknowledged, accepted.

Hughes: What happened to the fear when the virus was identified and eventually the test evolved?

Wofsy: I think it got worse in certain ways and better in certain ways, and it went through waves. There was the dietician; then we had to deal with the plumber cleaning the sink traps. Each time you thought you'd thought of all the things that had to be dealt with, there was a new one. And then the pregnant employees issue was big. We had to make the decision whether to treat pregnant employees differently, and that was years in the making, and we decided, No, you don't.

Hughes: Where did you make these decisions?

Wofsy: Infection control committee. Everything was so new and involved; we had this AIDS infection control task force [UCSF Task Force on AIDS] that published in the *New England Journal*. But then after a couple of years, things went back to the individual hospital infection control committees, and we made those decisions.

We started the health care worker study probably in 1984, 1985, to look at people who got needlesticks working with AIDS patients, and how we dealt with them. And now that's in its own department of occupational medicine.

Hughes: What were the results of that study?

Wofsy: The results were that people weren't getting infected, by and large. One employee did. So I think that the results of the study were positive, because it was a source of information. You had a sense that you could do something if you were exposed; you could be tested. We were a knowledgeable site; we were in the loop; we had access to the CDC.

Ward Atmosphere

Hughes: Would you talk about the atmosphere of the ward?

Wofsy: It was fun. The patients did interesting things with their rooms, and the nurses were bonded. I would say that unacknowledged but certainly playing a role is that at all times at least some not insignificant percent of the nursing staff came from the population most affected. And I think it makes a big difference. A lot of nurses were gay men; there were lesbian women who had particular interest in the epidemic; there were straight women. I don't think that there were a lot of straight men--well, I'm sure there were straight men who were nurses, but probably that [demographic group] was the lowest percent. The nursing staff, I'm sure, always included all sexual persuasions. Nor was it verbalized. You didn't know who was what; you had certain inferences and guesses, but that wasn't the topic of conversation.

The staff included a lot of members of the gay community. Their motivation was more than just the medical oath that they had taken. That's just the fact of it. It was their epidemic too, and I suspect some of them were infected.

The Ward as a Model

Hughes: What other facilities have been modeled after the ward?

Wofsy: One by one, major metropolitan cities went through the dilemma of whether to have a dedicated ward or whether to just fit people with AIDS into their existing hospital structure. So one of the things people took away, whether they were coming for a one- or two-day visit, or as part of this one- to four-week educational program [APEX], was the decision analysis of whether they should adopt such a ward for themselves. So part of the reason the

droves of visitors came through the AIDS unit was to learn how to organize such a unit and how they might apply it to their hospital.

After the unit had been open for maybe five or six years, we began to get visitors from other cities who had adopted the model, incorporated it, but modified it to their use. We began to realize that we were a little stale. We were a wonderful model for us, but it's like you notice your furniture is a little worn around the edges, and you keep thinking of it as your new sofa. For example, the model didn't have some of the features that were right for IV drug users.

There were innovative plans that had been incorporated elsewhere. Dick Chaisson, one of the residents here who then spent two years on the faculty, went to Johns Hopkins and took all that he had learned about our model, coupled it with some new and different ideas and a different population in Baltimore, and set up an inpatient unit which in many ways surpassed ours. That unit has done some things that are--I don't know whether I can say better, but are innovative. It works for them. It was because of the opportunity to watch this model evolve here, and take the best of it, and add elements to the model for the needs of IV drug users, and see the mistakes that got made here with housestaff, and think of a better way to educate housestaff, that Hopkins developed something that's equally good to better. The San Francisco model sprang up all over the U.S.

Hughes: In general, would you say that the changes made in the San Francisco model were ones of adaption to a specific circumstance, or was it more changing certain elements which didn't work as well as they might?

Wofsy: Adapting. We have a really good system, and I think we troubleshot what could be troubleshot. I don't think they came and saw the flaws and said, "Oh, let's get rid of them."

Hughes: Was the AIDS Clinic used as a model in a similar way?

Wofsy: I think so. But clinics have always existed, so I think that it was more how we did the clinic than that we did the clinic. Whereas, with the inpatient unit, it was <u>that</u> we did it and how we did it.

Hughes: So it was more conceptually revolutionary.

Wofsy: I think so. The clinic was not conceptually revolutionary. We did some quite startling things within it. But it's not

revolutionary to have a clinic dedicated to obstetrics, or renal dialysis, or what have you.

Hughes: When you say startling things within it, what are you thinking of?

Wofsy: Gee, they seem so unstartling now, but the relation of the nursing staff and the doctors--they were truly a team, more like a CCU [cardiac care unit]. In the CCU, the nurses and doctors really are professionals working together. We [in the clinic] were a team, so that our priorities and standards and expectations were a circle, not a hierarchy.

Then the other thing we did that was very--startling is too strong a word--is integrate patient care and research in one place. Many of the clinics that tried to do that weren't successful. They couldn't find a way to integrate, "I'm a research nurse; I'm a clinic nurse. I'm a research doctor; I'm a clinic doctor." They couldn't find the way to make it work together, and so they ended up splitting up, which was to the detriment of the patients and I think ultimately to the staff. We maintained clinical care and research in a single site. And that's a tribute to a lot of personalities who worked hard to do that.

Visitors

Hughes: Well, talk about the visitors who began to come to the ward and clinic.

Wofsy: Oh, people came in droves.

Hughes: When did they start to come?

Wofsy: Oh, back in about 1985, maybe even earlier. Bobbie Wilson, who was the first administrator [of AIDS/Oncology Services], took on the role of organizing the visitors. So if they came for a half-day, she'd arrange a program so that they'd talk to the right people. And then we got some money from Huey Lewis and the News [rock band] for education.

AIDS Provider Education and Experience [APEX]

Participants

Wofsy: I was keen to do that and took on organizing a program called APEX. The first one was four weeks--I can't believe we did it--but we brought them in for four weeks, and had a curriculum that ran eight hours a day for four weeks.

Hughes: What did you do?

Wofsy: I can't even remember. I can't believe it; it's so exhausting to think about!

Hughes: [laughs] And you were involved for all four weeks?

Wofsy: I ran it. I didn't do all the teaching, but I knew all of the participants and I looked after them.

Hughes: Were they all physicians?

Wofsy: It was designed for physicians. From time to time, we had nurses. And that's a whole story unto itself, because the people came from all over the world. They probably came from one of three motivations: One, they really were going to do AIDS work, and they took this information back and they used it. Two, they had an interest in the disease or the community for some personal reason, not necessarily their own; it might have been a family member or relative with AIDS. A surgeon came and took the program, and it never quite made sense. I had a feeling the interest was more personal. Three, another agenda.

There were a couple of interesting cases. A man came from China. That was our first program and we were naive. We didn't know about visas. He applied, got somebody to write the letter in English. China had just opened its borders. It was okay with us. The visa gave him a means to get out of China; he never went back. But he also had nobody here. It became an issue for us how to deal with this. His expectations were beyond anything that had been offered. And he's still here, not at the hospital, but he's been seen out in the community.

The other thing that's happened on a couple of occasions: Somebody came to get educated with the anticipation of taking a major position in AIDS--running a clinic--and after completing this intensive program, realized it wasn't for them. So people

have had many motivations over the course of time. We've probably had well over a hundred people come, probably a couple hundred.

Hughes: Anybody that cares to come is welcome?

Wofsy: We have an application. Well, I should go back: Huey Lewis and the News wanted to give monies to education. I was keen on that. Paul and I worked together. I developed the curriculum. We hired an administrator to deal with the scheduling and one thing and another. It was our child, this administrator's and mine. We applied for funding from the NIH, and it was not granted. The NIH really wasn't giving funds for that kind of thing at the time.

Initially we put too big an agenda on our course. It turned out that initially we either got people who were already doing what was being presented in our program in their own country or city, or people who had been exposed to HIV positives but hadn't really dealt with the medical problems. You can't mix them. You can't learn intensively about advanced HIV disease when you're really at the phase of counseling and testing, and vice versa. If you've already gotten to the point that you're really managing some of the infections, you don't want to relearn what you already have been through.

So we realized as we looked at the applications, we had to take a little bit more care to do one or the other. We've had as many as twelve people. It used to be mix or match--we'd have people from overseas, from the U.S., from California, from Iowa. We've had local programs; we had a half-day program for nurses.

The most ambitious was one program with the WHO [World Health Organization] that was for Eastern Europe, and this was again just after the borders were opened. I'm not astute about tensions in the Eastern Bloc. We ended up in one room for four weeks with a Russian and Ukrainian, two from Hungary--who in their own hospital have tensions between them--a husband and wife team from Poland, a man from Bulgaria, and, if you can believe it, at the time the war was breaking out in Yugoslavia, three from Yugoslavia representing every group that was at war with each other. They sat in a room together for four weeks, and they became each other's companions. So I'm not sure whether they got a medical course or a United Nations.

Hughes: [laughs] You might have helped the peace effort.

Wofsy: I think I may have helped the peace effort more than anything else. That was a really unique experience.

Hughes: You hadn't initially considered this aspect?

Wofsy: Well, we let the WHO make the selection of who the people would be, that there could be up to ten people. And then somebody from Yugoslavia who coincidentally was going to be here for another reason and joined the group.

APEX is my own child. Many of the things you and I have talked about involved many people taking different roles at different times. As I said, Paul was really the locomotive for the ward and the clinic. We worked together in many different ways and took different parts of them. This one, this APEX, was mine.

Community Visits

Wofsy: We incorporated community visits in APEX, which now are so commonplace that you can't even remember there was a time when that was unusual. But we kept adding interesting and unusual things, like the buyers' club. We went once to Quan Yin, where they do acupuncture. We went to places like Coming Home Hospice, and the AIDS Foundation, and all the places that you would logically think of in connection with AIDS support services. We went to private doctors' offices. We went to Project Inform. We went all over, as well as having workshops where we'd have faculty do a discussion of lymphoma or PCP. And participants would go to the clinic, the ward, and other sites within the hospital. And I think, to a person, they loved their time here.

Memories

Wofsy: I know another funny story. We had a group, about ten people--about a third from California, a third from other states in the U.S., and a third that was European. The hospital at that point, circa 1988, had just incorporated no smoking in the workplace.

To the Europeans, it wasn't so much that it was restrictive; it was unfathomable. They saw that no one was smoking inside, and they learned to go outside. The program was over at five o'clock, and it was held in a certain solarium on another floor. I remember I was making rounds, so I came back at about five-thirty, because my office was nearby. I saw lights in the solarium, and I went in. [laughing] An Austrian was sitting underneath the conference table smoking. [laughter] He hid.

Hughes: What the Americans had reduced him to!

Wofsy: Oh, I don't know that that relates to AIDS, but to me, that's the kind of memory that is incomparable.

The other memory is--you're not asking, but I'm going to tell it anyway: On a Monday, we started one of these [APEX] programs, and it was a small group, about six doctors. They had come in, and we had done the orientation. Tuesday, we had to run late. We couldn't get all the material done if we didn't schedule a particular lecture at five p.m. to six. We used the solarium in this brick building [Building 80] as our classroom. So we were having a lecture on how to conduct research in *Pneumocystis*. I was there, several faculty, and all these visitors. It was four minutes after five and the building began to shake. It was the Loma Prieta earthquake [October 1989].

I was conducting this course with some of my colleagues for these individuals, none of whom were from California, none of whom had ever experienced an earthquake. I realized that not only was there the responsibility for the curriculum, but for the safety of people who were not Californians, who don't have earthquake drills, who have never been through one before, and that we were in a brick building with glass walls. We got to safety, and the building didn't fall down. Okay, back to the questions.

Pneumocyctis carinii Pneumonia Research

Initial Interest

Hughes: Do you want to start with PCP studies?

Wofsy: Yes. I mentioned last time that Dr. John Mills, who was the chief of ID [infectious disease] when AIDS happened, happened to go on sabbatical and did research in a related area, but not because he was going to get involved in AIDS. The RFA [request for application] for the ACTG, AIDS Clinical Trials Group, came out, and in a legendary week or a weekend or what have you, John Mills applied and got one of the grants, with Paul Volberding as the co-investigator. So we became a recognized AIDS Clinical Trial Group, along with another fifteen or twenty other sites in the U.S.

At the same time that that was happening, John Mills, who didn't initially take such a keen interest in AIDS, did take a keen interest in *Pneumocystis*. He happened to have an already existing interest in PCP or *Pneumocystis* from some prior experience. Maybe he once took care of leukemia patients. For whatever reason, he had an interest and had actually written one or two review articles. Maybe someone assigned the topic to him. So he coincidentally had an interest in PCP.

That led to a very innovative idea of doing open trials in which fifteen or twenty patients would get a certain kind of therapy to see if it worked. It's not the most excellent science, because in the best science, you compare drug A to drug B and see which is better, or you compare drug A to placebo (to no treatment). But in this case, there was no comparison group. But the idea was that in an animal model, there were certain therapies that looked like they might work, and that before we got involved in a two-year, multi-multi-thousand-dollar study, let's get a certain number of patients, see if there were unexpected toxicities, and whether there was general benefit. Those kinds of studies wouldn't fly now. They wouldn't be of enough scientific rigor. But then it was rather innovative.

So John and I worked very closely together, as well as a few other people, and did some of these trials, and got them written up rather quickly, and then embarked on several comparative trials of different therapies. I forgot a piece, that I and four or five colleagues had in the very earliest years done a major comparative trial in PCP, so there are three factors: chief of ID is beginning to get interested in AIDS because of his preexisting interest in PCP and does studies; he applies and gets the ACTG money; and a group of us have worked together for another major study in *Pneumocystis* before those other two factors were active. So suddenly we became the national site doing studies on *Pneumocystis*.

Then it got so interesting that ID was doing studies; the pulmonary group was doing studies; the microbiology laboratory got interested in doing work, looking at PCP in the laboratory and how you could identify it and diagnose it. Then the pharmacologists got interested in looking at the pharmacology of the response to medication.

The *Pneumocystis* Study Group

Wofsy: I mentioned the things that are mine collaboratively and mine conceptually. It was mine conceptually that we needed to have a formal way we all got together to share our experiences and coordinate the studies. So we started what was then called the "*Pneumocystis* for Lunch Bunch." [laughter] We never got it printed, but we even had a logo. We would get together about once a month, multidisciplinary, and people would present the studies they were doing and get ideas. As the years went on, the group set priorities, because one of the people over in pulmonary would get a great idea for a study that was going to need 100 patients with *Pneumocystis*, while somebody over here was getting a different great idea and beginning to talk to funding agencies about money. Suddenly, everybody was assuming the patients belonged to them.

Hughes: And competing for money.

Wofsy: And competing for money.

I chaired the group, and then it became more officially the *Pneumocystis* Study Group. I chaired that from its informal start in 1984, and probably the last official meeting was in 1990, maybe even 1991. So it evolved as this informal discussion group, then became informally formal as a way of setting priorities, presenting data, networking for fellows who were getting involved and wanted to see the big picture, and then in its latter years there turned out to be some real clinical care issues that almost needed an agency to say, "This is the way we do it."

For instance, *Pneumocystis* was being treated in the general medicine clinic, the AIDS Clinic, the family practice clinic, the AIDS inpatient unit. But who is it who sets the standard for the way we do it here at this hospital? It's not the infection control committee; it's not each attending physician. So we used this mechanism [the study group] to come to a consensus on how we would go about treating, and then we sent bulletins out to the ER [emergency room], and family medicine, that the *Pneumocystis* Study Group says that these are the guidelines.

By about 1989 or '90, the AIDS Clinical Trial Groups had become so big, and they were conducting the major *Pneumocystis* research, that it no longer was really logical to have our own group. So it sort of dissipated in its own natural death.

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Wofsy: The AIDS Clinical Trial Group is a national network for the many different kinds of clinical trials for treatment of many conditions: *Pneumocystis*, cryptococcus, Kaposi's sarcoma. The idea is it's multidisciplinary; you have to set priorities; you can't study everything all the time. Now we're so used to the term "multidisciplinary," you can't imagine just the ID people getting together to do research, or just the doctors, because instantly you realize, "But you've got to have a pharmacist; you've got to have a nurse; you've got to have a this." But at that time, that wasn't the way it was.

The Impact of AIDS on Medicine

Hughes: Was it the epidemic that was the motor behind this emphasis on a multidisciplinary approach?

Wofsy: I think it was the epidemic and the volume of clinical research that was being done.

Hughes: Was what was happening in AIDS to a certain extent being translated to all specialties?

Wofsy: To some degree. I think clinical research really has taken on prestige.

Hughes: Did the multidisciplinary aspect become more of a desired criterion for other areas?

Wofsy: Multidisciplinarity is absolutely the norm now.

Hughes: Is it AIDS that is the impetus behind this change?

Wofsy: I don't know. To my eye, it's AIDS. It happened over that period of time. The other thing is, one magnifies one's own little sphere. The *Pneumocystis* Study Group wasn't some big thing in the world's eyes; it was our own internal multidisciplinary group.

Hughes: I wasn't really thinking it all stemmed from the *Pneumocystis* Study Group. [laughter] But a question that many people are interested in is, what general changes is AIDS making on the practice of medicine?

Wofsy: A national consensus group looked at just that question and concluded that AIDS really hadn't had a lot of impact. But it surely was a remarkable coincidence.

More on PCP Research

[Interview 3: January 19, 1994] ##

Deemphasis of PCP Research

Hughes: I think you have a few things to add about PCP?

Wofsy: Between the years of 1983 and currently, but predominantly for about six years from '83 to '89, San Francisco General was one of the main research sites for PCP treatment trials.[1] Dr. John Mills, who was the chief of ID, was the first chair of the OI subcommittee of the AIDS Clinical Trial Group. I was working with four or five PCP treatment trials. We had Ileana Medina, a special fellow here, who took on treatment trials as her research role, and one of the very active junior faculty members, Sharon Safrin, moved into the area of PCP treatment trials. So there was a very significant core of people interested in treatment.

There were only a few other sites in the U.S. where people were interested in doing PCP treatment trials, and so a lot of attention focused on what was coming out of our institution. By about 1989, the sites where research was conducted had diversified, and PCP, though still interesting, was dwarfed perhaps in terms of curiosity and interest by some of the other opportunistic infections, some of the new treatment trials coming out, new drugs being licensed or put up for licensure by the FDA, and so PCP actually moved away from the forefront as the prime OI of AIDS.

In fact, at the AIDS Clinical Trial Group meeting about a year and a half ago when there was a massive prioritization of where our research monies and efforts should go for opportunistic infections, it was stunning to all of us to realize that PCP actually came quite far down the list. We have four or five good drugs; we know a great deal about the disease, and that same kind of effort is now going into cryptococcus, cryptosporidium, and other diseases that there's somewhat less information about. So the efforts have shifted.

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[1] For Wofsy's and others' contributions, see, for example: Harry W. Haverkos. Assessment of therapy for Pneumocystis carinii pneumonia: PCP Therapy Project Group. *American Journal of Medicine* 1984, 76:501-508.

There was this golden era of PCP here at San Francisco General, and to some degree at UCSF as well. While we're still a focus, it just isn't a national focus to the same degree, and so we sort of crank out studies along with several dozen other sites in the U.S. It's sort of wound down.

PCP as a Career Stimulus

Wofsy: I would say PCP acted as the leaping-off point for several people's careers. Sometimes in an academic center, to get your career moving, there has to be something one sinks one's teeth into. Because PCP was such a focus, it functioned in that capacity, I think, for four or five people. So it was a very seminal disease in terms of training and getting people interested in doing research and directing their career towards AIDS. A number of people have redirected their career; mine is probably one of them. But it acted as something that got them to the next step, and now it's taken off in other directions.

Hughes: Did you make a conscious decision to minimize the time you spent on PCP, and actively decided to take something else up?

Wofsy: I think it was more actively taking something else up, and somebody else so naturally and logically taking PCP to its next logical step in an area where I didn't have particular skill. There was just a natural and comfortable evolution.

Hughes: For most people, is there a natural evolution of research interests?

Wofsy: I think my style is a little different. Yes, I think academically that does happen a fair amount. I think a lot of times, people try to retain something. But invariably, I think one site or individual will ultimately take a particular disease as their major thing. If you say the word "cryptococcus," you can name two or three sites where it's happening and they're sort of in charge.

Hughes: What did you mean when you said "my style"? What is your style?

Wofsy: Oh, I just have moved over two or three areas over the course of seven or eight years. It just turns out that I get things started. There are people who start things and then don't want to continue them through the ten-year development phase. There are others who are not starters, but like to get in after it's all off the ground. And then there are a few who do both. I think that I'm a starter.

I started the PCP Study Group. I've emphasized again and again, it sounds like I take individual credit. Not so. But at least I had a substantial role in getting that ordered, multidisciplinary, not overlapping, no infighting, collaborative effort underway. I started the epidemiologic research studies on women and prostitutes at risk for AIDS, and then moved that into the hands, appropriately, of somebody whose training was epidemiology. Then I took on the issue of education and set up educational programs for outside physicians, which have been quite successful. And then I got involved in the ACTG which others had done for five or six years, but that was new to me. I started the Women's Health Committee of the ACTG in 1991.

The Bathhouse Episode, San Francisco, 1983-1984

Debating Closure

Hughes: Did you have any particular role in bathhouse closure?

Wofsy: There were people at SFGH who got involved in the decision--Paul, Donald, myself; I can't remember who else was here. That was way early on when we were the three key people [associated with the AIDS Clinic]. I remember the bathhouse issue occupying just hours and hours and hours of discussions and meeting, and being politically correct, and then trying to be infectious-disease correct, and trying not to offend, and trying to think clearly, and trying to sort out issues for heterosexuals. One was grappling with having ease with a [gay] lifestyle that felt so different, realizing what's politically important to someone with a different lifestyle isn't what's in one's own visual field. And balancing that with how could people put themselves at risk like this by visiting the baths? How could this legally be happening?

So I think the learning curve was unbelievably steep for straight decision makers and for gay decision makers. The personalization removed the objectivity of decision making that would have happened if the issue had been over whether to put certain kinds of filters in the hospital ventilation system.

Hughes: Because the bathhouses were a symbol of gay liberation.

Wofsy: Because the bathhouses were a way of life. So even those who didn't use them--and there were many people who said, "I've never

been in one," or, "I certainly don't go regularly"--had this sense of preserving that culture, as it were.

And then it got into trying to sort out which gay leadership you felt was giving you the most accurate picture, because if one doesn't have any intuitive understanding of this, one has to get it from people who can explain it. And everyone had a different point of view.

Hughes: What was the forum for getting that understanding?

Wofsy: Hallways, administrative meetings.

Meeting with Bathhouse Owners

Wofsy: There was the meeting that was portrayed in *And The Band Played On*. But I remember a pre-meeting that happened in our conference room upstairs.

Hughes: Which meeting in *And the Band Played On*?

Wofsy: Well, there was a public meeting that was held at City Hall.[1]

The meeting I am referring to was with bathhouse owners and health people in 1983. I can't remember who all was in the room. I was not the only health representative. I don't recall forthrightness from the bathhouse owners, but rather this enormous posturing and a kind of denial that I'd only seen in patients with certain diseases, not with AIDS. Incredible attention to, "You have to teach us if Crisco isn't right. You need to be teaching us in the bathhouses, so that we can tell our customers the safe thing. We'll hand out information that K-Y is the thing to use, and not Crisco. We're not doctors; we don't know this stuff; you have to teach us this stuff. This is where people can get educated." I mean, an attention to minutiae, the tree right up close and personal, and an impossibility of seeing the forest.

Hughes: Were you there in an official capacity?

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[1] Shilts describes an emotional meeting at City Hall on March 30, 1984, in which Mervyn Silverman, director of the San Francisco health department, was expected to close the baths, but didn't until October. (Shilts, pp. 440-43.) See also: Randy Shilts. Silverman Delays on Gay Bathhouses. *San Francisco Chronicle*, March 31, 1984. (Gay and Lesbian Historical Society, folder: AIDS 1-3/84.)

Wofsy: It depends on what you mean by official capacity. The plan wasn't to leave the room and determine a policy; it was an information exchange. So we were there in an official capacity, but it wasn't for the purpose of formulating a specific plan. It was part of the whole process of seeing if it could get worked out by increasing understanding and dialogue, short of somebody having to close the bathhouses. I realized after that meeting that it didn't seem like it could get worked out.

Women with AIDS

The Mayor's Advisory Committee on AIDS

Hughes: In 1985, you became a member of the Mayor's Advisory Committee on AIDS. That committee actually was functioning in 1984, but I believe you were not a member of it.

Wofsy: I wasn't an original member.

Hughes: By 1985, the bathhouse episode had essentially been resolved.

Wofsy: Yes. By the time I was on the Mayor's Advisory Committee [1985-1988], I think that was over.

Hughes: So you were meeting with bathhouse owners because you were a physician who was seeing a lot of AIDS patients?

Wofsy: Right. It wasn't in a committee capacity. My involvement with the Mayor's Advisory Committee was because of my increasing understanding of issues about women and prostitutes. There was that whole era where they thought that, like in Africa, prostitutes were going to be the main line of AIDS into the heterosexual male population. So that was really why I was put on the Mayor's Advisory Committee. That was a transition point for me into a focus on women and AIDS.

Hughes: Were you considered the expert on women with AIDS?

Wofsy: Yes, absolutely. There's no question that's why I was appointed to the mayor's committee. But the appointees didn't have something after their name. It was sort of intuitively obvious. It was known that I was entering this area of research.

Hughes: You advised the mayor?

Wofsy: Feinstein, yes.

Hughes: Rather than the health director?

Wofsy: That's right. The health director was part of the committee, and that was [David] Werdegar. By the time I was on the Mayor's Advisory Committee, Silverman was gone. Since he was left with the legacy of closing the bathhouses, the bathhouse thing must have predated my being on the Mayor's Advisory Committee.

Hughes: Yes. Silverman closed the baths on October 9, 1984.[1]

Setting Up Research with Prostitutes

Hughes: Well, tell me when you first became aware that AIDS indeed could affect women?

Wofsy: Well, prostitutes were beginning to be smeared all over the literature because of the African connection. In 1984, I got into conversation with Judith Cohen, who was a Ph.D. working with Dr. Andrew Moss on epidemiological projects. I can't remember why or how we got into discussions about prostitutes in the U.S., and what role they might play in AIDS transmission. We didn't know each other--we had passed in the hall, sort of nodded, as you go to the drinking fountain. But I can't remember why we got into conversation. I think there probably were some newspaper articles at the time beginning to implicate prostitutes in the U.S.

Hughes: I know that there was a scare article in the San Francisco *Chronicle*.[2] The implication was that this woman was a threat to heterosexual white males.

Wofsy: I think that happened after Judith and I were involved.

I think we both came from the sense of human rights; we both objected to assumptions that weren't proved. For whatever reason, we decided to go in together to investigate this in response to an RFA, request for application, put out by the Universitywide Task Force on AIDS. Now, that RFA had come out I think in part in relation to conversations I had had with Merle Sande about our

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[1]See the oral history in this series with Dr. Silverman.

[2]For an account of this episode, see Randy Shilts, *And the Band Played On*, pp. 508-513.

interest in and concern about this area. So monies were targeted to look at this issue.

I remember putting in the grant application, having to get it together within ten days, not because we applied late, but because the RFA was dated with a very quick return.

Hughes: Why?

Wofsy: There were certain parties, I think, who could be expected to get their application in in a timely manner. The application went in, and we were awarded whatever the amount of money was to do the study.

The study was to look at the seroprevalence of HIV in sexually active women, both prostitutes and women who didn't receive pay for sex--a stunningly unimaginative study in 1994, and mind-boggling in 1984. In 1984, all anyone wanted to do was look at prostitutes. So the idea was mind-boggling that we wanted to compare sexually active women who were and weren't paid to see if there was any difference.

Soon thereafter, the Centers for Disease Control, not surprisingly, became involved in the issue of prostitution. They were only interested in prostitutes--no controls, no thank you, just get the prostitutes. CDC put out an RFA for a multi-center study that would look at and compare five cities. So we applied for that grant and received it, having gotten the pilot information from this other grant, and entered an era of prostitute work. So for about three years of my life, I learned an unbelievable amount about prostitutes. I met prostitutes; I thought about issues. It's been ten to twelve years of breaking down stereotypes and forming new ones, and that was the prostitute era.

I have to mention that the very first grant application that went in, you get a pink sheet, which is the evaluator's suggestions and evaluation of your grant process. Handwritten at the bottom, and I've xeroxed it somewhere and it's probably archived, is a note in bright red Marks-a-Lot that says something like, "Useless proposal," or "Stupid to fund this. Everyone knows prostitutes are the way AIDS is going to get into the heterosexual population." The comment came from an academic grant reviewer who was presumably unbiased, so the comment was stunning.

Enlisting Help from Prostitutes

Hughes: Tell me what a typical day on the prostitute project was like.

Wofsy: The kinds of things that we did which seem so obvious now were so unique then. It feels like the story of my life. There was a conference being held at the [San Francisco] Women's Center on issues facing women care givers. So while the subject was women with AIDS, it was really getting women together who were parole officers, social workers, nurses, doctors--how we approached issues that primarily affected men.

At this meeting, there were representatives of COYOTE, Call Off Your Old Tired Ethics. I can't remember if Margo St. James was there. I think she was. But a woman named Gloria Lockett was there. She made it pretty clear that she was an ex-prostitute. In the afternoon, we broke into small discussion groups. Judith Cohen and I had realized that if we were going to be able to do any kind of epidemiology amongst prostitutes, we would have to do it together with them, not just have them buy into it, but basically plan it together.

So at this small focused discussion group, the topic of which was prostitutes, the idea that you would have university investigators take blood from prostitutes was so outlandishly, incomprehensibly impossible, undoable, unthinkable.

Hughes: Why?

Wofsy: To start, you have to meet a prostitute. Now, everybody's met prostitutes and strippers. I mean, everybody has dinner with everybody now. But nobody did then. So you have to meet them, gain trust, ensure confidentiality, with people of all races. It is probably a place where the issue of ethnic diversity comes up instantly. It's a victimized group.

But in our discussion group, stunningly, this woman Gloria Lockett basically said, coming at it from a human rights of the prostitutes point of view, "Hey, those men are giving me disease; I need to know about it." It would be good for women to have an opportunity for HIV testing, because maybe they were getting things from those nasty men out there.

Somehow we worked it out, and by the time this grant application had to be completed in ten days or whatever it was, we had actually employed this woman [Gloria Lockett], ex-prostitute, to be an outreach worker. We went on outings. Ultimately, there was a van, but that was years later. I think we just all drove

down to a rented motel room, and then the ex-prostitutes who were in the employ of the university would go roaming out in the streets and find women who were prostitutes, offer them consent forms, condoms--everything was absolutely on the up and up.

If the women consented and said they'd like to be tested and have information, then the outreach worker would bring them back to the motel room and they would meet the nurse or the doctor, whoever. They would get a brief examination and blood tests, and condoms and bleach and so on.

Breaking Down Stereotypes

Wofsy: It started out with stereotypes. The first thing that just blew my mind was that there were absolutely no fishnet stockings. None. Driving down the street in Oakland, to me they looked as though they were all out shopping, just doing their day-to-day business--blue jeans, an old sweater. How men found them, who knows? There was nothing [suggestive] in their looks, body size, shape, clothing--just nothing. Most of the women seemed not to come from advantaged backgrounds, but that didn't distinguish these women from other women who were on the street in Oakland. So without the participation of the outreach workers who were ex-prostitutes, it would have been impossible to get cooperation and to have the women enroll in the study.

The other thing I remember about prostitutes is, we went to a meeting for the CDC in Atlanta. The CDC wanted the five cities that were going to be working on this project to hear from a prostitute some of the issues they had to deal with and be sensitive to. They had latched on in Atlanta to a call girl who came and spoke to us, and she just knocked our socks off. She was stunning. She would very much have been a comfortable contemporary of ours. Younger, but you didn't have a sense necessarily that intelligence, educational background, savvy were any different.

After our meeting, Judith Cohen, I, this woman, and several others went out to dinner at a very nice restaurant in Atlanta, what they would call upscale. We were chatting, and it was full of beautiful people, the way these upscale restaurants are, you know, looking like Ernie's or something. This woman looked around amused and she said, "They [restaurant patrons] all look like my customers to me." It was the most eye-opening thing, because she wasn't trying to impress or shock. She was just making a totally honest statement. What she was saying was, [the people in the

restaurant] might be prostitutes and customers. It had never occurred to me.

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Wofsy: The next step for me was that I wasn't really trained as an epidemiologist. Judith Cohen was getting increasingly involved as an epidemiologist, as well as at a community level. I had been principal investigator of the initial prostitute research. We transferred so that she would become the principal investigator of several of these studies, and then she went on to make additional grant applications. I focused my energies more on continuing the treatment trials and physician education. By 1989 or so, I would say she was almost autonomous. I really had very little direct involvement.

But for years, I continued to go in the van to some hotel room in the Tenderloin [District of San Francisco], and interview women, examine them, draw blood. I mean, unbelievable experiences.

Hughes: What did the women think of you?

Wofsy: They accepted me. I didn't have any natural rapport. I also didn't have a sense of distance. I was with this group of investigators that was accepted, and therefore I was accepted. I also took care to dress in a very comfortable, casual way, so that it didn't feel so different. I don't wear blue jeans, because blue jeans aren't my style, but I would wear some sort of casual cotton pants and cotton shirt.

Hughes: Did it make a difference that you were a woman?

Wofsy: Everybody was a woman.

Hughes: Was that deliberate?

Wofsy: Yes. There were no men involved in the study in any way or any capacity at any time. Yes, there was a statistician. But other than that, it was all women. The university was invisible. It had no meaning. We were just some group of women who was doing some study and giving out condoms. The mindset of how society arranges for these things to happen is not visible to the women we were seeing. The very large and ubiquitous "they" were testing, and "they" were giving out condoms and bleach, and "they" brought stuff for sandwiches along with them. "They."

Hughes: So in their minds, the fact that you were from the university didn't matter?

Wofsy: They signed a consent form, and the consent form was very carefully reviewed. This was not a "So if you just sign here, this is okay." Really carefully reviewed. The Eskimos have eight words for "snow," but to us it's white stuff and it's snow. I think the university and the government and Chevron were just all "they" to the prostitutes. I don't think "they" had any meaning. We always thought it was kind of cute that the university had ex-prostitutes in their employ.

Hughes: [laughs] I like that, too.

Fear of AIDS in Heterosexuals

Hughes: What was the AIDS world thinking about Africa in 1983 or 1984? My understanding is that the epidemic in Africa has always been heterosexual.

Wofsy: Right.

Hughes: Wasn't it irrational to expect the epidemic here to stay within the original four risk groups [homosexuals, intravenous drug users, hemophiliacs, and Haitians]?

Wofsy: That's what the group of us working on this women's study felt. Then we gradually began connecting with other people throughout the U.S. who were doing the same type of research, particularly through the CDC's study of five cities, because prostitute and woman were synonymous at that time. So the media calls would be, "Do you really think this [AIDS] is something that will ever happen in heterosexuals?" I can't remember for how many years the lead question was, "Is this really something that heterosexuals have to worry about?"

Hughes: How did you answer?

Wofsy: I would give percents, for example, of what percentage of AIDS patients were women; I would give information. There were actually two studies that were very good to extrapolate from, because they were published about women not knowing they'd been exposed to hepatitis B.[1] So you could back-extrapolate. In those

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[1]M. M. Jonas, E. R. Schiff, M. J. O'Sullivan, et al. Failure of Centers for Disease Control citeria to identify hepatitis B infection in a large municipal obstetrical population. *Annals of Internal Medicine* 107:335-337, 1987.

cases, the partners were often drug users or bisexual. So the women were infected with hepatitis B, which was found at the time their children were identified at birth as infected with hepatitis. So the publications had nothing to do with AIDS. One was from Cleveland, and one was from somewhere else where AIDS still was invisible.

But it was possible to use that data to extrapolate that women aren't going to know the things that their partners have been doing [sexually]. The study included an intensive epidemiologic questionnaire: Has your partner ever--? Does your partner associate with--? They went through quite a bit of information to see if these women could recall something about their partners that might have given them a hint of the hepatitis B risk activities, and they couldn't recall. So that information was very useful; I used those studies a lot in my early talks on AIDS.

Hughes: When had those studies been done?

Wofsy: In 1983, maybe. Just by coincidence.

Then there were a group in the U.S. who raised the flag about women and heterosexuals--it was mostly women: HIV is a disease for which gay men and women provide care, and straight men are in research and management roles. I suppose society in a way is like that in general, but it's very, very dramatic in AIDS.

The CDC's Approach

Hughes: You said that women and prostitutes were equated. But previously you had said that when the CDC put out that original RFA, they were very definite about restricting the study to prostitutes. I took from that that the CDC thought that drawing parallels between prostitutes and non-prostitute heterosexual women would be inflammatory.

Wofsy: Right. What I meant by that is that the only women who were going to be involved were women prostitutes.

M. L. Kumar, N. V. Dawson, A. J. McCullough, et al. Should all pregnant women be screened for hepatitis B? *Annals of Internal Medicine* 107:273-277, 1987.

Hughes: And that was okay because most of us don't have to deal with prostitutes?

Wofsy: Right.

Hughes: So explain the statement that you just made, that women and prostitutes were equated.

Wofsy: It wasn't that prostitutes were going to extrapolate to other women, but that people could in the anthropologic sense find themselves using the words like a thesaurus: CDC is doing a study of HIV in women. But people's mind bubble was: CDC is doing a study of HIV in prostitutes. The mind bubble was using the word 'woman' synonymously with 'prostitute.' AIDS in women and AIDS in prostitutes were the same, but AIDS in other women--mothers, sisters, cousins, et cetera--wasn't ever going to be an issue at that time.

Hughes: So what you're saying is that the CDC was protecting "respectable" women.

Wofsy: Right.

Hughes: And that was their deliberate aim?

Wofsy: No, I think from the CDC point of view, they correctly assessed that to test heterosexual women would be nonproductive and costly at that time, because they just weren't going to be infected. It wouldn't give you any meaningful information. So looking at it in a purely scientific sense, prostitutes in Africa were highly infected; prostitutes had a lot of sexual partners. If you're going to find HIV in women--I'm now being very rigorously academic--the group you are the most likely to find it in would be prostitutes, or women IV drug users. There was a lot of work going on with IV drug users at the time too.

So I gave it an anthropologic twist, because I was fascinated by what people did with it. But I could also do the absolutely straight research twist and say that definitely the best investment of money was to identify where high [HIV] prevalence was among persons of the female sex. And CDC were right about that. In some cities, there were no positives out of 100 prostitutes tested, so you can imagine how many positives there would have been just going into the Safeway and testing women randomly.

Hughes: So it made sense scientifically, what the CDC was doing.

Wofsy: Yes.

CDC Case Definitions of AIDS

The 1993 Definition

Hughes: It has only been since 1992 that the CDC definition of AIDS incorporated symptoms that pertain specifically to women.

Wofsy: Right. They proposed a new definition in '92, but it's officially called the AIDS definition of 1993. So there were definitions in '82, '86,'87, and '93.[1]

People who were not there at the time are frustrated that the original definition was made based on a bunch of opportunistic infections. I think the original definition was well conceived and people did the very best they could to describe the syndrome as they saw it then. HIV wasn't identified or even anticipated, and somebody came up with a definition that was no worse than the Jones criteria for rheumatic fever and probably better thought out.

Hughes: Explain that.

Wofsy: Oh, I'm sorry. There wasn't a blood test for rheumatic fever, which affected a lot of people in the United States and other countries in the forties. So a physician would diagnose rheumatic fever if a child had one item from a list of five things, and two items from another list of six things. So it was very analogous to HIV: You can have Kaposi's or *Pneumocystis* or cryptococcus. There was a menu of diseases to choose from. And because there wasn't a test, you had to take one disease from column A and two from column B in order to reach a diagnosis of AIDS.

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[1]CDC. Update on acquired immune deficiency syndrome (AIDS)--United States. *MMWR* 1982, 31 (no. 37):507-514.

CDC. Classification system for human T-lymphotropic virus type III/lymphadenopathy-associated virus infections. *MMWR* 1986, 35:334-339.

CDC. Revision of the CDC case definition for acquired immunodeficiency syndrome. *MMWR* 1987, 369 (no.S-1).

CDC. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR* 1992, 41 (no.RR-17).

Views on Simplifying the Case Definition

Hughes: Well, what would the critics have had you do?

Wofsy: There's a sense of frustration at how cumbersome the diagnosis is, and I agree. I think that if you could use the retrospectoscope, you would have changed the definition once the virus was identified and used some other parameters that could be established by a blood test. But now we're getting into my personal beliefs, which are politically flagrantly incorrect.

Throughout the eighties, my own beliefs, which I kept pretty much to myself because they were so politically incorrect, were that you attempt to simplify diagnoses for most conditions: something you can do by a biopsy and identify a specific cell type; you can do a blood test and the result is above or below a certain count. I was finding that I, who was virtually an AIDS historian, was forgetting. I couldn't rattle off the list of opportunistic infections associated with HIV any more. It was like being able to recite the alphabet. I was forgetting things and saying, "Herpes zoster, god, I just can't remember. Is it or isn't it an AIDS-defining condition?" And medical students surely were just going berserk.

Hughes: There was just too much to remember?

Wofsy: There was too much to remember. So there was a lot of misdiagnosis. But a very strong feeling that you certainly couldn't label a patient as HIV-positive. The proposal to use a certain CD4 [cell] cutoff as the definition of HIV made sense to me. And sensitivity about how that result got disclosed made a lot of sense to me. That is, those were things that required a lot of attention, thought, and detail.

Hughes: And that position was politically incorrect?

Wofsy: Yes.

Hughes: Why?

Wofsy: Because it has a big psychological impact to be diagnosed with AIDS, and a lot of people with a CD4 of 200, which was the cutoff that was chosen, are still feeling fine. So one then puts a very onerous label on a person who is feeling quite well. And I agree with that psychology; that is, I understand it and validate it. But at some point, one has a certain diagnosis, and people with diagnoses deal with them. It works, somehow. So it seemed

attractive to me to have some blood test; something that would quantitate the diagnosis.

Hughes: Did the HIV antibody test figure in the debate?

Wofsy: That just determines HIV positivity.

Hughes: So you're talking about AIDS itself.

Wofsy: The AIDS diagnosis, yes.

Arguments for Including Women's Conditions

Hughes: Well, two of the arguments in terms of the CDC definition are one, if the definition doesn't include you, then there are services that you are not eligible for. Second, if you look at the definition as a teaching tool--this is my own idea--and you don't include women's symptoms within that definition, then unless a physician sees a lot of women with AIDS and consequently knows what to look for, he's not likely to recognize a woman with AIDS.

Wofsy: I agree with both of those arguments.

Hughes: Were these arguments one reason for the preoccupation with the definition?

Wofsy: I think so, except that the way words were used by the audience involved in the debate was so different from the way I think or the way you articulately put together what I think is the crux of the issue, that I'm not sure I know. But I think that was very much a piece of it, and justly so. And so as we described in a letter from the women's health committee to the Centers for Disease Control about the definition, we felt that even though there wasn't good epidemiologic evidence of an increase in cervical cancer in association with HIV, there was epidemiologic evidence of an increase in the precancerous lesions, and that it was a valid and appropriate addition to the definition. We stayed out of politics; we just tried to cut it to the chase of what could be supported by science or epidemiology.

Women's Health Committee, AIDS Clinical Trial Group, NIH

Chair, 1991-1992

Wofsy: The other thing I did in women and HIV is the Women's Health Committee for the ACTG [AIDS Clinical Trials Group]. The AIDS Clinical Trials Group is the NIH's clinical research arm with about thirty-five sites, and we're one of them. In the years 1986, maybe 1987 and 1988, a small group of obstetrician/gynecologists were attached to the ACTG, largely because of perinatal [HIV] transmission trials looking to see if AZT would interrupt mother-to-child transmission. The ob/gyns formed a working group to discuss HIV related primarily to pregnant women, but from the pregnant woman's point of view as opposed to the fetal transmission point of view--a big research agenda.

To make a one-and-a-half-year story short, they petitioned the executive committee of the ACTG which ultimately agreed to make women's health an official scientific committee, just like opportunistic infection and primary infection. Rhoda Sperling, the obstetrician/gynecologist who had brought along the working group for a year and a half, was so obviously the person to chair this. In fact, it wasn't even a discussion topic.

She got so many death threats, because of anger over the perinatal transmission trials, that she didn't want to take on this responsibility. So the ACTG then opened up to look for a chair. Deborah Cotton, an internist, for whatever reason thought I would do a good job at it. I had never been to an ACTG meeting. She proposed my name. I went to an ACTG meeting in 1991, but there was so much anger and so many threats that I didn't want to take it on at that time.

Hughes: What was the source of this anger?

Wofsy: I can't remember. They would shut down research meetings.

Hughes: Women were protesting?

Wofsy: It was all parties other than heterosexual men. So it was gay men; it was heterosexual women; it was lesbians; it was blacks, Hispanics.

Anyway, I went to an ACTG meeting; I said I wouldn't do it. I didn't know what I was getting into. Then it went through a

formal nomination process, and things had calmed down a little bit by then. I was asked if I would chair it, and the co-chair was to be a certain obstetrician/gynecologist, Howard Minkoff, who is very well known and very politically astute. I thought that we'd be a good pair.

I agreed in spirit to do it, and then they realized that the co-chair couldn't be a man. So they identified another woman, Arlene Bardequez, to be the co-chair, not somebody I had met. I'll keep my account at the interview level, or it starts being psychoanalysis. Anyway, I accepted the chairmanship in May, 1991.

The ACTG meeting was in July, and we had to have a functioning committee by July. It had to be composed of who knew what, and I had never met the co-chair. So I arranged to go to New Jersey and meet her. We spent a day together, and then we took a train to Washington and spent twenty-four hours in Washington with key people in the ACTG and set up the committee.

Women Activists

Wofsy: The truth is, it's almost not possible to talk about it.

Hughes: Because it's too political?

Wofsy: It's so political and so personal that it's very hard to be objective. But if I can cut through it, what the committee I think proved was that women activists and some men for a couple of years had been very angry about the inattention to HIV issues in women. One of the reasons I took on the chairmanship, besides it being a challenge and all those things people pose to themselves, was it seemed an opportunity to work within the system for a lot of the things that were in fact unjust, that women had not gotten the upper end of things in HIV. It was an opportunity to really do something for women.

A tactic is to target an accessible person who has access to someone higher up who's not accessible. And that proved to be the Women's Health Committee. So from the very beginning, there was a great deal of anger from the activists, and not that nice sense of collaboration, of realizing we had to work together, that had happened when we first set up studies with prostitutes, but rather anger, pain, hurt--who knows.

The committee meetings were hard. The activists would take the seats in the front row around the table, so the investigators

had to either stand or take peripheral seats. I presume the activists had worked out tactics, which were to ask the same questions at every meeting again and again and again. Some of the questions were very good, and some of the women activists were very smart and contributed, or could have contributed, a lot to moving the agenda along in a positive way. But it really colored the experience, I think, for those of us who were involved in the committee in the first year and a half.

Hughes: Were you feeling split by wanting to get some of the activist issues on the agenda, but you were also a physician--

Wofsy: Right, I wanted to get the activist issues on the agenda. I realized that you have to put things on an agenda in a way that is extremely analytic, matter-of-fact. That's how things get on the agenda.

There was always such a brouhaha with the Women's Health Committee meetings that was like watching a swarm of bees: You look at the horizon and see where the action is. It turned out ironically to be the Women's Health Committee. A lot of other places as well, but it had sort of moved on. It hampered our ability to devote ourselves to the scientific issues that brought us together in the first place. It's hard enough to gain credibility with women investigators, and it can be hard sometimes when there's a lot of action and noise and voices to distinguish exactly who the factions are. I think that the women investigators and the activists sometimes looked a lot alike to the other members of the ACTG.

Hughes: And did you object to that?

Wofsy: It made it harder to move the research agenda along.

Hughes: Which had to be sold, whether you liked it or not, to the power structure which was largely composed of white males.

Wofsy: A women's research agenda has to be sold. There aren't men's and women's, but a research agenda has to be sold. It's a harder selling job when it's associated with a filibuster at the microphone, et cetera.

There was one Ph.D., but for the most part the activists didn't follow along with the details of the discussions about research. So when the discussion got technical, rather than saying, "Oh, good, the scientists understand and I don't, and that's what we need, somebody who understands this stuff and will get these studies done," the women suddenly felt we weren't paying

any attention to them, because the discussion stopped being understandable.

Accomplishments

Wofsy: But the Women's Health Committee, with all of that, did come together. It did provide a core that mixed--multidisciplinary again; history repeats itself--obstetrician/gynecologists, pediatricians, and internists. We got together; we didn't know each other; we had different styles. As the obstetrician/gynecologist said, "We're surgeons, and you're internists." So you're with women surgeons and internists, and despite all of that, we formed our committees; we got studies off the ground; we got policy making off the ground. What became clear is that both the women activists and the ACTG leadership to some degree expected the same thing of us, which was policy and sorting things out. To some degree, that agenda was sometimes bigger than the science, from both points of view. Nonetheless, again, with all of that, there were achievements.

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Wofsy: We set up some guidelines for inclusion of pregnant women in clinical trials. A study was undertaken to look at a treatment to prevent recurrence of cervical dysplasia.

The way the CDC definition of AIDS leads into this is that at our first meeting, when we were trying to prioritize the research agenda, what the activists in the audience wanted to talk about almost exclusively was the CDC definition. I sincerely couldn't understand, since it was women's health research that was needed, and there's no way that the women's health committee for a clinical trials group relates to the CDC definition, why so much focus went into the CDC definition. But I came to understand that for women with HIV, the symbolism of having a woman-specific diagnosis was profound.

If I were a tactician, I would look at any organized systematic body with power and get that body to work on my behalf. So from the activists' point of view, we were a committee with access to decision makers who could exert influence on making the decision about the CDC AIDS definition. And we ultimately did write a letter to the CDC commenting on what the Women's Health Committee felt were strengths and weaknesses of the proposed definition.

Hughes: You mean the 1993 definition?

Wofsy: Yes. This was probably back in 1992.

Hughes: Did you propose specific diseases, symptoms, that you thought should be included in the definition?

Wofsy: We pretty much took what was proposed and said either we endorse it or we would make this modification. We didn't get very dramatic. It was a good letter. It was an appropriate thing for our committee to do. There aren't very many organized committees that are part of a really systematic structure that focus on women's issues. When you think about it, there really aren't. So I came to understand that the Women's Health Committee was one of the places that potentially had power to influence, and that the CDC definition was what the women [wanted to augment].

More on Women with AIDS

More on Activists

Hughes: Were you on Dr. Sande's committee [AIDS Clinical Research Forum] which included activists?[1]

Wofsy: Oh, yes, I was on that committee.

Hughes: You said that the women activists at meetings of the Women's Health Committee were unwilling or unable to follow the science. My impression of male activists is that many are very knowledgeable about the science of AIDS.

Wofsy: I think the mean number of years of education of the first thousand patients with AIDS was sixteen years. That's a full college degree. I think that "male" by and large equals "gay male". I am positive that there are probably a fair number of non-gay men in ACT UP [AIDS Coalition to Unleash Power]; I don't think it's an exclusively homosexual organization. But I think that the articulate voices are those of people who assume leadership. That's the way leadership gets assumed.

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[1] For more on the committee, see the oral history in this series with Merle A. Sande.

I think that among the women activists, there were a number of very bright and educated women who often had an insightful way of seeing the problem and who really contributed. You had to stand back from the rhetoric and not take it personally, because there were major insights contributed by people dealing with the condition [AIDS] that were not seen by somebody looking at it more academically.

Gay men said from the get-go, "We are not victims." The women, while they didn't say, "We're victims," their language was victim language. And while there were some stunningly articulate and very well-educated women, the larger group of women was less educated than a comparable diversity of men. Sometimes the loudest voice, in my experience, was of a woman who had been the most victimized. Whereas in general, it seems to me that the louder voices among the men turned out more often to be those who had had some educational background related to the area of discussion. It was so emotional, it's hard to be totally objective.

Personal Impact

Hughes: What was this doing to you?

Wofsy: That actually has to be almost off the record. It's so emotionally charged, I think it's almost too hard to talk about. I can say in general that it was very hard.

Hughes: Was it because of the two roles that you were playing--women's advocate and physician?

Wofsy: Yes. I think that I was seen as very male, which I am.

Hughes: Why do you say that?

Wofsy: I have grown up being "the only woman in--"; I speak in the male voice; I can speak to men [in terms they understand]. I think it's an advantage in a committee chaired by a woman to be able to comfortably communicate with everybody. But I don't speak in the female voice in a professional arena. I speak in the male voice.

Hughes: Is that a deliberate choice?

Wofsy: [pause] The only way I can describe it is if you go to Spain, and you know Spanish, and everyone's speaking Spanish, it becomes counterproductive to speak English.

Hughes: It's the lingua franca.

Wofsy: It's the lingua franca, right.

It was very difficult to deal with those two roles simultaneously. I think that for others on the committee who sat through all of the same stuff, it was a show. The person in charge bears the responsibility to deal with many things simultaneously that others, even if they're prominent on the committee or have important roles, don't have to. There's a certain meeting at the ACTG that's closed. Meetings are open with the exception of the core committees, and so basically for four days all meetings are technically open. A person can go into any meeting. Most of them are so dry and dull and boring that people don't want to go to them.

It's in the bylaws that the core committee meetings are closed meetings for members only. At the first meeting, when many of the committee members really only knew each other by name--we were making eye contact for the first time--several activists sat down prominently at the table. So at the same time one is trying to chair a meeting, saying, "Well, hello, so-and-so, so glad you're here, and how are things in Louisiana?" one is having to decide what to do about this declaration. It was a very hard time.

Hughes: I can see that.

Wofsy: The Women's Health Committee now gets almost no activist attention. The time has passed. Now it's just a committee. It gets occasional attention.

Hughes: Is that because the definition now includes women?

Wofsy: Oh, no, it's just time. It was antibody testing, and all that stuff, which provoked attention.

Care for Women with HIV

Hughes: Where would a woman with AIDS or with HIV infection in those early days get medical care? What were her choices?

Wofsy: The issue of care for women--now I launch into lectures. Women with AIDS don't go to doctors with large gay clientele; they don't go to ID specialists for primary care. If they're an IV drug user, they may go to a physician who will quickly pick up on the

issues that affect IV drug users. But if that's not the case, the woman will go wherever people go--gynecologists, the clinic at jail, the family planning clinic. Now, everyone has some understanding of HIV, but it's just not high.

Hughes: In 1983, 1984, would any of those care-giving places have known much about women and AIDS?

Wofsy: No, they wouldn't know much.

Hughes: So probably there were missed diagnoses.

Wofsy: There were missed diagnoses.

I think what you're asking is, what if a woman was known to be HIV positive, where would she go? The woman could go where the men go. They'd call up the AIDS Clinic here, or in New York, the Gay Men's Health Crisis: [in high voice] "Hi, I'm Sally. Is this the Gay Men's Health Crisis? I need you!" So technically women had access, but they were never the primary concern of anybody there.

There were never very many, so women didn't find each other. And they didn't have anything in common. Two gay men with AIDS may have very little in common, but at least they share the sense of gayness. Whereas two women with HIV, one may be a computer salesperson in the Sunset, and the other may be a drug user who lives south of Market, and they're not going to have a lot of things to talk about together.

Hughes: Why the lack of emphasis on treatment in women?

Wofsy: Because what emerged pretty early on was the disease, at least in broad strokes, is fairly similar for men and women, except for gynecologic conditions, and everybody does this [shrugs] to gynecology, men and women alike.

Hughes: Why?

Wofsy: People don't like it. It's time-consuming; you have all this equipment. You get rusty if you don't do a gynecological exam frequently. It involves sensitivities that are much more acute than those of the rest of the physical exam. There's this mindset that gynecology isn't part of the routine exam. Yet gynecology is really a part of primary care and really should be just a normal part of the exam.

Hughes: You're an infectious disease specialist; presumably, you hadn't done any gynecology since medical school.

Wofsy: I was in the ER for about six years, so I did a lot of pelvic exams. But I really didn't anticipate spending a lot of time doing pelvic examinations as an infectious disease specialist. It really didn't enter my head why that should be required.

Hughes: So you could understand the reluctance from a personal standpoint.

Wofsy: Right, and also from the experience of doing a pelvic. It requires a lot of steps. They're not all that complicated, but anything you don't do often, you get rusty at, and you don't do it very well.

Funding

Hughes: How readily was money available for research on questions related to women with AIDS?

Wofsy: The rhetoric is that it wasn't available at all. The reality is, there were always pockets of money targeted at women. They tended to be in epidemiologic issues rather than treatment issues. So the rhetoric is definitely true in the larger sense, but not with the absoluteness that comes across. The other thing is that an ingenious investigator could always have gotten money. But somebody has to care, and that often has to be a woman investigator or a man who is investigating women's diseases, and there aren't many of those. So the relative paucity of money and the paucity of [interested] investigators go along together.

Research Networks

Hughes: Was a network established amongst investigators interested in AIDS in women?

Wofsy: Oh, yes. We all got to know each other very quickly. There was the ACTG network; there was a network within the CPCRA [Community Programs for Clinical Research on AIDS], which is the community-based research group. The people who had done the CDC prostitute study were the beginning of a network. There was an RFA in 1992 to look at the natural history of HIV in women called the WIHS [Women's Interagency HIV Study].

In 1990 the NIH had a meeting about women in AIDS, the first ever. That's a whole other political story, but from that ultimately came an RFA with money to do a natural history study of HIV in women. It was to be multi-site, and four sites were going to be CDC-funded, four sites NIH-funded, and they were going to work collaboratively. Four CDC sites got funded about a year and a half ago; four NIH sites just got funded; we are one of them. Any time there is a pot of money, it brings people out of the woodwork. You ended up knowing who was applying for what, and all of the women investigators are networked through one of three or four different channels. I don't think anyone ended up applying who isn't linked in somewhere.

If it sounds like the old boys' network, it is. Just the texture is different. It's given me a lot more understanding of the old boys' network, and some of the benefits we all derive from it. [laughs]

The Federal Government and Women with AIDS

Hughes: I'd like to quote from Gena Corea's book, *The Invisible Epidemic*. She says, "...the federal focus was on pediatric AIDS, even though there were many more women infected than children and even though pediatric AIDS was in fact a reflection of AIDS in women."[1] Do you buy that, and what are the implications if you do?

Wofsy: I buy it except that [sighs] it's complicated. Pediatricians care about peds [children]. Internists care about men. I absolutely agree, but that's the whole issue--women are invisible. There has to be somebody who's the advocate, and there isn't any advocate.

Hughes: Do you credit HIV with the current focus on women's health problems?

Wofsy: You mean a general focus?

Hughes: Yes, I mean the fact that the NIH has targeted women's health problems.

Wofsy: I would have thought HIV was almost solely responsible, until I got invited to a meeting sponsored by the Office of Women's Research at NIH, which included HIV, but HIV was a fly speck. It was domestic violence, accidents, homicides, osteoporosis, heart

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[1] Corea, p.45.

disease. By the time the whole day had been spent listening to the laundry list of issues that affect women, I wasn't sure I could feel that HIV had taken the leadership role. I think it's just a natural evolution of the eighties, and of women achieving positions of being advocates and investigators.

Women's Attitudes toward Drug Trials

Hughes: Do you have anything to say about the fact that most drugs used to treat HIV have been tested on gay, white men?

Wofsy: Yes, I have two quotes that I use. One is that women are collectively eager and individually extremely reluctant to enroll in research studies. The other quote is from somebody who said, "If there is a good study, gay men will be there at five in the morning, waiting in line. Who's going to wheedle and cajole women to be in a study with a line around the block? Who's going to pay attention to the people that have to be begged and pleaded with, and who's going to be begging and pleading?" As a political statement, women really want research trials. Actually being in the trials may be a very different story.

Hughes: Why are women reluctant?

Wofsy: I think there are a couple of reasons. I don't have any data for this, but I think that because 50 percent of women with HIV are African American, and because of their experience with Tuskegee [syphilis experiment], they have very real and concerned suspicion of the research establishment. Although when you look at enrollment of women in research trials, it's largely African American. So people are getting connected; they're working it out somehow.

There's always the thing about childcare. I'm really not sure that childcare isn't a smoke screen. It's one of a number of factors. But it's an enormous investment of time and effort to be in a research study. It's more attractive if it's the only drug available--but most research studies aren't like that. They're really comparing A to B, and you could probably get A prescribed by your doctor anyway. I think it's multifactorial, where it fits in life's priorities for a lot of women. You could wipe childcare out of the equation, and women still are very reluctant to enroll in studies.

Perceptions of Women with AIDS

Hughes: In a 1987 interview, you were quoted as saying that the Third International Conference on AIDS with its focus on women as "vessels of infection [for men] and vectors of perinatal transmission [to fetuses], left the impression of women as "almost an invisible pass-through."[1]

[tape interruption]

Wofsy: It has to do with sophistication of listening. If I say, "In the [AIDS] literature, women are described as vectors of disease and vessels transmitting to children," or what have you, a certain way of listening--I shouldn't call it unsophisticated--will hear that as, "Well, I'll tell you what I think of women with HIV." And in actuality I'm saying the opposite. It is part of being quoted that you learn to live with.

Part of the male voice sometimes is that the listener projects on you anger, and then doesn't intentionally misquote, but could misinterpret what's being said. It's a very sophisticated, subtle line to say, "That's the way women with AIDS are portrayed," and not have to go on to say, "And fuck them anyway for saying that." [laughter]

I wrote an editorial for *JAMA* in 1987 that got a lot of attention.[2] I discussed those issues about women as vectors. In the editorial, I carefully laid out that that's how women are seen, not that's what they are. The editorial got a lot of play, *Newsweek* and *Time*, and the whole nine yards. Somebody picked it up and thought, Gee, that's interesting. [reading] "To date, women have received more attention for their potential role as infectors than for the problems they face as infectees."[3] This was really a new thought back then. Now, everybody understands this.

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[1] Corea, p.82.

[2] Constance B. Wofsy. Human immunodeficiency virus infection in women. *Journal of the American Medical Association* 1987, 257:2074-2076.

[3] *JAMA* 1987.

Speaking on AIDS[1]

Hughes: Well, I know you have done, and I presume are still doing, a lot of talking on the subject of AIDS.

Wofsy: I think people who deal with AIDS got to be very good speakers. It sort of goes with the territory. There was a lot of practice. Under fire, one was dealing with public speaking as well as academic speaking, whereas I think in cardiology, for example, one tends to have a wide audience--new students to fellows--but within the medical framework. Community speaking is part of community service. So I think people who dealt with HIV became very good at speaking, and I did too.

I didn't start out that way. When I did my infectious disease fellowship in 1980 and '81, except for some small talks to groups about urinary tract infections, I really didn't have any speaking experience. My first speaking experience was actually in the realm of infectious disease. I was asked to give a talk on pneumonia to replace somebody who was called out of the country. So he lent me his slides. I got through the talk, and it was probably a satisfactory talk. It was my first to a group of 300 people or so.

Practice makes perfect. I got very good at talking. And at talking on television, and talking on the radio, and talking everywhere. I became known for the brevity and terseness of my sound bites. I'm going on and on and on, but I assure you, I could convey the same information in approximately five minutes of terse sentences.

Hughes: We're looking for texture, not terseness. [laughter]

Wofsy: I'm a texture person. Do other people whom you interview do this? Do they say, "God, what we lived through?"

Hughes: They do to a degree.

Wofsy: I spoke on every national television show at one time or another, it seems like. I gave a plenary talk at Stockholm for the Fourth

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[1]This section was moved for better chronology from its original position earlier in the transcript of this interview session.

International Conference on AIDS [1988].[1] I just couldn't believe I was asked to give a plenary talk. It just didn't come together, and I remember sitting in the hotel room at six a.m. looking at the slides, and they were dancing around in front of my eyes. I couldn't get them hitched together. The talk was at ten. I had to take a train. I ultimately put them in the best order I could and said, "All right."

You had to have two copies of your slides, because they had to project them from two carousels to two screens. So I got them in the carousels somehow. The room was huge. It was a Cow Palace. Something happens. I couldn't have been more comfortable if I had been eating a picnic lunch with my kids. The projectionist got a slide out of order, and he spoke only Swedish, and somehow that had to be dealt with--and it was fine.

I got a lot of very extraordinary feedback for that talk. It touched a chord. It was stuck in with a lot of more didactic talks, so that people stayed in the room. Normally, they try to leave the room for the patient-care type talks.

Hughes: Patient care is what you talked about?

Wofsy: Patient care. I was more reminiscing than anything.

But now, things have changed with talks. I think AIDS led the way for a certain kind of talk, a way of being more human, expecting speakers to be good instead of the dry old talks in medical school. Teachers are usually good, but people who give informational talks--[sighs] often the slides are disorganized; it's sort of a joke. AIDS speakers got good. And they raised expectations about speaking. A new generation has learned from that and is improving the model.

Hughes: What are the ingredients?

Wofsy: Clarity, conciseness, lack of bombosity, modernism--getting accustomed to things being new, learning that change happens like [snaps fingers] that. I go to a talk in a non-AIDS field, and a slide will have at the bottom, "1986"; something hasn't changed since 1986 in who knows what field. Or even 1991. I think we in the AIDS field are just used to change. We can make a u-turn on a dime, psychologically, mentally, with the epidemic, and I think you get good at it in a lot of aspects. You do a lot of talking,

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[1]C. B. Wofsy. AIDS care: Meeting the health care needs of the HIV infected. Plenary presentation, Fourth International Conference on AIDS, Stockholm, June 12-16, 1988.

and people call you on things. I think with AIDS, everybody is just so accustomed to being challenged--

Hughes: There in a sense are no rules.

Wofsy: There are no rules.

Hughes: There's no channel along which one is supposed to think.

Wofsy: That's right. There's no pathway to follow. We made it.

Hughes: But how long can that last?

Wofsy: Oh, it's over now. It's over.

SFGH Physicians in the Early Years of the Epidemic

Hughes: The epidemic is scientifically interesting, but I think it's much more than that. How do you feel?

Wofsy: What I think is that HIV took people instantly out of the realm of the office or the ivory tower. I, Donald, Paul, and many others like us, have undergone an evolution of life experiences that couldn't have been imagined before HIV and would not have been part of any other occupation. It would be wrong to say I understand the television industry, but I have glimpses into the television industry and print media that I don't think I could get in any other way. I've gone into churches that are denominations or beliefs that I wouldn't otherwise have known were out there. Not to mention my exposure to gay and straight, and up and down, and north and south, and east and west, and pink and blue.

You used the word texture. I sometimes forget that texture has been part of this last decade. I keep reemphasizing it isn't unique to me, but I think there is a core that had this experience that isn't true of the people who are now coming into the HIV field. They're not on national television, because the nature of the disease has changed. It's not what national TV needs. I did five one-hour specials with KPIX, dozens of hours of live television. Just that alone was a really interesting experience to have had.

The '81 group spent years thinking we could get a handle on the epidemic, somehow, some way. I think each person would put it very differently, but if somebody dissected the words, it would come down to a commonality that if this, then that. I don't think

there's any illusion about our control now. I really think that in our own naive way, we thought we could find the brain of the elephant. And now it's so clear, we've got one person at the foot and one at the trunk and one at the tail, like anything else.

Let's be realistic--the epidemic brought enormous personal and professional advantage. When else does a good physician but not an Osler end up on national television and dining with governors and the minister of health of China? I just don't think it happens that way that much.

Hughes: You were in the right place at the right time.

Wofsy: Or the wrong--that's the yin and the yang. The wrong place at the wrong time, and the right place at the right time.

Hughes: You could have ducked out, as some people did. And you didn't.

Wofsy: No. We--I use the collective "we" because this cohort of several of us here have gone through this together. I think a lot of our experience feeds on that. That is, in one way or another, one individual's advantages sometimes trickle down. I certainly have gotten enormous advantage from Paul's and Donald's visibility. But I think vice versa is also true. There just gets to be this known cohort [of AIDS physicians] here. Somebody always seems to be able to address any topic. "Well, if so-and-so can't, then so-and-so will." So there's definite, enormous advantage in the cohort that an individual, no matter how experienced, good, charismatic, wouldn't have. We have the advantage of being the San Francisco model and having a group. We've helped each other, I think. But HIV is a new disease now, and on to a new generation.

More on the AIDS Provider Education and Experience

[Interview 4: February 1, 1994] ##

Educating Physicians No Longer in Training

Hughes: We've mentioned APEX, but I understand you wish to say a little more.

Wofsy: Right. APEX is an acronym for AIDS Provider Education and Experience, named thusly because we knew everything had to have a

handle. AIDS really changed things; acronyms had to be very user friendly. So when we put together our educational program for physicians, we started out that way.

Huey Lewis and the News, a rock group, gave money that they wanted targeted to education. It was a relationship and a contact that largely went through Paul Volberding, but I had immense interest in this concept of educating physicians who were no longer in training. After much discussion together, we put together a program. An administrator was hired, and I directed the program. We also applied to the NIH for some funds that were becoming available for this purpose, and they ultimately didn't fund anybody for it, but it was a very nice program proposal.

What evolved was one- to four-week programs for physicians who were no longer in training to come here to San Francisco General Hospital and learn about HIV. The first few programs we designed for a lot of people, ten to twelve people. The people came from all over the United States; in fact, I'd say about a third came from states other than California, a third came from California, and then a smattering came locally or internationally. In the original groups, it was people who expected to go into AIDS work, who had been designated by an employer or by their own self-interest, or they may have had a private situation that caused them to want to take this training. We learned over the course of time that for people not yet providing AIDS care, you can't talk about advanced aspects of the disease, because they're not ready to absorb it.

As we did this over the years, and it spanned about eight years, 1986-1995, a trend became stunningly obvious: Although our goal was to train more people to take care of patients with HIV, the people who wanted to take the training were the people who were already doing the best they could in their communities. So the level of expertise of the trainees began to equal that of the trainers. And what they were learning was the San Francisco model, the geographic variability, and what turned out probably to be the most important thing they got out of their training was that they had been here. To say that they had done a training program here carried a lot of credibility when they went back home.

Hughes: That implies that San Francisco General, and, by extension, the APEX program, had a reputation.

Wofsy: It had a reputation, yes.

Other AIDS Education Programs

Wofsy: Two or three years ago, one of our programs was sponsored by the ID Society of America. The education was extended so that there are now four or five infectious disease programs linked with AIDS programs at hospitals across the United States which are offering the same kind of physician training. The applicants can decide which hospital they want to go to.

Another trend emerged, and that was, though there was curiosity about San Francisco, it no longer matched the demographic and patient population that people elsewhere were faced with. And though the training was of extraordinarily high level in meeting people who were in CMV [cytomegalovirus] research, PCP, et cetera, our circumstances, which are still predominantly with homosexual men, didn't match the milieu of the trainees. Some of the East Coast sites became more desirable for training programs, and from everything I can infer, it had to do with the demographics, not with the faculty.

We also did a program with Eastern Europe, in which the WHO sponsored a program that I developed over about a year. Perhaps it was my political naivete: We designated Eastern Europe, and I said I wanted it to be physicians only, because it had been my experience that it's hard to train doctors and nurses together. WHO had the responsibility for choosing. So they ended up choosing individuals from Yugoslavia, Poland, Hungary, Russia, and Bulgaria. The Yugoslavians were from what proved to be opposing factions, and war broke out while they were here. From Russia, one turned out to be from the Ukraine and one from Russia. It turned out to be a United Nations more than a training program. But it was a stunning experience for them, and for us.

Hughes: In a political sense or in a medical sense?

Wofsy: In both, I think. I actually have seen many of the people at other conferences, and ultimately went to Russia, Budapest, and Prague last fall,[1] and met with one of the individuals leading this delegation of doctors. So we actually made return visits to some of the doctors who came here.

Most recently, we have extended the program to work with the family practice program at SFGH and do one-week targeted programs, mostly for people within California who are in family practice. A

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[1]In October 1992, Wofsy went to Eastern Europe as delegation leader of a program called Management of HIV Disease in Eastern Europe.

consequence of that has been that we've trained maybe fifty physicians and a few nurse practitioners and PAs [physician's assistants] who work in the local or nearby jails, district health centers, Kaiser [Permanente]--I don't think we've had any school-based trainees. So the way we do things here has in a very personal way been extended to many of the key providers in other community clinics and centers around the Bay Area.

Hughes: How well does the program translate?

Wofsy: It translates extraordinarily well. There's face-to-face, first-name contact; there's validation; there's reciprocation. Kaiser isn't just a name out there; we know the people at Kaiser who are setting the guidelines and the policies. So I think it's been a really big plus for the program, and I hope for them as well. Okay, that's the end of my radio broadcast. [laughter]

Hughes: Is the program discontinued?

Wofsy: No, it's ongoing. The money from Huey Lewis and the News ran out, and so there isn't one large umbrella of independent source funding. So what we've done is affiliate with groups--WHO, the ID Society of America, the Health Resource Service Agency, through the family practice program. And that's actually been rather successful.

Hughes: How unusual is it in the field of infectious disease to have training in a specific disease?

Wofsy: I think it's extremely unusual. Again, AIDS has led the way. In the last year, there was an application made from the pulmonary group of the ID society which wants to provide training in tuberculosis in a rather similar style, very much the same model, to that that we've used for HIV. TB is becoming epidemic so that they are intending to bring people from all over to spend time in the TB clinic, the laboratory, et cetera. The idea that you want to come on site is very important. The CDC, Centers for Disease Control, has long had various programs where you can go for training in epidemiology or other subjects.

Hughes: As time went on you found that certain aspects of APEX worked and certain didn't?

Wofsy: You bet. Oh, it was stunning. There's nothing to match experience. You can plan and plan and plan, but you just can't anticipate what's going to happen. And the other thing is that what one group loves, the next group doesn't. So you take pains to incorporate that particular speaker or that particular site

visit, and the next group goes, "Oh." So then you eliminate it, and the next group wants it. [laughter]

Hughes: I gather from your comments that there are similar training programs now in other places in the country?

Wofsy: Oh, yes, all over. I want to take pride in and credit for what our program has done in developing something that was at the time unique, and at the same time not imply that everything that has evolved nationally is a direct consequence of it. These things have a way of synergizing by word of mouth and experience and one thing or another.

Different Programs for Physicians and Nurses

Hughes: Would you explain your comment that you find it difficult to teach physicians and nurses together?

Wofsy: That has two prongs: If I give a lecture to doctors or nurses, I basically give the same lecture. But if people are coming here for on-site experience, it's been my experience that the physicians in the course want to push the outer envelope of their didactic knowledge more than the practical experience. The nurses, it's been my experience, come because they want to see, feel, do; their didactic knowledge, though it always could be expanded, isn't the area where their mission is, but rather to see and be with other nurses. So it really needs to be two parallel programs in order for the doctor and the nurse in that unit to have had the experiences they need to carry out their work.

The doctor very often is going to be a leader, a teacher, an academician, and wants to come home with knowledge and enhanced teaching and lecture skills. The nurse is often going to be setting up the program, and needs to go home with a lot of real how-to information. It's not that one is less or more intellectual than the other, but their goals of what they need to come home with are rather different.

Now, in cases, we were easily able to arrange a lot of cooperation: The head nurse on 5A would take the nurse from Poland and spend the day with her. But it takes a lot of extra time and you have to put it together on the spot. It worked very beautifully; people were really wonderful about accommodating.

AIDS Medicine as a Specialty

Hughes: Is AIDS medicine likely in the future to become a board-certified specialty?

Wofsy: I don't think so. To say you need a specialty implies that it will go on for the foreseeable future. So in certain ways, there would be a negative momentum on the part of everybody to institutionalize AIDS to that degree. From a practical point of view, cognitive specialties are already struggling to survive with health care reform. There is an intent to limit the number of specialists.

I think what's likely to evolve is that internal medicine will quasi-specialize, that is, general internists will not have a formal subspecialty but a concentration area, and that some will have concentration areas in HIV/AIDS. Infectious disease is looked upon as the specialty that does advanced AIDS medicine, and oncologists will be very loath to give up the chemotherapy. Bottom line is, I think it won't become a specialty.

The Role of Medical Specialties in AIDS Research

Hughes: Is there a struggle among the specialties to maintain a toehold in AIDS research? I'm thinking particularly of the oncologists and dermatologists who were the first in the AIDS field in San Francisco.

Wofsy: I don't think they're trying to maintain a toehold. I think this may be one of the few institutions left in which AIDS is in the Division of Oncology--the academic division it sits in is oncology.

Hughes: That's probably historical.

Wofsy: That's historic. I can't think of any other situation in which that's the case. Four or five of our faculty members are oncologists; that's unheard of. For instance, at the AIDS Clinical Trial Group in Washington, the oncology committee has a reasonably small membership compared to infectious disease, and that probably is reflective of the general situation.

Hughes: Oncology dominated at first, even at the level of NIH; the first conference sponsored by the federal government on what later

became known as AIDS was sponsored by NCI [National Cancer Institute].[1]

Wofsy: I didn't realize that, but it makes sense.

Hughes: Then, as we all know, there was a struggle between NCI and NIAID [National Institute of Allergy and Infectious Disease] over which was going to take charge of this epidemic.

Wofsy: Yes.

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Wofsy: I don't work with the trauma center, but I know it's a pretty important thing to this institution, and I'm glad they're here, because indirectly, everybody benefits. I think there's probably a lot of occult realization that the hospital has now become renowned for trauma and AIDS.

Hughes: Was the money used for AIDS activities largely appropriated specifically for AIDS work, or did it have to be weaseled from other programs?

Wofsy: That's an area that I had less to do with, and if I commented it would be so much hearsay; I think that others have probably been able to answer more forthrightly.

UCSF-San Francisco General Relationships

Hughes: My impression is that the KS Clinic faded after the movement of AIDS activities to San Francisco General. Is that indeed the case, and was there tension between San Francisco General and UCSF groups?

Wofsy: I can speak as someone who was involved but not a confidante of those who might know private thoughts. It looked rather smooth to a knowledgeable but not inner-inner-inner-circle observer. Conant was a dermatologist. For him to do the full spectrum of care for a systemic disease didn't make sense at that time. Kaposi's is a dermatologic condition. When it was clear that much more systemic disease was going to happen, and that Paul, by his personality and

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[1] On September 15, 1981, the National Cancer Institute and the Centers for Disease Control sponsored a workshop on Kaposi's sarcoma and opportunisitic infections.

drive and his affiliations with multidisciplinary faculty and energies here, was interested in taking on the care of patients with HIV, and that UC seemed to have zero enthusiasm for becoming a hospital for taking care of AIDS patients, and Merle, the chief of medicine, was supportive here, an evolution seemed to happen. Now, the internal tensions I don't recall becoming a topic of common gossip.

Hughes: Why do you consider yourself not to be a member of the inner circle?

Wofsy: I was part of twenty million meetings as part of this epidemic. I was never part--nor excluded--from meetings that involved decisions about use of space at UC, patient flow, whether to invite patients here, what proportion of AIDS patients to have. Those decisions were simply happening at meetings for which I wasn't present and have no recollection of feeling that I should have been.

Hughes: Who was making decisions of that nature?

Wofsy: I think probably Paul and Marcus, along with appropriate administrators.

Hughes: Would Dr. Sande have been involved?

Wofsy: Dr. Sande would definitely have been involved, directly or indirectly, and may well have been in the room.[1]

Hospital Facilities for AIDS Patients

Hughes: Do you remember discussions relatively early on about hospital beds, and the fact that hospital facilities here were in danger of being overwhelmed by AIDS patients?

Wofsy: Absolutely. Those meetings I attended. When the inpatient [AIDS] unit [Ward 5B] was set up, it was to have twelve beds. There were two AIDS patients in the hospital, and we spent more time deciding who would be in the other beds than we did on infection control, yadda yadda. By the time it opened, all the beds were full [with

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[1]Dr. Wofsy added the following comment during her review of the draft transcript: "In retrospect I think I'm wrong. I think I was on the inside."

AIDS patients]. It became very clear that there were going to be a lot of AIDS patients.

My memory is that the debate had more to do with housestaff education than with physician exhaustion. That is, we had always been a hospital that provided the physician-in-training with a very wide spectrum of clinical experiences. When you start having 20 percent of the patients you're caring for with one disease, you lose the breadth of experience and become a mini-specialist in that area. So Merle was very outspoken; at one point he put a ceiling, no more than 33 percent, as I recall, on the number of AIDS patients to be admitted.

I remember being in a number of meetings with community doctors and Department of Public Health officials. I remember trucking down to the health department many times to meet with people, basically to state that everybody had to take care of this epidemic; everybody had to work together to create AIDS facilities at each hospital, et cetera.

I can only speculate that there were some rather interesting meetings, San Francisco General versus UC. It was one thing to have people in the derm[atology] clinic taking care of AIDS patients, but the common understanding was that decision makers were not anxious to have the patients in the hospital at UC. They ultimately named the clinic, which opened in 1984, the Adult Immunodeficiencies Clinic.

Hughes: That terminology was not coincidental?

Wofsy: It was not coincidental. Now you laugh in your sleeve, but at that time there was a pediatric immunodeficiency clinic, so having an adult immunodeficiency clinic seemed like the mirror image.

[tape interruption]

Community AIDS Physicians

Hughes: We haven't talked about the role of community physicians in terms of their interaction with what was going on here and also the role they played in the community.

Wofsy: That will get into the Donald Abrams oral history.[1] I don't think I would have been that aware of it without AIDS, but there was a

[1] See the oral history in this series with Donald I. Abrams.

group of physicians which had large gay practices. One speculates that many were themselves gay; I don't think that was always the case. These physicians, therefore, didn't take long to become experts. It was perhaps because of their lifestyle, or the lifestyle of the clients they served--not their training--that made them become experts in AIDS. And because San Francisco, like New York, probably has one of the biggest and most visible gay communities in the world, there were a lot of specialists pretty quickly in HIV.

I can't remember in detail the events leading up to the CCC, the [San Francisco] County Community Consortium, but Donald was instrumental at all levels. In fact, as I recall, there were a couple of meetings to get academicians in the community together. I think Paul's recollection is that he appointed Donald to chair a committee. To an insider's observation--I am an insider here--Donald showed unbelievable independent drive and motivation and organizational skills that wouldn't necessarily have been predicted for Donald that put this all together. He became a glue that held the physicians, chaired the committee, had vision, knew how to keep them together. [tape interruption]

At about this time, an RFA for funds to actually do community-based research came out. He applied, and this group then became a formal research group, the County Community Consortium. No one had done any research, and I for one was very skeptical. It seemed very altruistic. The community physicians would do part of the research, but it didn't look like they had experience in running clinical trials. And I think I was proven wrong; they were very good.

Hughes: You were worried about scientific credibility?

Wofsy: Yes. Minor worry, not major. I don't want to make this a topic heading: "Wofsy Worries." They were so driven and sure they could do it. But faced with the big machine here at the university, this plan didn't seem real likely to succeed.

I went to the meetings reasonably religiously for several years. They met--probably still do--on third Wednesdays. They instituted all kinds of things--community grand rounds--and it was really a stunningly organized effort. I was very, very impressed with Donald--his bright and gifted personal style, his energy in motion. You could only admire how he put this together, kept it together, and imaginatively put some structure to it. He has many talents, but that wasn't one I would have predicted.

Hughes: Was this idea unique?

Wofsy: Oh, yes, everything that's been done is unique. [laughter] Now they're everywhere.

Hughes: But this was the first. Are you aware in the history of medicine of community physicians so deliberately being pulled in to what previously had been an academic domain?

Wofsy: I don't think I can think of any other disease where the community physicians were getting the disease, or at risk for it. I really think that makes a difference.

Hughes: What about the role of Bay Area Physicians for Human Rights?

Wofsy: I don't know very much about BAPHR, but I know that many of these community physicians were part of it, and that it was a resource for patient referral. I never was at a meeting, so I don't know what their mission is, or what other things they did. And I don't know whether the membership is superimposed on the membership of the Community Consortium. It's always been grassroots, never gotten huge, never heard gossip or scuttlebutt. It seemed to me to be a respected organization that was taking on a responsibility for finding resources, doctors, referrals, for people who had HIV.

The San Francisco Model of AIDS Care

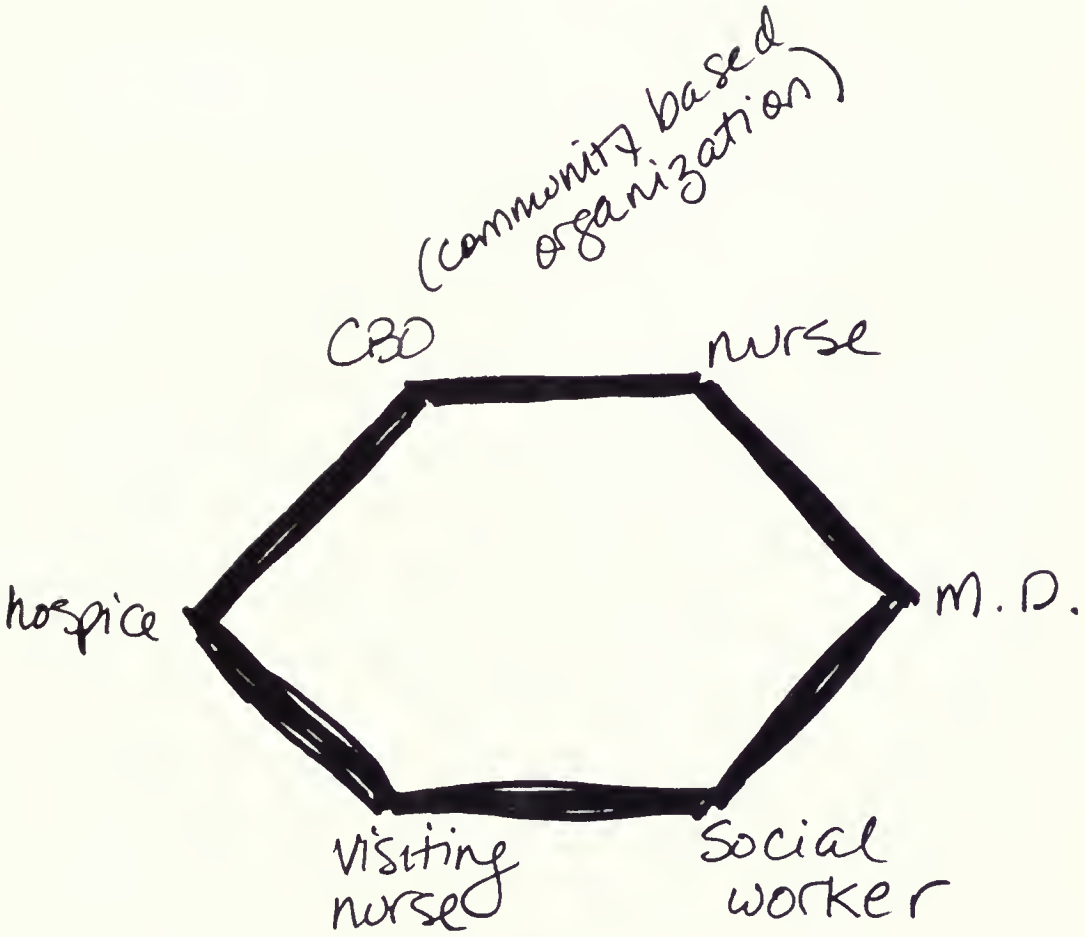
Hughes: What does the San Francisco model mean to you?

Wofsy: What the San Francisco model means to me is a multidisciplinary mechanism of care and services. I'll draw it and I'll verbalize it as I used to give it in talks. Normally, there are organizational hierarchies where there's a box at the top, and then more boxes, and then lines coming on to more boxes. In its most simplistic role in medicine, there's the doctor and the nurse, and then the social worker, and then the hospital aide. That hierarchy would outline this way--doctor, nurse, patient, head social worker, social service aide, floor manager, yadda yadda.

With AIDS, I drew a picture that was like this [demonstrating; see diagram next page].

Hughes: A hexagon.

Wofsy: A hexagon, in which the leader, the one at the top, is from whatever discipline is needed most then. So during the part of the disease's history where it was really all diagnostics, the


(community based organization)
CBO
nurse
hospice
M.D.
visiting nurse
social worker

physician is in charge. Toward the later stage of disease, the hospice manager is the one who's in charge. If it's a research study, the research nurse may be doing the day-to-day management, which technically doesn't seem much different than this. [points to first diagram]

I think what it has to do with is respect for or understanding of how the lattice is structured on the part of other people. So you could turn this hexagon into the clinic setting, where it would be nurse-social worker-doctor; or the city, where it would be public health department-university professor-city treasurer.

I am not trying to be a Polyanna. There were fights like in any family. But I think there was a tacit understanding that everyone in the city was really doing something quite unique and in their own world. Even if you bitched and griped, you recognized that part of what made this whole thing so spectacular was that other person or that other agency, even if you were in direct competition. So if the mayor had an advisory committee, if someone was out there working with needle exchange, if certain people were very skilled at being lobbyists up in Sacramento, we had all the components of a comprehensive response to the epidemic. And, if not working together, at least they didn't work destructively against one another, and they all somehow came together to serve the people of San Francisco. So it's pretty Polyanna, but it's probably at the base true, as long as the people with AIDS in San Francisco were gay men.

Hughes: Well, this model grew up around that population. So what does this say about the model being replicable elsewhere?

Wofsy: It's said the model doesn't work elsewhere, and I disagree. The analogy is things like dialysis units where people have chronic diseases, and someone has to understand the inner workings of that machine--filters and membranes and pore size--and it's not the doctors. And someone else has to understand everything there is about veins. I think they work together in professional collegiality, and to some degree isolation, that is slightly analogous to the AIDS situation. So I think the model is translatable.

The big factor is the support being from the patients themselves. In other places where the patients are disadvantaged, the patients don't function as part of the support structure. They're a stressor; they're what the mission is all about.

Hughes: That hexagon you described is a collaboration. Has that sort of collaboration operated anywhere else?

Wofsy: The reputation of New York was that it didn't. New Yorkers had the reputation that all they ever did was scream at one another. None of us were there, so I don't know. They've done some pretty remarkable things.

Other UC Campuses

Wofsy: In Los Angeles, the other big California city affected by the epidemic, some of the wrangling going on within the major academic institution, UCLA, was legend. Gossip made its way 500 miles north like that [snaps fingers].

Hughes: What factors had the most effect on the way the epidemic was approached in Los Angeles?

Wofsy: I think the biggest one was that Mike Gottlieb, who was essentially the initial identifier of the epidemic, for whatever reason didn't retain his position at UCLA.

Hughes: What effect did that have on the city's response to the epidemic?

Wofsy: I don't know, because I think in the academic community, your major contacts are your academic peers, and so the major sister institution in Los Angeles wasn't a very active player in the epidemic. By and large you don't see the other community service agencies, et cetera, getting involved with AIDS. I've been on the board of the San Francisco AIDS Foundation for three years. Because of my natural inclinations and interest, I was somewhat more aware of AIDS Project Los Angeles and some innovative things that were going for women with AIDS; it was not a vacuum down there at all.

But from the academic point of view, people who wanted to do AIDS had to really push and struggle and work to do it. So academically, less has come out about AIDS from UCLA than from the other UC campuses. San Diego turned out to be a real charger.

Hughes: In terms of research?

Wofsy: Yes, research. For UCLA, I think of AIDS Project Los Angeles and an extensive community-based network. In San Diego, I don't know squat about their community-based organization, but the university does wonderful work.

Hughes: Does that boil down to individual capability?

Wofsy: I think so.

Hughes: What about the players at SFGH?

Wofsy: There was at least one player, or maybe just one, in each position, and real winners. Nobody was assigned to do what they did; they just did it.

Establishing Boundaries at San Francisco General

Hughes: Do you recall maneuvering in the early stages of the epidemic to carve up the turf?

Wofsy: There were always big maneuverings at the boundaries. Big ones.

Hughes: What are you thinking of when you say that?

Wofsy: I think the boundaries included Dr. John Mills as the chief of ID, and Paul Volberding with the AIDS program. This was John Mills' old office. So the ID division, by circumstances much too long to go into history, actually sat here right in the middle of the hallway of the AIDS program. I think Merle was shoring up and pounding away at the boundaries. The person and the place begin to become the same.

Hughes: Individuals' boundaries?

Wofsy: No, the boundaries of the programs. [pause] There are legendary boundary issues in various laboratories and one thing and another, but that's all so much hearsay that it doesn't bear mention on my part.

Hughes: What in the end establishes an individual as the owner of a piece of turf? I'm sure it is more than just publication.

Wofsy: [laughs] I don't know what; jockeying for position, respect, authority, charisma, predatoriness. I don't think it's any different in AIDS than in anything else in life.

Hughes: Many of the early players in the epidemic were not well established in their careers, because they were young. I'd put you in that category--you needed a place.

Wofsy: Right.

Hughes: You began with PCP. I'm realizing that was a natural way for you as an ID person to go, but was there more than that? Was there a realization that this was an area that could be claimed and used to establish yourself academically?

Wofsy: At the beginning of the epidemic, my view was it didn't look like anything anybody was ever going to want, not because they were afraid of it--it didn't look like anything. It looked like a 3,000-piece jigsaw puzzle that only a fool would spend his time on, while other people could productively do something that had fewer pieces and more instant completion. So I think that even the concept of turf or territory related to AIDS was just not there. It was, if anything, "Why that? Why don't you get on with your career, instead of chasing dismal things at the end of dark rainbows?"

KS was the lead, so there was really something tangible to grab on to initially as the concrete entity. It looked like KS was all there would be, this unusual cancer, and that was it. It took a while for any territory to come into it. I think it was obligation to the affected patients. I think it took three or four years for professional advantage to come into play.

AIDS and the Doctor-Patient Relationship

Hughes: Has the epidemic affected the doctor-patient relationship?

Wofsy: I'm trying to think how to respond to this. [pause] I've been at the county hospital since 1974, and the county hospital is a place that serves people who don't have anybody else. This sudden influx of highly articulate, young, questioning people was stunningly stimulating and held the physician to the kind of expectation that private patients hold their physicians to, in a setting in which the amenities simply weren't there. I think that the San Francisco model painted AIDS as a special disease, and painted people with AIDS as more deserving of better care, from the health care provider and the system, than for other diseases.

It was a model of addressing the whole life of the patient, as opposed to heart disease which addresses bypass surgery, diet, exercise. But I really can't think of anything I've ever heard in a cardiology lecture that addressed where the person lives, whether somebody is going to form an apartment complex for people with bad congestive heart failure who can't sleep with their spouse any more at night because they wheeze and get up, and people get terrified about sudden death--I mean, it just doesn't

happen. There is a place where the medicine ends, and then the person lives out their disease. I think that AIDS set up the model that the clinical providers take care of everything. That was projected back to the health providers as a sense of pride on the one hand and responsibility on the other.

I realized for myself that I, as probably a lot of people who deal with a lot of dying patients, was getting too close and I had to back up and develop my own training about how to deal with patients who were dying. This is something that oncologists probably get a little during their fellowship, where they're being guided about how to deal with dying patients while intensively working with people who aren't going to have a good outcome. So in the AIDS epidemic this had to happen on the spot without specific training.

Maybe starting four or five years ago, the expectation that AIDS is a disease that encompasses all of one's persona, and that the medical system takes care of everything because it understands and doesn't judge, has expanded to populations that are very disadvantaged and have many more serious life consequences than AIDS. They expect the ubiquitous "they" will do for me; "they" will get it taken care of, both on an individual basis and as an advocate for other serious life traumas--legitimate, horrible things about people's lives. So somehow AIDS and spousal abuse, or physical abuse to women, get linked up in a way so they start to become hard to separate. Somehow those lobbying/advocacy efforts all come together. I remember we were stunned the first time someone came to the AIDS Clinic because of physical violence.

This concept of total care has moved over into a new population which we can't handle well. And so we're having to retool to nurture and distance to selected advocacy. Choose your cause: needle exchange, or homeless, or whatever; you can't do the whole plate. Maybe I'm just speaking for myself, but it certainly was true of me. I had to realize those things.

The other thing the epidemic did is encourage this concept of the physician-patient team. We were involved in the care of articulate people, and, without even thinking of it, I lost any concept of paternalism in medicine. You know, "I [the physician] tell you what to do." I also, I hope, never gained, "What do you [the patient] want to do?" I think that's absolutely horrible to impose on patients. I'm not sure what to do, and I went to medical school and took all this training; how could a patient possibly know? But I learned in my work with AIDS patients to make recommendations and talk the recommendations over back and forth.

I find it very unrewarding now to take care of patients with whom there is no exchange. "Now, I want you to take this medicine. This is a good, strong medicine for you. It's a powerful medicine. It will work for your infection." If I can't get any shade of discussion or education or nuance in there at all, I find it frustrating.

I've had the benefits of public practice, with all of its altruism and MASH-unit kind of staff associations, and the very best of private medicine in terms of a young, intellectually challenging patient population, all under one roof, the best of both worlds. And it now makes it hard when I don't have that intellectual stimulation going back and forth between the patient and me. I don't mean the patient has to be bright, but just generates some sense of resistance back and forth. I can deal with a very uneducated patient who says, "Now, is that a good medication for my heart?" I can change my language to have a dialogue, and then that's very satisfactory.

Hughes: That dialogue format is not the way that physicians in this country in the past have been taught to interact with patients.

Wofsy: I think it is now. There are a lot of articles now--the *Annals of Internal Medicine* in the last few years has started sections that deal with the art of medicine, being a doctor. There are opinion pieces on how to empathize that aren't soupy and sentimental, but are sort of clinical. There are four or five basic personality styles in patients; a physician has to learn how to approach different kinds of behaviors. So there's a lot coming out about how to relate in a dialogue to patients. I think AIDS led that a lot. And no, it's not traditional.

Total Care of the Patient

Hughes: Is total care also something that the AIDS epidemic contributed to medicine? Had there been that concept in any other phase of medicine?

Wofsy: I may have a different opinion than some of my colleagues. I think total care is more than medicine can do. The thing I've found the most personally difficult is the lack of a boundary between me as a doctor and providing for me as a person.

I'm going to be tangential: the CDC is beginning to approach life as a health issue. In other words, the bulletin of the Centers for Disease Control [*Morbidity and Mortality Weekly*

Report] devotes the overwhelming majority of its publication to infectious diseases, and then occasionally to abortion, motor vehicle accidents, et cetera. But now, as we're turning to prevention of violence as a vaccine as it were, in a way society is looking at life harm as bad for health. But as a physician, I find there are limits to what I can give. Medicine is much more than prescriptions and diagnostic tests and cold, didactic interaction. But when a patient says, "My life is broken, and you, collectively, need to fix it," I don't have that responsibility.

Hughes: Did you feel at one stage that you did?

Wofsy: Yes. I felt in the years early on, when the disease was mostly affecting gay men, that the doctor needed to do the advocacy, the lobbying against the social disservices, the injustices, the discrimination against gay men. Who else was going to do it? Who else saw the issues? And then later lots of people became involved. So everyone--the doctor, the nurse, the social worker, the ACLU [American Civil Liberties Union], everyone--began to play a role. And now I see it in San Francisco with other populations. For example, homelessness and AIDS get linked in the same sentence.

Hughes: So it's quite clear that no one profession can handle all the dimensions of the problem.

Wofsy: Yes. It may be so clear to my colleagues that it doesn't occur to them to talk about it, but I am aware that I feel, as I did early in the epidemic, and I'm getting over it, that we have to solve all these problems.

Hughes: Is there an element of personal protection in this? I read into some of the things that you've said in the course of the interviews that in the early years of the epidemic, for you and maybe for others who were directly involved, your personal life was put more or less on hold; everything was subsumed to the epidemic.

Wofsy: Yes. There's no question about that. So what's the question?

Hughes: Well, it's more or less a statement. I also gather from what you're saying that that particular approach was really not sustainable.

Wofsy: It was not sustainable. And I wish some wise person had been around to say that. [laughter]

Hughes: Your family didn't say that to you?

Wofsy: You don't listen to your family. Everyone you're working with is doing the same thing, so that's the norm. And then everyone who's not your family goes, "Oh, I don't know how anyone could do what you're doing." And that's no basis for judgment either. There's a reaction, "Oh, God, I couldn't deal with people who are dying." So then you've got them to educate, too.

We take a weekly vacation each year to a family camp. There were years, literally years, where, except for my inner circle of three or four families who go the same time each year so we know each other well, it was almost a conspiracy of silence in which what I did as a physician didn't come up. It was almost unspoken that I and my close friends would deflect anything that would bring in the word "AIDS" into the conversation. I couldn't bear to hear the word; I couldn't bear to have it brought up; I couldn't bear the curiosity. And I think a lot of people had the same experience at that time: "Just don't discuss it." This was between the years of maybe 1983 and 1988--just don't talk about it. Now, who could care? We're so tired of reading about AIDS in the paper.

Hughes: Was that part of the distancing, trying to keep your professional and your private life separate?

Wofsy: I think so, yes.

Impact on Family Life

Hughes: What did the epidemic do in those early years to your family life?

Wofsy: Hard to know. In 1982, when I first started, my son was eight, and my daughter was four. Well, there are two things. One is that my husband, who's also in academics,[1] was enormously supportive. I think no woman could conceivably have done this without an extraordinarily supportive partner. (I'm so used to politically correct language, I don't even say husband or wife, but partner!)

Travel came into the picture very early, and it just became a way of life. So in terms of the kids' resenting it, it just didn't come up. I remember dropping my daughter at school one day--she may have been in the second grade--and I said, "Bye!"

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[1]David Wofsy is professor of medicine and microbiology-immunology at the Veterans Administration Medical Center, an affiliate of UCSF.

She said, "I'll see you tonight." I said, "Oh, no, I won't be home tonight." And she said [brightly], "Oh! Where are you going?" And I said, "Well, Atlanta." And she said, "Oh! I'll see you tomorrow?" And I said, "Yeah." And she said, "Okay, see you tomorrow." [laughter]

Hughes: Just what Mom does.

Wofsy: That's what Mom does. And I think to my kids, frankly, it looked very glamourous. I was on television. They pick up the paper, I'm in the paper; I'm getting awards. From their very narrow point of view, they have a famous mom. Someone at school saw your mom on television: that's a famous mom. And I think somehow the issue of doing good things for people came across. We'd go to the international AIDS meeting, and they came sometimes. I don't think kids think of it, but they began to link up some special trips and Mom's meetings. I think if you ask them, they would see only the advantages. I don't think that they would verbalize disadvantages, but they may have been present at the time.

I think it was a big hardship for David, because he also had an academic career, and I traveled more and was rushing off to meetings. He did much more with the children. He's inclined to do a lot anyway, but he did more than would have fallen on his plate under other circumstances.

The international AIDS meeting, God forbid, was held in a different major European city every year for seven consecutive years. That's a lot of international travel by the time you're done. Now people in academics travel a lot, but I think we AIDS physicians were six years ahead.

Publication

Hughes: Do you want to comment on publication in AIDS, particularly the tension between the need to get new information out to where it could be applied, and the academic need to preserve that information until it had been peer reviewed and then published?

Wofsy: I remember being horrified in situations where somebody would make comments before something had been published in peer-reviewed literature. I remember making tangential allusions to a new finding and wondering, "Oh, my God, what's the *Chronicle* going to say tomorrow? Oh gee, does that mean it can't ever be published?"

I think that quick publications, news magazines, things that tell of research in progress and preliminary trends that need exploration, are a big step forward.

Hughes: Do they preclude publication elsewhere?

Wofsy: Not now. It has also been my observation over time that activists will say, "We can't get information. You're withholding information." And I'm sometimes frustrated because I have just been to nine meetings of varying levels of sophistication at which I thought I would fall asleep hearing the same information again and again and again, where the presenter seems like he's on autopilot.

I realize what the person is really saying is, "I don't have information in the language that's targeted at me specifically, where someone is really leading me through." That's what they mean. "Information out there" means to me, "information that I understand and relates to my particular circumstances."

Hughes: Is that part of a physician's responsibility?

Wofsy: No, I don't think so.

When I say activists, that's a broad term, because activism implies somebody branching off the mainstream. It may be an affected person who is quite a shy, retiring sort, who just says, "I really want to know."

Hughes: What you're talking about is the loosening of boundaries between public and professional knowledge.

Wofsy: Right.

Hughes: Is that a movement that's been prompted by the epidemic? Did AIDS lead the way?

Wofsy: To my view, it has. There was a meeting headed by Jonson, a medical ethicist--

Hughes: Al Jonson, yes.

Wofsy: --in which fifteen or so opinion leaders got together and asked, "Has AIDS really made a substantive effect on the practice of medicine?" And he gave a grand round saying, "No." These opinion leaders felt that if AIDS had never happened, things essentially wouldn't be much different now; changes in certain legal issues related to medicine aren't traced to AIDS. His argument was

rather plausible, the way well-articulated arguments are. I don't buy it.

Hughes: Tell me why.

Wofsy: Perhaps because I was in medicine for a hunk of time before AIDS. You get to compare and contrast. It seems to me that everything one can come up with in medicine first happened in the AIDS arena: short-tracking medications for licensure, parallel track, durable power of attorneys becoming routine, anti-discrimination legislation, changes in the way the physician interacts with the patient. But I'm sure others could be more articulate.

Ethical Issues

Hughes: AIDS raises a lot of delicate ethical issues concerning confidentiality and personal rights versus public rights. Please comment.

Wofsy: The physician is principally involved with individuals, one at a time, who collectively are his or her patients. And, in the traditional setting, maybe in hospital committees, he deals collectively with patients. Except for those who became involved in health care policy, I think the majority of one's colleagues really have a focus on the individual patient's life.

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Wofsy: They constantly found problems in that the goals of society and medicine were often diametrically opposed. An example is, lack of disclosure of HIV test results for the individual patient is iron-clad. Looked at from the societal point of view, to be unable to test and unable to have a nomenclature [HIV positivity or negativity] in which to converse back and forth and deal with the individual's health issue is ludicrous. And yet, to generalize the individual issue, which is one of non-discrimination, lack of disclosure of HIV status, and protection of individual rights made the job of being a doctor extremely difficult and fraught wtih charting subterfuge.

We used to teach medical students what euphemisms to use. It was crazy. How they were not to state "the person with HIV" but to hope that the next physician would be able to decipher their medical record note to understand what this person was really sick with so that the person would get reasonable care.

Experiencing the Epidemic

Hughes: There are a lot more questions I could ask, but I think the time has come for you to set the record straight in any way you wish.

Wofsy: Let me just think for a second. Well, I'll just be personal, and it may be generalizable.

AIDS has occupied more than a decade of my professional life, and was superimposed on the very heart of the upbringing of two children, the most productive personal as well as professional years, those very high activity years. Things seem like the norm if you and the people closest to you are doing those things. I think I'm now able to reflect that this hasn't been the norm, and that we--many of the people who have come up in our conversations --lived through a period of medical history that's not unparalleled, but is unique within the academic and medical practice world, and that we have this unspoken thing in common with each other that must be true of people who were in World War II or who spent a sustained period of time under extraordinary conditions. When you step back from it, you say, "Oh, that wasn't normal, everyday life." It's those who have been doing it for ten years and more that share something unspoken that's unique and that was not normal and usual.

The other thing is that sometime fairly early in the epidemic, providing public information, public service, through the media and newspapers and videotapes and church groups--that is, the community--became a part of medicine. It introduced me to a world that I had been absolutely blind to when I was in medicine before HIV. It's been too much and too hard, but it would be hard to give up almost any of the experiences. If I had to go through and say, "Put a red line through that one," it would be hard to know which experience to put the red line through. However, I think things don't need to be quite so densely packed, and I can relax a little.

Hughes: Which I hope you are now doing.

Gender and Sexual Preference

Hughes: Has it made any difference, the fact that you are a woman in a leading position in the epidemic?

Wofsy: I think in the way that AIDS was ahead of its time in being multidisciplinary, it also may have been four or five years ahead of its time in looking a little less at the sex or sexual preference of people who were interested in getting involved, and more at what they did. If you're willing to do it [AIDS work], great. We don't care if you've got polka dots.

I think that some of the opportunities I've had have come about because "we should have a woman"--on the panel, on the committee, in the discussion, in whatever way. I consider that to my advantage. Nothing comes in a vacuum. Everyone is given opportunities for a variety of reasons, the bulk of which are competence, and then there are a whole lot of other shades of grey around it. So I've been glad for those opportunities. Your question raises a whole lot of complexities about women in more senior positions, which I think are the subject of another book.

Hughes: I'll come back for that one in a few years. [laughter] Well, thank you, Dr. Wofsy.

Transcribed and Final Typed by Shannon Page

TAPE GUIDE--The AIDS Epidemic in San Francisco: The Medical Response, 1981-1984: Volume III

Note: Because large portions of the transcript were relocated, cut, and amplified on in this oral history, it was not possible to create a meaningful tape guide to the Arthur J. Ammann, M.D. interviews.

APPENDICES

APPENDIX A: AIDS CHRONOLOGY[1]--by Sally Smith Hughes

1968-1970 David Baltimore and Howard Temin independently discover reverse transcriptase, a marker for retroviruses.

1974 Charles Garfield founds Shanti Project to provide free volunteer counseling to people with life-threatening illnesses.

1976 Robert Gallo isolates T-cell growth factor (interleukin-2), allowing T-cells to be cultured in vitro.

1978 San Francisco Mayor George Moscone assassinated; Dianne Feinstein becomes mayor.

1980 Gallo demonstrates that retroviruses (HTLV-I and HTLV-II) can infect humans.

1981:

February Michael Gottlieb, UCLA, diagnoses Pneumocystis carinii pneumonia [PCP] in two homosexuals.

March Gottlieb diagnoses another case of PCP in a homosexual.

Sandra Ford, drug technician for Centers for Disease Control [CDC], officially notes increase in requests for pentamidine, for treatment of PCP.

Constance Wofsy diagnoses CNS toxoplasmosis in gay patient at San Francisco General Hospital [SFGH].

April Gottlieb diagnoses two more cases of PCP in homosexuals.

Two Kaposi's sarcoma [KS] cases in San Francisco and Stanford announced at UCSF dermatology grand rounds.

May/June Donald Abrams and others see cases of PCP in gay men at SFGH.

June 6 - CDC's Morbidity and Mortality Weekly Report [MMWR] publishes Gottlieb and Wayne Sandera's report on PCP in 5 gay men.

June 8 - First meeting of CDC Kaposi's Sarcoma/Opportunistic Infection [KSOI] Task Force, headed by James Curran. Purpose to characterize syndrome and determine frequency, risk, and etiology. Surveillance and case file for KS and PCP initiated.

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[1] This chronology is an ongoing working draft created to assist the oral history project; its focus is San Francisco and its accuracy contingent upon the many sources from which it was derived.

June (late) First case of KS diagnosed in gay man at SFGH.

July City of San Francisco establishes reporting and case registry system for KSOI.

July 3 - First press report of syndrome appears in New York Times.

MMWR reports Kaposi's sarcoma in 26 gay men.

July 13 - First article on KS in New York Native.

August CDC requires health departments to notify CDC of all KSOI cases.

Aug. 28 - MMWR reports first heterosexuals, including first female, with KSOI.

September CDC begins case-control study with 50 gay KSOI patients and 120 "healthy" gay ccontrols to determine factors in homosexual environment possibly causing KSOI.

Sept. 15 - CDC and National Cancer Institute sponsor workshop on KS and opportunistic infections. CMV leading candidate for cause.

Sept. 21 - First KS Clinic and Study Group held at UCSF.

October Friedman-Kien et al. begin study of clinical course of KS in gay men.

November Shanti begins to focus on psychosocial problems of people with KSOI.

December First clinical descriptions of immunosuppression in IV drug users.

John Ziegler, Conant and Paul Volberding receive $50,000 from American Cancer Society to support KS Clinic at UCSF; first grant awarded for AIDS.

CDC investigators suspect that causal agent of AIDS is infectious but cannot provide irrefutable evidence. Others support "lifestyle" hypothesis.

Reagan proposes massive cuts in CDC budget.

Dec. 9 - Marcus Conant passes out flyers on KS at American Academy of Dermatology meeting in San Francisco.

Dec. 10 - Durack at Duke suggests amyl nitrites ("poppers") might cause immune dysfunction.

New England Journal of Medicine article links immune deficiency to T4 helper cell/T8 suppressor cell ratio.

1982:

Early 1982 Syndrome is named gay-related immunodeficiency disease--GRID.

January First case of immune deficiency linked to blood products is reported in a hemophiliac.

Helen Schietinger becomes nurse-coordinator of KS Clinic at UCSF.

San Francisco health department makes first request for tax funds to support AIDS prevention and community services; Board of Supervisors appropriates $180,000 for AIDS programs.

March 4 - MMWR lists four risk groups for AIDS--homosexuals, hemophiliacs, Haitians, and IV drug users [IVDUs].

April Congressional subcommittee hearing in Los Angeles on AIDS, Henry Waxman (D-CA), chairman.

May (Mother's Day) Conant, Frank Jacobson, and Richard Keller write articles of incorporation for Kaposi's Sarcoma Research and Education Foundation, predecessor of San Francisco AIDS Foundation.

May 15 - Friedman-Kien et al. publish study showing promiscuity greatest risk factor for KS. Authors support immune overload theory of AIDS causation.

June 18 - CDC reports cluster of PCP and KS cases in LA and Orange County, suggesting infectious agent is cause of AIDS.

June 26 - UCSF Nursing Services sponsors conference, Kaposi's Sarcoma and Pneumocystis Pneumonia: New Phenomena among Gay Men.

July CDC, FDA, and National Hemophilia Foundation representatives meet to plan risk evaluation of blood products for hemophiliacs.

July 9 - CDC publishes first report of 31 cases of opportunisitic infections in Haitians.

July 13 - First international symposium on AIDS, at Mt. Sinai Medical Center, New York, sponsored by Mt. Sinai and New York University schools of medicine.

July 16 - MMWR reports first three cases of PCP in hemophiliacs, representing first cases of KSOI caused by blood or blood products.

July 21 - KS Foundation operates hotline for advice and referrals regarding AIDS, KS, and opportunistic infections [OIs].

July 27 - CDC adopts "acquired immune deficiency syndrome--AIDS" as the official name of the new disease.

August CDC asks blood banks not to accept high-risk donors; CDC recommends hepatitis B core antigen testing.

Aug. 13 - National Cancer Institute [NCI] issues RFA for research on AIDS.

Sept. 24 - CDC publishes first official definition of AIDS: a disease due to defect in cell-mediated immunity occurring in people with no known cause for immune deficiency.

First? published use of term "AIDS", in MMWR. Rapid adoption of term thereafter.

October KS Research and Education Foundation contracts with San Francisco Department of Public Health [SFDPH] to provide AIDS education services in San Francisco.

Oct. 29 - UCSF Departments of Medicine and Dermatology and Cancer Research Institute sponsor program in medical education, Acquired Immunodeficiency Syndrome and Kaposi's Sarcoma. Almost 200 physicians and scientists attend.

November MMWR suggests that hospital staffs caring for AIDS patients use hepatitis B precautionary measures.

December Shanti makes first in series of contracts with SFDPH to provide counseling services and a housing program for people with AIDS [PWAs].

Dec. 1 - House of Representatives votes $2.6 million to CDC for AIDS research.

Dec. 4 - CDC presents Blood Products Advisory Committee with evidence of AIDS transmission through blood supply; no official action taken.

Dec. 10 - Ammann, Cowan, Wara et al. report first case of possible transfusion AIDS, in MMWR.

Dec. 17 - MMWR reports four cases of unexplained immune deficiency in infants.

Late 1982 Most investigators convinced that AIDS is caused by an infectious agent.

Nation's first AIDS specimen bank established in UCSF School of Dentistry, coordinated by KS Clinic.

1983:

Early — New York City health department establishes formal AIDS surveillance program.

Beginning of bathhouse crisis. Formal AIDS infection control guidelines instituted at San Francisco General Hospital.

January — Montagnier, Barré-Sinoussi, and Chermann at Pasteur Institute, seeking to isolate an AIDS virus, begin to grow cells from lymphadenopathy patient.

President of New York Blood Center denies evidence of transfusion AIDS.

Orphan Drug Act becomes law, giving exclusive marketing rights, tax breaks, and other incentives to companies developing drugs for rare diseases.

Jan. 1 - First outpatient clinic dedicated to AIDS (Ward 86) opens, at San Francisco General Hospital.

Jan. 4 - CDC national conference to determine blood bank policy re blood screening for AIDS; no consensus.

Jan. 7 - CDC adds heterosexual partners of AIDS patients as fifth risk group for AIDS.

Montagnier et al. find traces of reverse transcriptase in lymphadenopathy cell cultures.

San Francisco's Irwin Memorial Blood Bank [IMBB] adds medical history questions designed to screen out donors from high-risk groups.

Jan. 14 - National Hemophilia Foundation asks blood and plasma collectors to screen out high-risk donors.

Jan. 19 - Irwin Memorial Blood Bank adds more questions about medical history of potential donors.

February — At Cold Spring Harbor Workshop on AIDS, Robert Gallo suggests that a retrovirus probably causes AIDS and presumes a variant of HTLV-I or HTLV-II.

Feb. 3 - Physicians from UCSF KS Study Group urge IMBB to use hepatitis B core antibody test to screen out blood donors with AIDS.

Feb. 7 - IMBB launches confidential questionnaire designed to detect potential blood donors with AIDS. Bay Area Physicians for Human

Rights urges potential donors to refrain from donating if they have AIDS symptoms.

March — CDC establishes clinical definition of AIDS in attempt to standardize epidemiological surveillance.

UCSF Task Force on AIDS created, mainly to establish infection control policy.

California requires reporting of AIDS cases, but not AIDS -Related Complex [ARC].

Public Health Service [PHS] recommends members of high risk groups reduce number of sex partners.

Mervyn Silverman, SFDH director, forms Medical Advisory Committee on AIDS.

Mar. 4 - MMWR first refers to "high risk" groups: gays with multiple sex partners, IVDUs, Haitians, and hemophiliacs.

CDC states that "available data suggests that AIDS is caused by a transmissible agent."

Mar. 17-19 New York University sponsors AIDS symposium.

Mar. 24 - FDA issues blood donor screening guidelines.

April — Congressman Phillip Burton dies; Sala Burton eventually elected to his seat.

City of San Francisco and Shanti open hospice-type care center for neediest AIDS patients.

Conant, Volberding, John Greenspan, Frank Jacobson, and others persuade Willie Brown to ask for $2.9 million in state funding for AIDS research.

April 11 - Date NCI officials later cite as when NCI became committed to finding AIDS etiology.

April 14 - Irwin Memorial Blood Bank [IMBB] adds donor sheet designed to screen out donors at high risk for AIDS.

April 26 - Recall of San Francisco Mayor Feinstein, supported by White Panthers and some gay groups, fails.

May — NIH announce $2.5 million for AIDS research. NCI and NIAID issue RFA [Request For Applications] for research on an infectious agent.

Heat treatment to reduce infectious agents in transfused blood approved by FDA.

San Francisco health department issues first brochure on AIDS.

Feinstein declares first week in May AIDS Awareness Week.

May 2 - "Fighting for our Lives" candlelight march in San Francisco to bring attention to AIDS; similar march in NYC.

May 6 - Journal of the American Medical Association [JAMA] press release: "Evidence suggests household contact may transmit AIDS."

May 12 - UCSF announces receipt of $1.2 million for AIDS research; Paul Volberding, principal investigator

May 20 - Montagnier publishes discovery of "T-cell lymphotrophic retrovirus," later called lymphadenopathy-associated virus (LAV).

May 23 - San Francisco Board of Supervisors votes $2.1 million for AIDS programs, $1 million of which is for out- and inpatient wards at SFGH.

May 24 - Edward Brandt, Assistant Secretary of Health, declares AIDS research #1 priority.

May 31 - Health department director Mervyn Silverman, backed by Feinstein and San Francisco Board of Supervisors, requires city bathhouses to post public health warnings about contracting AIDS.

June UC issues guidelines to protect AIDS patients and health workers.

San Francisco Men's Health Study begins to recruit participants.

Feinstein chairs first U.S. Conference of Mayors Task Force on AIDS.

July California legislature approves $2.9 million for AIDS research.

Donald Abrams begins work at SFGH AIDS Clinic, bringing 200+ lymphadenopathy patients from UCSF.

July 26 - 12-bed inpatient Special Care Unit (Ward 5B) opens at SFGH--first dedicated AIDS hospital unit in U.S.

July 28 - Universitywide Task Force on AIDS created to advise UC president on guidelines for and coordination of state-supported AIDS research at UC.

August — Willie Brown, Rudi Schmid, Conant and other AIDS researchers criticize UC for delays in releasing state funds for AIDS research.

September — At Cold Spring Harbor NCI meeting on human T-cell leukemia retroviruses, Montagnier et al. report LAV-like viruses in 5 lymphadenopathy patients and 3 AIDS patients, selective affinity of LAV for CD4 helper lymphocytes, and evidence of similarities between LAV and lentivirus causing equine infectious anemia. Gallo presents findings of HTLV-I in 10% of AIDS patients; doubts LAV is retrovirus.

UC states that there is no scientific reason for healthy medical personnel to be excused from caring for AIDS patients.

Bureau of Infectious Disease Control, SFDPH, begins active surveillance of AIDS cases in San Francisco.

Sept. 13 - Montagnier sends Gallo sample of lymphadenopathy-associated virus [LAV].

Sept. 21 - UCSF Task Force on AIDS publishes infection control guidelines for health care workers caring for AIDS patients.

November - KS Research and Education Foundation contracts with State of California Department of Health Services to provide information and referral services on AIDS to other counties.

Mika Popovic in Gallo's lab discovers method for growing AIDS virus in T-cells.

San Francisco Department of Public Health asks for legal option to make baths off-limits to PWAs. Lawyers decide that medical uncertainties about AIDS prevent such action.

Jay Levy obtains six viral isolates from AIDS patients but decides not to publish until further proof.

December - Pasteur Institute applies for U.S. patent on diagnostic kit based on ELISA test for LAV antibodies.

Feinstein votes against live-in lover legislation, angering gay community.

AIDS Clinical Research Centers established with state funding at UCSF and UCLA to collect clinical and laboratory data.

National Association of People with AIDS formed.

Entry "AIDS" added to Cumulated Index Medicus.

Council of State and Territorial Epidemiologists passes resolution making AIDS a reportable condition.

Hospice of San Francisco contracts with SFDPH to include AIDS patients in its care of terminally ill.

1984:

January — Annals of Internal Medicine reports case of heterosexual transmission of AIDS before overt manifestation of disease (hemophiliac to wife).

American Red Cross, American Association of Blood Banks, and Council of Community Blood Centers oppose proposal to screen out high-risk groups from blood donor pool.

Jan. 6 - CDC updates its definition of AIDS.

Jan. 12 - NEJM publishes CDC documentation of first 18 transfusion-associated AIDS cases.

February — Chermann in talks in U.S. states that French have discovered AIDS virus.

March — President of New York Blood Center continues to deny HIV transmission by blood.

Larry Littlejohn, gay activist, sponsors San Francisco ballot initiative to close baths.

Mar. 2-4 - 19th Annual San Francisco Cancer Symposium, "Cancer and AIDS". Conant, Abrams, Wofsy, Ziegler, Volberding speak.

March 6 - Blood industry task force meets on surrogate testing; blood bankers oppose it.

March 26 - Government allots $1.1 million to develop AIDS antibody test to seven institutions, including Irwin Memorial and Stanford blood banks.

April — Feinstein issues first formal statement that Silverman should close baths. Silverman responds that he will formulate guidelines banning sex activity in baths that spreads AIDS.

NIH applies for patents on Gallo's AIDS antibody test, a diagnostic kit based on Western blot technique.

April 9 - Silverman and state and San Francisco health officials outlaw sex in bathhouses, rather than close them.

April 24 - Margaret Heckler, Secretary of Health and Human Services, announces discovery by Gallo et al. of AIDS virus, that an AIDS test will be available soon, and that a vaccine will be available in 18-24 months. Gallo had not yet published his results.

May Gallo publishes four reports and Montagnier one, in Science, linking AIDS with a new retrovirus which Gallo calls HTLV-III and Montagnier calls LAV.

Board of Supervisor's president Wendy Nelder chides Silverstein for "shameful" delays in proposing sex guidelines for baths. Silverman replies that he is waiting for board to transfer authority to regulate baths from police to health department.

Rock Hudson diagnosed with AIDS.

May 1 - IMBB and other Bay Area blood banks begin testing blood for hepatitis B core antigen.

Summer Silverman orders bathhouse surveillance for unsafe sex.

June Board of Supervisors committee delays action on giving health department authority to regulate baths until after Democratic National Convention in San Francisco.

IMBB adopts directed blood donation program.

July Democratic National Convention in San Francisco.

August After gay lobbying, Board of Supervisors tables move to give Silverman regulatory power over baths, killing his idea to promulgate sex guidelines for baths.

Levy et al. isolate virus, ARV, which they claim to cause AIDS.

September Chiron Corp. announces cloning and sequencing of ARV genome.

Giovanni Battista Rossi in Italy isolates AIDS virus.

October Feinstein forms Mayors Advisory Committee on AIDS.

FDA approves Lyphomed's injectable pentamidine for PCP and gives it orphan drug status.

Bureau of Communicable Disease Control, SFDPH, begins surveillance of average monthly AIDS bed census.

Oct. 9 - Silverman closes baths and private sex clubs as "menace" to public health. Baths reopen hours later.

November Gallo et al. clone HTLV-III.

Nov. 28 - San Franciso Superior Court Judge Roy Wonder rules baths can remain open if monitored for safe sex practices every 10 minutes.

December Montagnier et al. report cloning of LAV; they also report CD4 molecule as LAV receptor.

Silverman resigns as director of SFDPH.

90 reported cases of transfusion AIDS; 49 reported cases of Factor VIII hemophilia cases.

CDC recommends use of heat-treated blood products for hemophiliacs; other specialists differ. Heat-treated blood products become commercially available.

National Kaposi's Sarcoma Reasearch and Foundation renamed San Francisco AIDS Foundation.

Dec. 26 - Simon Wain-Hobson, Pierre Sonigo, Olivier Danos, Stewart Cole, and Marc Alizon at Pasteur Institute publish LAV nucleic acid sequence in Cell.

1985:

January Gallo et al. publish full nucleic acid sequence of HTLV-III.

Jan. 14 - Irwin Memorial Blood Bank prohibits males having more than one sex partner to donate blood.

February FDA approves Gallo's AIDS diagnostic kit based on Western blot technique.

Feb. 1 - Paul Luciw, Jay Levy, Ray Sanchez-Pescador et al. at Chiron publish ARV nucleic acid sequence.

Feb. 7- Dan Capon, M.A. Muesing et al. at Genentech publish ARV nucleic acid sequence.

March San Francisco County Community Consortium founded for community-based AIDS drug testing.

March 2 - FDA approves Abbott Laboratory's commercial test for AIDS. Red Cross contracts with Abbott, one of five companies supplying test, and in days phases in test. Britain and France delay testing six months to introduce their own antibody tests.

March 3 - IMBB introduces genetically engineered hepatitis B antibody core test.

March 4 - First International Conference on AIDS, Atlanta

March 6 - IMBB institutes anti-AIDS virus antibody test, the first blood bank in U.S. to do so.

March 14 - San Francisco Chronicle reports army study showing AIDS transmission through heterosexual contact.

Spring California legislature and Gov. Deukmejian approve bill banning HIV antibody testing without subject's written informed consent, except at test sites where testing is anonymous. Bill also bars employer and insurance company discrimination on basis of AIDS status. $5 million appropriated to establish HIV community test sites. Disclosure of test results to third party must be improved in writing by test taker.

April CDC drops Haitians from high risk groups for AIDS.

May US Patent Office awards patent on Gallo's antibody test.

Summer AIDS diagnostic kits using ELISA become commercially available. California law mandates every county to offer AIDS test at public health centers; guidelines for preserving confidentiality.

June American Association of Blood Banks, American Red Cross, Council of Community Blood Centers agree not to begin "look back" program to identify people who have received AIDS-infected blood.

National Institute of Allergy and Infectious Diseases [NIAID] creates first AIDS Treatment Evaluation Units, predecessor to AIDS Clinical Trial Groups (ACTGs).

California public health clinics begin testing for AIDS.

June 24 IMBB adds bar codes for confidential exclusion of blood units.

September Mathilde Krim and Michael Gottlieb found American Foundation for AIDS Research [AmFAR], merging AIDS Medical Foundation of New York and National AIDS Research Foundation of Los Angeles.

Martin Delaney and others found Project Inform.

October Public's awareness of AIDS rises with Rock Hudson's death.

Congress allots $70 million to AIDS research day after Hudson's death.

December Pasteur Institute sues for share of royalties on AIDS antibody test.

CDC first considers vertical transmission of AIDS virus; advises infected women to "consider" delaying pregnancy until more known about perinatal transmission.

CDC contracts with San Francisco AIDS Foundation to develop materials for anonymous AIDS testing sites.

Late in year Department of Defense announces that new recruits will be screened for AIDS and rejected if positive.

Third UC AIDS Clinical Research Center founded at UCSD. Goals of three centers broaden to include rapid evaluation of new therapeutic agents.

13-year-old Ryan White, a hemophiliac with AIDS, is barred from school in Indiana.

CDC expands surveillance definition, in light of HIV antibody test.

KEY PARTICIPANTS
in San Francisco AIDS History, 1981-1984

Appendix B

*[1]Donald A. Abrams, M.D., AIDS clinician and member of original AIDS physician team at San Francisco General Hospital (SFGH); early research on AIDS-associated lymphadenopathy (swollen lymph glands); organizer of County Community Consortium.

*Arthur J. Ammann, M.D., pediatric immunologist at University of California, San Francisco (UCSF); conducted early studies of AIDS-associated immune deficiency in adults and children; reported first case of transfusion AIDS; currently head of a pediatric AIDS foundation.

Francoise Barré-Sinoussi, retrovirologist at Pasteur Institute and member of team which isolated AIDS virus.

Edward N. Brandt, Jr., M.D., Ph.D., Assistant Secretary for Health, U.S. Department of Health and Human Services, 1981-1984.

Conrad Casavant, immunologist in Department of Laboratory Medicine and associate director of Clinical Immunology Laboratory at UCSF; died of AIDS in 1987.

Jean-Claude Chermann, retrovirologist at Pasteur Institute and member of team which isolated AIDS virus.

*Marcus A. Conant, M.D., clinical professor at UCSF, and dermatologist with private AIDS practice; diagnosed first case of Kaposi's sarcoma in San Francisco; founder of first AIDS clinic (at UCSF); medical activist at local, state, and federal levels.

James W. Curran, M.D., M.P.H., epidemiologist and director of AIDS research at Centers for Disease Control (CDC), Atlanta, Georgia.

William Darrow, CDC sociologist.

Larry Drew, virologist at Mt. Zion Hospital, San Francisco.

*Selma K. Dritz, M.D., M.P.H., epidemiologist at San Francisco Department of Public Health (SFDPH); tracked early AIDS cases in San Francisco; addressed medical and community groups on AIDS recognition and prevention.

Gaetan Dugas, French-Canadian airline steward who was among first to be diagnosed with AIDS; sometimes mistakenly referred to as "Patient Zero" and held responsible for early dissemination of AIDS.

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[1] The asterisk indicates that the individual has been interviewed for the AIDS oral history series.

Edgar Engleman, M.D., medical director of Stanford University Hospital blood bank.

Anthony S. Fauci, M.D., director of AIDS activities at National Institute of Allergy and Infectious Diseases, later director of Office of AIDS Research, currently director of NIAID, National Institutes of Health (NIH).

*Donald P. Francis, M.D., D.Sc., epidemiologist and virologist at CDC in Phoenix and Atlanta; conducted early epidemiological and virological studies of AIDS; later became CDC advisor on AIDS to California Department of Health Services; current director of research on AIDS vaccines at a biotechnology company.

Robert Gallo, M.D., retrovirologist at National Cancer Institute, NIH, involved in controversy with Pasteur Institute over isolation of AIDS virus and patent rights to HIV test.

*Deborah Greenspan, D.D.S., D.Sc., clinical professor of oral medicine at UCSF; identified AIDS-associated hairy leukoplakia; instrumental in establishing infection control procedures in dentistry.

*John S. Greenspan, D.D.S., Ph.D., professor of oral biology and oral pathology at UCSF; organized and directs UCSF AIDS specimen bank; current director of UCSF AIDS Clinical Research Center.

Margaret Heckler, Secretary of U.S. Department of Health and Human Services, 1983-1985.

Harold Jaffe, epidemiologist with the AIDS program at CDC.

*Jay A. Levy, M.D., virologist and professor of medicine at UCSF; second to isolate AIDS virus; devised early AIDS diagnostic test and heat treatment to rid blood of HIV.

Luc Montagnier, virologist and member of Pasteur Institute team which isolated AIDS virus.

*Andrew R. Moss, Ph.D., M.P.H., epidemiologist at SFGH; conducted early epidemiological studies of AIDS in San Francisco showing high incidence in gay community; later work focused on AIDS incidence in drug users and homeless.

Herbert A. Perkins, M.D., scientific director (later president) of San Francisco's Irwin Memorial Blood Bank; involved in formulating national blood bank policy regarding blood screening for HIV; currently represents blood bank in legal cases associated with transfusion AIDS.

*Merle A. Sande, M.D., professor of medicine and chief of medical services, SFGH; chairman of AIDS advisory committees at university, health department, and state levels.

Randy Shilts, journalist who covered AIDS for San Francisco Chronicle; author of And the Band Played On: Politics, People, and the AIDS Epidemic; died of AIDS in 1994.

*Mervyn F. Silverman, M.D., M.P.H., director, San Francisco Department of Public Health; center of controversy over closure of San Francisco bathhouses; current director of American Foundation for AIDS Research.

*Paul A. Volberding, M.D., oncologist and chief of AIDS Services, SFGH; member of original AIDS physician team at SFGH; prominent AIDS clinician.

Girish Vyas, Ph.D., professor of laboratory medicine, UCSF.

*Warren Winkelstein, M.D., M.P.H., epidemiologist at University of California School of Public Health; director of early on-going epidemiological study of AIDS (San Francisco Men's Health Study); member of panel deciding in June 1994 to disprove expanded clinical trial of two AIDS vaccines.

*Constance B. Wofsy, M.D., infectious disease specialist at SFGH; member of original AIDS physician team at SFGH; authority on Pneumocystis carinii pneumonia and women with AIDS.

*John L. Ziegler, M.D., oncologist at Veterans Administration Medical Center, San Francisco; authority on AIDS-associated lymphoma and Kaposi's sarcoma.

APPENDIX C

Curriculum Vitae

ARTHUR J. AMMANN

Current Position: Chairman of the Health Advisory Board
Pediatric AIDS Foundation, Santa Monica, CA
Director of:
The Ariel Project for Prevention of HIV Transmission
from Mother to Infant, Novato, CA

Date of Birth: August 12, 1936 - Brooklyn, New York
Married: Marilyn J. Mihm - 1960
Children: Kimberly and Scott

Former Position: Genentech 1985 to 1992:

1987 Associate Director Pharmacological Sciences
Lead a group of five Ph.D.s, two post doctoral students and nine research technicians in the preclinical development of tumor necrosis factor and interferon gamma. Established relevant biologic activity for each molecule appropriate for clinical development. Prepared the preclinical investigational New Drug applications and summary presentations for the FDA.

1989 Director Collaborative Medical Research
Established a Collaborative Research Program for external development of products. Collaborators included 39 individually funded projects and 57 non-funded projects at University Medical Centers and National Institutes of Health. Total annual budget of over 1.5 million dollars. Established a wound healing program to evaluate the effect of growth factors on wound healing and bone repair. Evaluated transforming growth factors alpha and beta, insulin-like growth factor, growth hormone and various vehicles for drug delivery. Also developed outside collaboration with four investigative groups. Resulted in Investigational New Drug application for transforming growth factor beta.

Director, Clinical Research Infectious Diseases
Primary responsibility for clinical development of recombinant CD4-IgG and recombinant gp120 as a vaccine and therapeutic. Developed Investigational New Drug applications, phase I protocols and established study sites involving university centers, AIDS Clinical Trial Groups, AIDS Vaccine Evaluation Groups and Community Based Clinical Trial Groups. Genentech representative for various AIDS related activities including Institute of Medicine, Keystone Symposia and Pharmaceutical Manufacturing Association.
Presentation of scientific programs representing preclinical and clinical development to pharmaceutical companies. These companies included: Fujisawa, Mitsubishi, Boehringer Ingelheim, Vestar, British Biotechnology, California Biotechnology, Bristol Myers, 3M, Johnson and Johnson, Oncogen, Collagen, Telios, Serological, Alpha Therapeutics, Glyco.
Provided scientific planning for developmental and clinical products which have immunologic applications: tumor necrosis factor alpha and beta, interferon gamma, pulmonary surfactant, transforming growth factor beta, recombinant CD4-IgG, recombinant AIDS vaccine gp120, insulin like growth factor, human growth hormone and monoclonal antibody to adhesion molecules.

Patents Written

1988 Treatment of bacterial and fungal infections using tumor necrosis factor

1988 Interferon gamma and Interleukin 2 synergy

1989 Method of inducing bone using transforming growth factor beta

1990 Method of treating periodontal disease using transforming growth factor beta

1990 Method of treating lung disease using interferon gamma

1991 Treatment of HIV associated immune thrombocytopenia

Education

1950-1954 Brooklyn Technical High School, Brooklyn, NY

1954-1958 B.S. in Biology - Wheaton College, Wheaton, IL

1958-1962 M.D. - New Jersey College of Medicine, NJ

Training

1962-1963 Internship: Jersey City Medical Center, Jersey City, NJ

1963-1965 Residency: Department of Pediatrics, University of California, San Francisco, CA

1965-1966 Chief Resident:Department of Pediatrics, University of California, San Francisco, CA

1966-1968 Captain, U.S. Air Force, Travis Air Force Base, CA

1968-1969 Fellowship in Immunology, University of Minnesota Medical Center,Minneapolis, MN

1969-1971 Fellowship in Immunology, University of Wisconsin Medical Center, Madison, WI

Licenses and Certifications

1963 Diplomate, National Board of Medical Examiners

1964 Licensure, California

1967 Diplomate, American Board of Pediatrics

1968 Licensure, Minnesota

1974 Diplomate, American Board of Allergy and Immunology

1974 Fellow, American Academy of Pediatrics

Appointments

1966-1967	Director, Newborn Service, David Grant Air Force Hospital, CA
1966-1968	Clinical Instructor, Department of Pediatrics, University of California, San Francisco
1967-1968	Chief, Pediatric Research, David Grant Air Force Hospital, CA
1968-1969	Fellowship, U.S.P.H.S., University of Minnesota Medical Center, Minneapolis
1969-1971	Research Associate, Special Fellow, U.S.P.H.S., Department of Pediatrics, University of Wisconsin Medical Center, Madison
1971-1973	Assistant Professor Pediatrics, Director Pediatric Immunology/Rheumatology and Pediatric Clinical Research Center, Department of Pediatrics, University of California, San Francisco
1973-1978	Associate Professor Pediatrics, Director Pediatric Immunology/Rheumatology and Pediatric Clinical Research Center, Department of Pediatrics, University of California, San Francisco
1978-1985	Professor Pediatrics, Director Pediatric Immunology/Rheumatology and Pediatric Clinical Research Center, Department of Pediatrics, University of California, San Francisco
1985-1987	Associate Director Pharmacological Sciences, Genentech, Inc., South San Francisco, Adjunct Professor of Pediatrics, University of California, San Francisco
1987-1989.	Director Collaborative Research, Genentech, Inc., South San Francisco, Adjunct Professor of Pediatrics, University of California, San Francisco
1989-Pres.	Director Clinical Research, Genentech, Inc., South San Francisco, Adjunct Professor of Pediatrics, University of California, San Francisco

Honors and Awards

1967 United States Surgeon General Award for Research

1968 United States Public Health Service Fellowship

1975 Visiting Professor, University of Arizona, Tucson, AZ

1977 Herbert C. Miller Visiting Professor, University of Kansas Medical Center; E. Mead Johnson Award for Pediatric Research, New York, NY

1978 Ross Award for Pediatric Research, Carmel, CA

1979 Outstanding Alumnus Award and Jaegers Lecturer, New Jersey College of Medicine; Visiting Professor, University of Arizona, Tucson, AZ, Alpha Omega Alpha

1980 Citation Classic, Current Contents "Thymosin Activity in Patients with Cellular Immunodeficiency", NEJM, 292:70-74, 1975

1981 Alberta Heritage Foundation, Visiting Professor University of Calgary, Alberta, Canada; Alberta Heritage Foundation, Visiting Professor University of Edmonton, Alberta, Canada;

1982 Matteri Memorial Lecture, Portland, OR

1984 Visiting Professor University of Florida, Department of Pediatrics
Olympic Torch Runner for University of California

1985 Visiting Professor, University of Iowa Medical Center, Department of Pediatrics, Iowa City, IA; Citation Classic, Current Contents "Nucleoside Phosphorylase Deficiency in a Child with Severely Defective T-cell Immunity and Normal B-cell Immunity", Lancet 1:1010-1013, 1975; Visiting Professor, University of Tel Aviv Medical Center, Tel Aviv, Israel; Visiting Professor, Gaslini Institute, Genoa, Italy

1986 Keynote Speaker, International Congress of Reproductive Immunology, Toronto, Canada; Bella Shick Memorial Lecture, Brookdale Hospital, Brooklyn, NY

1987 Distinguished Alumnus Award, New Jersey College of Medicine, Newark, NJ; Featured speaker, Madison General Medical and Surgical Foundation, Guy F. Forbeck Foundation Memorial Lecture

1988 Visiting Professor, Baystate Medical Center, Springfield, MA;
Special Award from the American Medical Association for Contributions to the Burton Lectureship Award, American Academy of Pediatrics

1989 Robert Dashbasch Memorial Lecture, Mills-Peninsula Hospital, San Mateo, CA

1990 Benjamin Kagan Honorary Lecture. Cedars-Sinai Hospital, Los Angeles, CA

1991 Honorary Judge Silvarado Concourse d'Elegance. Fundraiser for Pediataric AIDS, Silverado Country Club, Napa, CA

Membership in Professional and Other Organizations

1961 Charles Berry Research Society

1966 Society of Air Force Internists and Allied Specialists

1971 Western Society for Pediatric Research
Society for Pediatric Research

1975 American Association of Immunologists
American Society for Microbiology
American Academy of Pediatrics

1978 American Federation for Clinical Research

1980 New York Academy of Sciences
American Association for Advancement of Sciences

1983 Toland Society, University of California
Board of Directors, Association of Program Directors, General Clinical Research Centers, National Institute of Health
Chancellor's Associates University of California

Service to Professional Publications

Annals of Internal Medicine	Ad hoc referee
Clinical and Experimental Immunology	Ad hoc referee
Journal of Clinical Immunology	Editor
Journal of Immunology	Ad hoc referee
Journal of Immunology/Immunopathology	Ad hoc referee
Journal of Lab/Clinical Medicine	Ad hoc referee
Journal of Pediatrics	Ad hoc referee
Pediatric Research	Ad hoc referee
Pediatrics	Ad hoc referee
Thymus	Ad hoc referee
Biotechnology Therapeutics	Editor

Professional Consultantships, Site Visits and Special Task Force

1971-1975	Consultant, Family Practice Program, Santa Rosa Community Hospital
1971-1976	Consultant, Bacterial Vaccines, NIH Allergy & Infectious Disease
1971-1985	Consultant, Valley Medical Center, Fresno, CA Consultant, Travis Air Force Base, Fairfield, CA Consultant, Letterman Army Hospital, San Francisco, CA Consultant, Oakknoll Naval Hospital, Oakland, CA Consultant, Children's Hospital, Oakland, CA
1974-1978	Site Visitor, General Clinical Research Centers
1975-1978	Site Visitor, National Cancer Institute
1975-1976	Consultant, NIH Task Force on Clinical Immunology
1980-1985	Board Member, Immunology Research Foundation; Consultant, Sickle Cell Disease and Immunologic Abnormalities, National Institutes of Health
1981	Consultant, National Institutes of Aging
1983	Consultant, Centers for Disease Control on Priorities in AIDS Investigations
1983-1985	National Association of Clinical Research Center Program Directors; Chancellors Committee on AIDS; University of California Central Committee for AIDS Clinical Activity; Special Consultant CDC Task Force on Pediatric Acquired Immunodeficiency; Consultant, American Academy of Pediatrics Infectious Disease; Committee on Acquired Immunodeficiency Syndrome in Pediatrics; Consultant, American Medical Associations for Recommendation Regarding AIDS Diagnosis and Treatment; American Academy of Pediatrics Red Book Committee on Infectious Disease
1983-1986.	University of California AIDS Task Force
1983-1988.	University of California Research on AIDS Task Force American Medical Association Task Force on AIDS
1984-1985	American Medical Association Advisory Committee on the Immunologic Aspects of AIDS
1985	Advisory Committee to the American Red Cross on Unique Risks of Transfusions in Infants; State of California Task Force on AIDS Subsection on Pediatric AIDS Site Visit, University of Washington Medical Center Primate Center
1986	State of California Task Force on AIDS Grant Review American Medical Association Council on Immunotherapy
1986-pres.	American Foundation for AIDS Research Scientific Review Board; American Medical Association Council on Scientific Affairs for AIDS
1987	Special Grant Review on AIDS for National Institutes of Health; State of California Task Force on AIDS Grants;American Medical Association Council on Scientific Affairs for AIDS; American Medical Association Council on Immunotherapy; Food and Drug Administration Task Force on Standards for Nutritional Evaluation in Children

1987-Pres.	American Foundation for AIDS Research Scientific Review Board
1988	Task Force on Defining Research Directions in Pediatric AIDS for American Foundation for AIDS Research; National Institutes of Mental Health Task Force on priorities on AIDS research.
1988-Pres.	Chairman, Scientific Policy Committee, American Foundation for AIDS Research
1988-Pres.	Board of Directors, American Foundation for AIDS Research
1989-Pres.	Chairman, Scientific Advisory Committee.Pediatric AIDS Foundation; Chairman, Workshop on Passive Immunotherapy Sponsored by American Foundation for AIDS Research; International AIDS Meeting Abstract selection committee
1990	Advisory Committee Member for National Institutes of Mental Health; Committee on HIV Infection of the Central Nervous System
1990-Pres.	Chairman Samuel Jared Kushnick Foundation
1991	Keystone Directions in Pediatric AIDS Research planning committee
1992	Institute of Medicine. AIDS Meeting planning committee

Public Service

1966-1968	Captain U.S. Air Force
1971	Guest Speaker, Eau Claire Womens Club, Eau Claire, WI, "Correcting defects through transplantation"
1972-1974	Neighborhood Environmental Impact Group
1975	Guest Speaker, Intervarsity Christian Fellowship Assoc., When does life begin - when does life end"
1975-1978	Summer Physician University of California Alumni Camp
1975-1981	California Youth Soccer Coach
1975-1985	Lecture Series, Marin Covenant Church
1976-1978	Board Member, Marin Covenant Church
1979	Guest Speaker, North Park College, IL
1979	Presentation - "Autoimmune Disease and Immunodeficiency" - State Legislature UCSF
1979	Guest Speaker, Seminary Womens Club, Tiburon, CA
1979	Guest Speaker, Marin County Rotary Club
1979-1984	Marin County Young Life Committee
1980	Summer Physician, Malibu Teenage Camp, Canada
1981	Physiologic Consequences of Stress, Lecture to Northern California Certified Public Accountants
1981	Guest Speaker, Community program sponsored by Santa Rosa YMCA
1984	Guest Speaker, San Francisco Christian Businessmen, Medical ethics in today's society Guest Speaker, San Rafael Rotary, biomedical technology
1985	Marin County Workshop on Parenting, Fairfax, CA Marin Community Video, Update on AIDS.Search Committee Senior Pastor, Marin Covenant Church, Marin County, California Board of Elders, Marin Covenant Church, Marin County, CA
1986	Marin County Task Force on AIDS American Foundation for AIDS Research Scientific Advisory Committee Board of Elders Marin Covenant Church Care of the Elderly, Community Conference, San Rafael, CA. Speaker at the San Rafael Rotary 20/20 AIDS and blood transfusions.
1987	House of Representatives Hearing on AIDS (Testimony). AIDS and the School. Richmond Unified School District. Marin County Public Health Committee on AIDS. AIDS: The New Epidemic. Marin Covenant Church. Marin County, CA. The Community Response to AIDS. Marin General Hospital,.Marin County, CA. Who is my neighbor? A conference on AIDS. First Presbyterian Church of Berkeley, Berkeley, CA. AIDS Public Health Concerns, State School for Rehabilitation of the Blind. Albany, CA.
1988	AIDS Seminar. Formulating your Christian Response,. Walnut Creek Presbyterian Church, Walnut Creek, CA. Biomedical Technology and the New Ethics, National Conference for Christians and Jews, Carmel, CA. AIDS and the Family, Family Forum for Single Adults, Sponsored by Marin Covenant Church, Marin County, CA. Board of Directors, American Foundation for AIDS Research..Speaker Marin Health Forum, Marin Community College.University Service -Campus, School and Departmental
1989	Congressional testimony. House of Representatives. HIV and children. Attending Pediatric AIDS Clinic, Oakland Children's Hospital. Lecture on Ethics of AIDS Treatment. American Scientific Affiliation. Stanford University
1990	AIDS and your health. Marin Covenant Church, San Rafael, CA California AIDS Leadership Committee. Subcommittee on recommendations for infants and children. House of Representatives Testimony. Priorities in Pediatric AIDS. Representative Barbara Boxer
1991	AIDS and the Church. Redwood Covenant Church, Santa Rosa, CA

Scientific review of grants for American Foundation for AIDS Research.
Scientific review of grants for Pediatric AIDS Foundation
Congressional Advisory Group Priority in AIDS Research. Appropriations Committee, Senator Tom Harkins
California AIDS Leadership Committee. Subcommittee on recommendations for infants and children.

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43. Cashman D, Martin DW, Ammann AJ: An in vitro model for T-cell dysfunction associated with purine nucleoside phosphorylase deficiency. Clin Res. 26:183A, 1978. Presented at Western Society for Pediatric Research, Carmel, CA.

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45. Barnard JL, Wara WM, Ammann AJ, Wara DW: Assessment and compliance of cancer patients receiving Irradiation and Immunotherapy. Presented at American Society of Therapeutic Radiologists, 1978.

46. Wara DW, Goodman JR, Ochs HD, Ammann AJ: Leukocyte tubular reticular structures (Viral Particles) In mothers with discold lupus erythematosus and their sons with chronic granulomatous disease. Cell Metabolism, 1978.

47. Martin DW, Gudas LJ, Cohen A, Ammann AJ: The common molecular mechanism of immune dysfunction in the inherited deficiencies of adenosine deaminase and purine nucleoside phosphorylase. Presented at American Society for Clinical Investigation, 1978.

48. Fujiwara P, Ammann A, Wara D, Cowan M: Aging and immunologic function: In vitro lymphocyte response to thymosin (Bovine fraction 5). Presented at American Aging Association, 8th Annual National Meeting, 1978, San Francisco, CA.

49. Sweetman L, Packman S, Yoshino M, Cowan M, Wara D, Ammann A, Nyhan W: Biotin responsive multiple carboxylase deficiency. Pediat Res. 13:426,1979.

50. Ammann AJ: Immunological aberrations In purine nucleoside phosphorylase deficiencies. Presented at Ciba Foundation on Enzyme Defects and Immune Dysfunction, London, England, November, 1978.

51. Barrett DJ, Cowan M, Guenther D, Ammann AJ, Wara DW: Thymosin effect in patients with DiGeorge Syndrome. Ped Res. 12:477, 1978. Presented at Society for Pediatric Research, New York, NY.

52. Cowan MJ, Wara DW, Packman S, Ammann AJ, Yoshino M, Sweetman L, Nyhan W.: Abnormal immune function associated with biotin responsive enzyme deficiency, Fed Proc. 38:1222, 1979. Presented at American Association of Immunologists, Dallas, TX

53. Barrett DJ, Wara DW: Helper cell function of human fetal thymocytes. Presented at FASEB, Dallas, TX, 1979. Fed Proc. 38:1222, 1979.

54. Addiego JE, Ammann AJ, Schiffman G, Baehner R, Higgins G, Hammond D:.Antibody response to pneumococcal polysaccharide vaccine (PPS) administered before treatment of patients with Hodgkin's Disease (HD). Presented American Society of Hematology, Phoenix, AZ, 1979.

55. Wara DW, Barrett DJ, Ammann AJ, Cowan MJ: In vitro and In vivo effects of thymosin FV on cellular immunity in children with primary Immunodeficiency. Presented at New York Academy of Sciences, New York, NY, 1979.

56. Barrett DJ, Ammann AJ, Wara DW, Ayoub EM: Suppressor/helper cell function in children with autoimmune disease. Presented at Society for Pediatric Research, San Francisco, CA, 1980.

57. Barrett DJ, Ammann AJ. Pneumococcal vaccine in sickle cell disease: IgG and IgM antibody response. Presented at Society for Pediatric Research, San Francisco, CA, 1980.

58. Sander JE, Nathan M, Cowan MJ, Packman S, Ammann AJ, Wara DW: Intermittent ataxia and Immunodeficiency with multiple carboxylase deficiencies: A biotin responsive disorder. Annals of Neuro, 1980.

59. Chudwin DS, Wara DW, Cowan MJ, Ammann AJ: Childhood mixed connective tissue disease. Presented at Society for Pediatric Research, San Francisco, CA, 1981.

60. Barrett DJ, Ammann AJ, Ayoub EM: Pneumococcal polysaccharide in Hodgkin's Disease. Presented at International Symposium on the Streptococcus and Streptococcal Diseases, 1981.

61. Chudwin DS, Wara DW, Lameris-Martin NB, Ammann AJ: Effect of antibody concentration on opsonic requirements for phagocytosis in vitro of streptococcus pneumoniae types VII and XIX. Clinical Res. 1982. Presented at Western Society for Pediatric Research, Carmel, CA, 1982.

62. Chudwin DS, Caufield MH, Ammann AJ, Wara DW: Increased opsonic activity In sickle cell patients after pneumococcal Immunization. Presented at Society of Pediatric Research, Washington, DC, 1982.

63. Chudwin DS, Wara DW, Cowan MJ, Ammann AJ: Patients with abnormal lymphocyte phenotypes have low responses to phytohemaglutinin and allogeneic cells. Presented at American Association of Immunologists, New Orleans, LA, 1982.

64. Weintrub P, Ammann AJ, Abrams DI, Shuman MA, Addiego JE, Cowan MJ, Koerper MA. Altered T-cell Immunity hemophiliacs receiving frequent factor VIII concentrated. Blood 60:244. Presented to American Society of Hematology, Washington, DC, 1982.

65. Barrett DJ, Ayoub EM, Ammann AJ. IgG and IgM pneumococcal polysaccharide antibody responses in infants. Society for Pediatric Research, Washington DC, 1982.

66. Ammann AJ. Combined T and B cell immunodeficiency disease. Pediatric Hematology and Oncology, Erice Sicily, 1982.

67. Ammann AJ. Severe combined immunodeficiency diseases. Pediatric Hematology and Oncology, Erice Sicily, 1982.

68. Chudwin DS, Ammann AJ, Caufield MH, Wara DW. Opsonic activity in sickle cell disease after pneumococcal Immunization, National Sickle Cell Meeting,Washington, DC, 1982.

69. Weintrub P, Ammann AJ, Abrams DI, Shuman MA, Addiego JE, Cowan MJ, Koerper, MA. Altered T-cell immunity In hemophiliacs receiving frequent factor VIII concentrate. American Society of Hematology, 1982.

70. Savouret JF, Chudwin DS, Wara DW, Ammann AJ, Cowan MJ, Miller WL. Childhood mixed connective tissue disease is characterized by antibodies to U7 ribonucleoprotein. Western Society for Pediatric Research, Carmel, CA, 1983.

71. Parkman R, Remold-O'Donnel E, Kenney DM, Cairns L, Cowan M, Ammann A. Immunodeficiency due to lymphocyte GPL-115 deficiency. Society for Pediatric Research, St. Louis, MO, 1983.

72. Cowan MJ, Hellmann D, Chudwin D, Wara DW, Chang RS, Ammann AJ. Maternal transmission of acquired immunodeficiency syndrome (AIDS). Society for Pediatric Research, St. Louis, MO, 1983.

73. Lawrence DN, Spira TJ, Ammann AJ Shannon K, Gordon S. Variable patterns of T-cell subset abnormalities in blood donors linked to recipients withsubsequent acquired immunodeficiency. International Congress of Immunology, Kyoto, Japan, 1983.

74. Weintrub PS, Ammann AJ Abrams Dl, Cowan MJ, Drew WL, Addiego JE. T-cell immunity and CMV infection in hemophiliac patients. Western Society for Pediatric Research, Carmel, CA, 1983.

75. Ammann AJ, Cowan MJ, Wara DW. Acquired immunodeficiency in children. New York Academy of Sciences. New York, NY, 1983.

76. Shannon KM, Ammann AJ, Cowan MJ, Abrams D. Assessment of monocyte-macrophage antigen presentation In homosexual men with Kaposi's Sarcoma. Western Society for

Pediatric Research, Carmel, CA, 1984.

77. Shannon KM, Ammann AJ, Cowan MJ, Abrams D. Assessment of monocyte-macrophage antigen presentation in acquired immunodeficiency syndrome. Triservice Research Society, Reno, NV, 1984.

78. Cowan M, Ammann AJ, Wara DW, Weintrub P, Pabst H, Martin N, Arias N. Mismatched bone marrow transplantation using soybean agglutinin negative marrow cells. Society for Pediatric Research, San Francisco, CA, 1984.

79. Perkins H, Goldman H, Rosenschein S, Ammann AJ, Dritz S. AIDS transmission by voluntary donors. American Association of Blood Banks, 1984.

80. Ammann AJ, Kaminsky L, Levy JA. Antibody to AIDS associated retrovirus in pediatric patients with primary and secondary immunodeficiency diseases. International Conference on Acquired Immunodeficiency Syndrome, 1985.

81. Perkins HA, Rosenschein S, Echenberg D, Ammann AJ, Levy JA. Risk of AIDS from blood donors who subsequently develop AIDS. International Conference on Acquired Immunodeficiency Syndrome, 1985.

82. Cowan MJ, Shannon K, Wara DW, Ammann AJ. Rejection of bone marrow transplant and resistance of alloantigen reactive cells to in vivo deoxyadenosine in a patient with adenosine deaminase deficiency. Society for Pediatric Research, 1985.

83. Cowan MJ, Ammann AJ. Restoration of in vitro function of adenosine deaminase deficient lymphocytes by interleukin 2. Society for Pediatric Research. 1985.

84. Palladino MA, O'Connor. JVO, Shalaby MR, Ammann AJ. Tumor necrosis factors alpha and beta: their role in homeostasis. Endocrine Society 1985.

85. Culver KW, Ammann AJ, Partridge JC, Wong DF, Cowan MJ. Abnormal mitogen responses in infants born to intravenous drug abusers. Society for Pediatric Research. Washington, DC. 1986.

86. Ammann AJ, Palladino MA, Volberding P, Abrams D, Martin NL, Wert R, Conant M. Tumor necrosis factor alpha and beta in AIDS related complex and acquired immunodeficiency syndrome. American Federation for Clinical Research. Washington, DC. 1986.

87. Palladino MA, Krams S, Wara DW, Shalaby MR, Ammann AJ. Tumor necrosis factor alpha and interferon gamma induce neutrophils from normal and Chronic Granulomatous Disease patients to release superoxide. American Federation for Clinical Research. Washington, DC. 1986.

88. Matthay K, Wara DW, Ammann AJ, Cowan MJ. Mismatched bone marrow transplantation using soybean agglutinin processed T-cell depleted marrow. XI International Congress of the Transplant Society. 1986.

89. Ammann AJ. Fetal and Neonatal Graft vs Host and Immunodeficiency Disease: Engraftment by Maternal Cells. International Society for Reproductive Immunology. Toronto, Canada. 1986.

90. Shalaby MR, Shepard HM, Hirabayashi S, Figari I, Ammann AJ. The role of recombinant tumor necrosis factor alpha in the regulation of in vitro cell mediated immune response in mixed lymphocyte culture. Reticuloendothelial Society. Denver, CO 1986.

91. Palladino, M.A., Ammann, A.J., Shepard, H.M., Lewis, G., Figari I. and Lakides, G.

Regulation of tumor necrosis factor alpha, tumor necrosis factor beta and interferon gamma by cyclosporin A. Clinical Immunology Society. Baltimore, MD. 1986.

92. Czarniecki, C.W., Chiu, H.H., McCabe, S.M., Figari, I.S., Ammann, A.J., and Palladino, M.A. Regulation of cytokine production and class II antigen expression by transforming growth factor beta. UCLA Symposium on Growth Factors. Keystone, CO. 1987.

93. Billings, R.E., Chen S.A., Hollenbach, S., Ammann, A.J., Patzer, E., Hobson, W., and McCalden, T.A. Tumor necrosis factor alpha does not mediate the hemodynamic responses to endotoxin in baboons. American Heart Association on Molecular Biology of the Cardiovascular System. Boston, MA 1987.

94. Billings, R.E., Chen S.A., Hollenbach, S., Ammann, A.J., Patzer, E., Hobson, W., and McCalden, T.A. Comparison in baboons of the hemodynamic responses to tumor necrosis factor and endotoxin. American Heart Association on Molecular Biology of the Cardiovascular System. Boston, MA 1987.

95. Shalaby, M.R., Shepard, H.M., and Ammann, A.J. The in vitro immunosuppressive activities of recombinant human transforming factor beta. 11th International Reticuloendothelial Society. Kauai, HI. 1987.

96. Ballard, P.L., Liley H.G., Gonzales, L.W., White, R.T., Benson, B.J., and Ammann, A.J. Interferon gamma and surfactant synthesis in human fetal lung.Society for Pediatric Research. St. Louis, MO 1988.

97. Ballard, P.L., Liley, H.G., Gonzales, L.W., White, R.T., Benson, B.J., and Ammann, A.J. Effect of Interferon gamma on surfactant synthesis in human fetal lung. Western Society for Pediatric Research. Carmel, CA 1988

98. Shalaby, M.R., Fendly, B., Sheehan, K., Schreiber, R., Ammann, A.J. Antibody to recombinant murine tumor necrosis factor prevents splenomegaly in the graft vs host reaction (GVHR). Federation of American Socities for Experimental Biology. Las Vegas, NV Vol. 2 p. 1848, 1988.

99. Billings ER, Chen SA, Hollenbach S, Ammann, AJ, Patzer E, Hobson W, McCalden TA. The role of tumor necrosis factor alpha in endotoxin shock. Western Pharmacology Society 1990.

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101 Collier A, Katzenstein D, Coombs R, Holodly M, Mordenti J, Arditti D, Ammann AJ, Merigan T, Corey L, Safety and Pharmacokinetics of intravenous recombinant CD4 immunoadhesion (rCD4-IgG) VI Internation AIDS Conference, San Francisco, CA Abstract SB480 1990

102 Davey R, Davey V, Polis M, Falloon J, Kovacs J, Zunich K, Ammann AJ, Metcalf J, Amantea M, Masur H, Fauci A, Lane HC. A phase I trial of receombinant human CD4 immunoglobulin G (rCD4-IgG) in HIV-1 infection. VI International AIDS Conference, San Francisco, CA Abstract SB481 1990

103 Weintrub P, Yogev R, Conner E, Wilfert K, Mordenti J, Ammann AJ, Safety and pharmacokinetics of recombinant CD4 in children with HIV infection. IV international AIDS Conference, San Francisco, CA Abstract FB23 1990

104 Chen TL, Bates RL,Xu Y, Ammann AJ, Beck SL, Biochemical and cellular events in healing ulcer wounds: the effects of recombinant transforming growth factor beta-2 American Society for Cell Biology, San Deigo, CA 1990

105 Beck LS, Ammann AJ, Casey F, Aufdemorte TD, Amento EP, TGF beta accelerates bone repair in baboons 1990

106 Hodges TL, Kahn J, Kaplan L, Volberding P, BouvierL, Mordenti J, Ammann AJ, Groopman J, Allan JD, Phase I study of the safety and pharmacokinetics of recombinant human CD4 immunoglobulin G (rCD4-IgG) given by intramuscular (IM) injection in patients with AIDS and ARC. VI International AIDS Conference, San Francisco, CA 1990

107 Yarchoan R, Pluda JM, Adamo D, Thomas RV, Mordenti J, Goldspiel BR, Ammann AJ, Broder S, Phase I study rCD4-IgG administered by continuous IV infusion to patients with AIDS or ARC. VI International AIDS Conference, San Francisco, CA Abstract SB479 1990

108 Duliege AM, Uttenbogaurt CH, Landers DV, Fong S, Hayes EF, Ammann AJ, Ochs HD, In vitro effects of rCD4-IgG on human thymocytes and cord blood lymphocytes. VII International AIDS Conference, Florence, Italy 1991

109 Coombs RW, Collier AL, Gibson JW, Nelson KE, Chuloupka K, Ammann AJ, Corey L, Keystone Meeting: Prevention and treatment of AIDS, Keystone, CO 1992

Letters

1. Ammann AJ. Reply to "Respiratory complications of ataxia-telangiectasia", NEJM, 281:1019, 1969.

2. Ammann AJ. Immunoglobulin assay. Lancet 1:527, 1970.

3. Hong R, Ammann AJ. Ataxia-telangiectasia, NEJM, 283:660, 1970.

4. Ammann AJ, Hong R, Good RA. Reply to "Healthy IgE deficient persons", NEJM, 283:542, 1970.

5. Ammann AJ, Hong R. Selective IgA deficiency and autoimmunity. NEJM, 284:985, 1971.

6. Cederbaum SD, Niwayama G, Stiehm ER, Neerhout RC, Ammann AJ, Berman W, Jr.Combined immunodeficiency manifested by Letterer-Siwe syndrome. Lancet1:958, 1972.

7. Ammann AJ, Tooley WH, Hong R. Toxic epidermal necrolysis. Lancet 11:4840485, 1972.

8. Ammann AJ. Leiner's disease and C5 deficiency. J. Pediat 81:1221, 1972.

9. Ammann AJ. Comment on Dr. Needleman's letter, re: Association between susceptibility to infection and radio-chemotherapy. Ann Int Med, 79:151, 1973.

10. Wara DW, Reiter EO, Ammann AJ, Kaplan SL. T-cell rosettes in thyrotoxic Grave's disease. NEJM, 289:1145, 1973.

11. Ammann AJ, Wara DW. Reply to "Use of thymus in millipore chambers for immunologic reconstitution". NEJM, 289:982-983, 1973.

12. Ammann AJ. Reply to "Severe sepsis in patients splenectomized for blood dyscrasia", J Amer Med Assoc, 227:214, 1974.

13. Ammann AJ. Significance of elevated IgM level in children with repeated respiratory tract infection. J Amer Med Assoc, 230:1443, 1974.

14. Wara DW, Ammann AJ, Goldstein AL. Reply to "Transfer factor, thymosin and E rosettes", NEJM, 292:869, 1975.

15. Ammann AJ. Blood replacement for the patient with selective IgA deficiency. J Amer Med Assoc, 232:202, 1975.

16. Wara DW, Ammann AJ, Lipow HW, Diamond LK. Rosette forming cells. Lancet 1:1298, 1975.

17. Wara DW, Ammann AJ. Effect of thymosin on B lymphocyte function. NEJM 293:507, 1975.

18. Ammann AJ, Wara DW. Maternal-fetal graft versus host reaction. J. Pediatrics, 87:329-330, 1975.

19. Ammann AJ, Addiego J. Immunodeficiency in familial erythrophagocytic lymphohistiocytosis. Lancet, 789, 1978.

20. Ammann AJ, Diamond LK. Indications for pneumococcal vaccine in patients with impaired splenic function. NEJM, 299:778, 1978.

21. Ammann AJ, Blood disorders and AIDS. Consultant 24:17, 1984.

22. Ammann AJ, Etiology of AIDS. JAMA Sept. 14, 252:1281-2, 1984.

23. Ammann AJ, Cowan M, Wara D, Heyman M, Thaler MM, Buckley R, Lawton A, Vogler LB, Hirschhorn R. Alpha-fetoprotein levels in immunodeficiency. NEJM, 314:717-8, 1986.

24. Ammann AJ, Sherman BM. Effect of growth hormone therapy on immune function. J Pediatr., 110:663-665, 1987.

University of California Service

1971-1985	General Clinical Research Center Advisory Committee.
1971-1985	Pediatric Clinical Research Center Advisory Committee.
1971-1977	Pediatric Clinical Curriculum Committee-3rd year students.
1971-1972	Ad Hoc Committee on Human Experimentation, Academic Senate.
1971-1973	Department of Pediatrics Affirmative Action Committee.
1972-1980	Department of Pediatrics Intern Selection Committee.
1973-1975	Utilization Review Committee-Executive Medical Board of UCSF.
1973-1976	Curriculum and Education Policy Executive Committee - Pediatrics.
1973-1985	Ad Hoc Peer Review Committee for Faculty Promotion, UCSF.
1973-1978	Pediatric Postgraduate Committee.
1973-1985	Moffitt Addition Planning Committee.
1974-1985	Immunology Graduate Student Selection Committee.
1974	Organizing Committee for Symposium on "Laboratory Diagnosis of Immunologic Disorders".
1976	Thesis Committee - Timothy Terrill.
1977	Thesis Committee - Constantine Tsoukas.
1977	Organizing Committee, "Update Rheumatology-Immunology Advances", Continuing Education.
1978-1985	Ad Hoc Peer Review Committee. Outside reviewer University of California, Irvine.
1979	Fellow Education Committee Department of Pediatrics.
1979	Thesis Committee - Leroy Kondo.
1979	Thesis Committee - JoAnn Honn.
1980	Search Committee Director Outpatient Unit -Pediatrics.
1981	Search Committee Pediatric Cardiology position.
1981-1985	Moffitt Modernization Ad Hoc Committee on Pediatric Space.
1982	Thesis Committee - Geoffrey Davis.
1982-1984	Pediatric Executive Committee.
1982-1985	Pediatric Department Advisory Committee.
1982-1985	University of California, AIDS Infectious Disease Task Force.
1982-1985	University of California, Research on AIDS Task Force.
1983-1985	Chancellors Committee on AIDS.
1983-1985	Pediatric Inpatient Program Committee.
1983	Search Committee - Pediatric Cardiology.
1983-1985	Dean's Committee on Bone marrow Transplantation.
1984	Search Committee - Oral Biology.
1984	Visitors Committee for the Italian Ministry of Health, Education and Health Engineering.
1985-1988.	University of California Task Force on AIDS.
1988	Health and Medical Apprenticeship Program. IDS 130. University of California, Berkeley.

APPENDIX D

Biographical Sketch

Paul A. Volberding, MD
Professor of Medicine
University of California, San Francisco
Director, Center for AIDS Research
Director, AIDS Program and Medical Oncology
San Francisco General Hospital

AIDS Program
San Francisco General Hospital
995 Potrero Avenue, Ward 84
San Francisco, CA 94110

Phone: 415/476-4082, ex., 110
FAX: 415/476-9233
Internet: pvolberding@sfaids.ucsf.edu

Dr. Paul Volberding is a Professor of Medicine and the Director of the Center for AIDS Research at the University of California, San Francisco, and Director of the AIDS Program and Medical Oncology at San Francisco General Hospital. He received his undergraduate and medical degrees at the University of Chicago and the University of Minnesota, respectively, and finished training at the University of Utah and the University of California, San Francisco, where he studied for two years as a research fellow in the virology laboratory of Dr. Jay Levy, later a co-discoverer of HIV Dr. Volberding's professional activities have centered at San Francisco General Hospital where he established a model program of AIDS patient care, research, and professional education. His research career began with investigations of HIV-related malignancies, especially Kaposis Sarcoma. His primary research focus, however, shifted to clinical trials of antiretroviral drugs. He has been instrumental in testing many compounds, but is best known for groundbreaking trials establishing standards of care for the use of zidovudine in asymptomatic HIV infection. Dr. Volberding has written many research and review articles. He is the co-editor in chief of the *Journal of Acquired Immune Deficiency Syndrome*, and is the founder and Chair of the Board of the International AIDS Society - USA. He is also the co-editor of *The Medical Management of AIDS*, the most widely used textbook of HIV medicine, now in its fifth edition.

APPENDIX E

PAUL A. VOLBERDING, MD

Curriculum Vitae

OFFICE ADDRESS UCSF AIDS Program
San Francisco General Hospital
995 Potrero Avenue, Ward 84
San Francisco, CA 94110

PHONE 415/476-4082 ex. ~~84232~~ 110
FAX 415/476-9233
INTERNET ~~volber@itsa.ucsf.edu~~ pvolberding@sfaids.ucsf.

EDUCATION AND DEGREES

1971	University of Chicago, A.B.
1975	University of Minnesota, M.D.
1978	American Board of Internal Medicine
1981	Medical Oncology, Board Certified

MEDICAL LICENSE California

PRESENT POSITION

Professor of Medicine
Director, Center for AIDS Research
University of California, San Francisco

Director, AIDS Program and Clinical Oncology
San Francisco General Hospital

AWARDS

1983-1986	American Cancer Society, Junior Clinical Faculty Fellow
1984	Bay Area Physicians for Human Rights, Community Service Award
1987	Better Health & Living Magazine - for Contributions to Medicine
1987	San Francisco Examiner (San Francisco 39ers) - for Community Service
1987	International Association of Business Communicators SF Chapter - Distinguished Communicator Award
1987	GQ - The Glenlivet Award for Singular Style
1988	The American Academy of Oral Medicine Award for Distinguished Service
1988	Pruitt Lecturer, Mayo Clinic
1989	Scripps Hospital, Bernard Lee Schwartz Lecture
1989	Arts for Life, Special Humanitarian Award
1989	American Medical Association, Award for Health Education
1989	AIDS on the Front Line, Second Annual AIDS Conference, Certificate of Appreciation
1990	Professional Achievement Citation/University of Chicago Alumni Association
1991	American College of Physicians, Richard and Hinda Rosenthal Foundation Award
1991	L.I.F.E. Outstanding Achievement Award, Florence, Italy
1994	The American Academy of Oral Medicine, The Samuel Charles Miller Award
1994	Lifetime Achievement Award, Annual Houston Conference on AIDS in America
1994	Outstanding Achievement Award, University of Minnesota, Medical School
1994	Distinguished Alumnus Award, Phi Delta Theta International Fraternity
1995	*San Francisco Focus* Magazine, Bay Area Brain Trust Award
1995	American Medical Writers Association, Honorable Mention Award.

MEMBERSHIPS IN SCIENTIFIC & PROFESSIONAL ORGANIZATIONS

1982-	American Association for Advancement of Science (Fellow, 1996-)
1982-	American Society of Clinical Oncology
1982-	American College of Physicians (Fellow, 1986)
1982-1993	American Cancer Society, San Francisco Unit (Member, Board of Directors)
1984-1995	American Society of Hematology
1984-	San Francisco Medical Society
1984-	California Medical Association
1984-	American Medical Association
1984-	American Federation for Clinical Research
1986-	Western Society of Clinical Investigation
1987-	Clinical Immunology Society
1988-	International AIDS Society
1988-	Clinicians for Health Care Equality
1989-	Western Association of Physicians
1995-	The California Academy of Medicine

COMMITTEES

University/Local

1982-1986	Chairman, Cancer Committee, San Francisco General Hospital
1983-1987	AIDS Task Force, University of California, San Francisco
1985-1986	Ethics Committee, University of California, San Francisco
1985-1987	California Medical Association AIDS Task Force
1983-1989	AIDS Advisory Committee, San Francisco Department of Public Health
1984-1988	San Francisco Mayor's AIDS Advisory Committee
1987-1990	Ad Hoc Search Committee for Director of the AIDS Research Center, University of California, San Francisco
1988-	AIDS Coordinating Council, University of California, San Francisco
1989-1990	Committee on Equal Opportunity of the San Francisco Division of the Academic Senate
1990-	Shanti Project's Advisory Committee
1991-	Council member/AIDS Clinical Information Network
1993	Board of Directors, American Cancer Society, San Francisco Unit
1993-	HIV-Related Malignancies Program (Chair) for the UCSF Cancer Center
1994-	Honorary Board Member and Volunteer, Project Open Hand
1995-	Fundraising Advisory Committee, University of California, San Francisco.
1995-	Committee on Academic Planning & Budget, Academic Senate, University of California, San Francisco.

National

1986-1987	National Academy of Sciences (Institute of Medicine) AIDS Policy Review Steering Committee
1986-1987	American Medical Association AIDS Panel
1986-1987	American Institute of Biological Sciences AIDS Research Review Committee
1986-1988	NIH AIDS Drug Selection Committee Member
1987-1988	Office of Technology Assessment, Panel Member, Use of Laboratory Tests in Insurance
1986-1987	National Institutes of Health AIDS Executive Committee Consultant
1986-1992	National Institute of Allergy and Infectious Disease AIDS Clinical Trials Group Executive Committee (1987-88) Chair, Oncology Subcommittee (1990-) Chair, Primary Infection Phase I Working Group
1987-1994	AIDSFILMS, Board of Advisors

1987-1990	National Academy of Sciences (Institute of Medicine) AIDS Activities Oversight Comm
1987-1989	American Foundation for AIDS Research (AmFAR) Scientific Advisory Committee
1987-	National Cancer Institute, Extramural Advisory Board, PDQ Database Underwriting
1988-1991	National Sheriffs' Association AIDS Advisory Board
1989-1993	Am Med Assoc Diagnostic and Therapeutic Technology Assessment Reference Panel
1992-	Institute of Nutritional Genetics & Molecular Medical Science, Scientific Advisory Board
1992-1994	Co-chair, Institute of Medicine Round Table on AIDS Drug & Vaccine Development
1993-	Senator Dianne Feinstein's AIDS Advisory Group
1994-	Chartwell Home Therapies HIV Medical Advisory Board
1994-	National Policy Advisory Board for the HIV Cost and Services Utilization Study. RAND.
1995-	Honary Board Member, AIDS, Medicine & Miracles.

International

1986-	Founding Member, Advisory Committee, International AIDS Society
1987-	British Columbia Provincial Advisory Committee on AIDS
1990-1992	President, International AIDS Society
1993	Scientific Advisory Committee, Munich AIDS-Days Conference

Editorial Boards

1985-	AIDS Knowledge Base, [computer database], editorial board
1986-	The AIDS Record (Newsletter)
1986-	AIDS Research and Human Retroviruses (Journal)
1986-	AIDS File (Newsletter)
1987-	AIDS and Public Policy (Newsletter)
1987-	AIDS Patient Care (Journal)
1988-	AIDS (Journal)
1988-	The Journal of the Acquired Immune Deficiency Syndrome (Co-Editor-in-Chief)
1990-	Oncology Times (Journal)
1990-	AIDS Information (Journal)
1995-	AIDS Abstracts (Journal)

Conference Committees

1985	Organizing Committee and Plenary Speaker, First International AIDS Conference, Atlanta, Georgia
1986	Organizing Committee and Plenary Speaker, Second International AIDS Conference, Paris, France
1987-1990	Co-Chair, Medical Management of AIDS, San Francisco, California
1987	Organizing Committee, Third International AIDS Conference, Washington DC
1988	International Advisory Committee, Fourth International AIDS Conference, Stockholm, Sweden
1989	International Advisory Committee, Fifth International AIDS Conference, Montreal, Canada
1990	Co-Chair, Sixth International AIDS Conference, San Francisco, California
1991-1993	International Advisory Committee, Seventh, Eighth, Ninth International Conference on AIDS, Florence, Amsterdam, Berlin
1994-	International Advisory Committee, XI International Conference on AIDS, Vancouver, Canada

Journal Reviews

Blood
New England Journal of Medicine
Journal of Clinical Oncology
Annals of Internal Medicine
Gastroenterology

Journal of Clinical Immunology
The Lancet
Public Health Reports
Journal of the American Medical Association
Journal of Investigative Dermatology
Science

TRAINING & EXPERIENCE

1968-1971	Virology Laboratory Assistant Dr. Marc Beem, University of Chicago
1970	National Science Foundation Summer Research Program University of Chicago, laboratory of Dr. Marc Beem Reversibility of rhinovirus neutralization
1971-1975	University of Minnesota School of Medicine Avian type C virus receptor research, Dr. Charles Moldow
1975-1978	Medicine Internship and Residency, University of Utah Medical Center, Salt Lake City, under the direction of Dr. George Cartwright
1978-1979	Clinical Fellow in Hematology/Oncology University of California San Francisco, under Dr. Stephen Shohet Clinical research conducted with Dr. Michael Friedman on therapy of hepatic tumors
1979-1981	Research Fellow in Hematology/Oncology University of California San Francisco Research conducted in the laboratory of Dr. Jay A. Levy studying mechanisms controlling infection with xenotropic type C retroviruses Continued clinical research with Dr. Michael Friedman on the therapy of hepatic tumors
1981-1986	Assistant Professor of Medicine University of California San Francisco
1986-1990	Associate Professor of Medicine University of California San Francisco
1990-Present	Professor of Medicine University of California San Francisco
1981-Present	Chief, Medical Oncology Division San Francisco General Hospital
1984-Present	Chief, AIDS Program San Francisco General Hospital
1988-Present	Director, Center for AIDS Research University of California San Francisco

PUBLICATIONS

ORIGINAL ARTICLES

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APPENDIX F

DECLARATION OF PAUL A. VOLBERDING, M.D.

I, Paul A. Volberding, M.D., do hereby make the following declaration in support of the Application for a Temporary Restraining Order and Order to Show Cause Re: Preliminary Injunction:

1. I attended the University of Minnesota School of Medicine from 1971 to 1975, and received my M.D. degree from th institution in 1975. From 1976 to 1978, I did an internship an residency in Internal Medicine at the University of Utah. From 1978 to 1981, I had a Hemotology/Oncology Fellowship at the University of California at San Francisco ("UCSF"), and thereafter joined its faculty. From 1981 to 1982, I was the medical oncology consultant to the Malignant Melanoma Clinic at UCSF.

2. I am currently an Assistant Professor of Medicine a UCSF and Chief of Medical Oncology at San Francisco General Hospital ("SFGH"), and have been so employed since July 1, 1981 In addition, I am Director of the Acquired Immune Deficiency Sydrome ("AIDS") Clinic at SFGH and Co-director of the Kaposi's Sarcoma Clinic at UCSF. I serve on the Boards of Directors of the American Cancer Society/San Francisco and the AIDS & KS Research and Education Foundation. Over the past several years I have written or participated in the writing of numerous professional articles on AIDS and Kaposi's Sarcoma. My curriculum vitae, which includes a complete list of my

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publications, is attached hereto as Exhibit 1 and incorporated herein by reference as though fully set forth.

3. In my capacity as Chief of Medical Oncology and Director of the AIDS Clinic at SFGH, my major responsibility is to oversee the diagnosis and treatment of all patients at SFGH with AIDS, herein defined to refer to patients meeting the criteria of the Center for Disease Control ("CDC") in Atlanta (which includes the presence of diseases considered diagnostic of an underlying immune deficiency such as Kaposi's Sarcoma, central nervous system lymphoma, or infections such as pneumocystis pneumonia). I also treat patients, supervise six full time physicians, six nurses and approximately thirty clerical and other staff members, and supervise the training of medical students in the treatment of patients. At the present time, I have approximately 300 patients with AIDS or AIDS-related diseases.

4. The first contact that I had with AIDS was in July, 1981, when I commenced my employment at SFGH. The week before I began, the first patient with Kaposi's Sarcoma was admitted to that facility. In the course of obtaining a medical history, the patient related that he previously had been employed at a gay male bathhouse, where he had had numerous sexual contacts with patrons. Attached as Exhibit 2 hereto is a picture of the patient taken approximately two months after his admission in July, 1981. He died in October, 1981. Kaposi's Sarcoma normally does not affect people until they are in their 70's or 80's.

During my medical school training, residency and oncology fellowship, I had never seen a patient with Kaposi's Sarcoma. Therefore, it was striking to me to see a 22-year old man with a very aggressive form of this disease. That same week, the CDC had just published its first report alerting physicians to the possibility of a new disease affecting homosexual men associated with Kaposi's Sarcoma, and I became very interested in further studies of the syndrome. Over the next two to three months, I saw several more patients with Kaposi's Sarcoma at SFGH.

5. In my capacity as a medical oncology consultant to the Malignant Melanoma Clinic at UCSF, I met Dr. Marcus Conant in September, 1981. I mentioned to him that I had several patients with Kaposi's Sarcoma. He took me to see several of his Kaposi's Sarcoma patients at UCSF. On the basis of our experience and the reports that had been published suggesting that this was a new disease affecting homosexual men, we realized that we would be seeing more cases because of the large number of risk group members in San Francisco. Therefore, we started a Kaposi's Sarcoma Clinic at UCSF, which I believe was the first facility devoted to AIDS in the entire country.

6. Over the next year, Dr. Conant and I saw ever increasing numbers of patients affected by Kaposi's Sarcoma, and became very alarmed when we saw that the disease was extremely aggressive and rapidly fatal. We quickly realized that we would be better able to study the treatment of Kaposi's Sarcoma in AIDS in a more controlled fashion if patients were referred to a

single facility. Because of my special interest in the syndrome, we decided that all patients with Kaposi's Sarcoma would be referred to the Oncology Clinic at SFGH for protocol therapy, where there would be controlled treatment with careful follow-up and the use of both conventional and experimental drugs.

7. Based on the clinical appearance of patients with AIDS and the concentration of the disease in specific risk groups, AIDS researchers suspected from the start that the disease was caused by an infectious agent, most likely a virus. The findings of numerous published investigations strongly suggested an infection and destruction of the cells in the immune system. Recently, investigators in both the United States and France identified a new viral agent in patients with AIDS or in AIDS risk groups. The current view is that this virus, variously termed LAV or HTLVIII, causes AIDS by preferentially infecting and damaging T-lymphocytes (cells of the immune system). The infection of the cells is chronic, but viral shedding of the infected cells may be intermittent. Thus, after exposure to the virus, outcomes for the infected person may include the development of AIDS, the development of immunity to AIDS, or a chronic carrier state. In those infected individuals who develop AIDS, the breakdown in their immune system causes an increased susceptibility to a wide variety of clinical problems, including infections and cancers, most of which ultimately are fatal.

The form of AIDS I personally have been most involved with is a common malignancy, Kaposi's Sarcoma ("KS"). This disease is

a tumor of the cells lining the lymphatic vessels. These vessels normally function to drain fluids from body tissues. KS, unlike most cancers, does not have a primary site with secondary sites of involvement. Rather, it can affect many regions of the body simultaneously. Prior to the AIDS epidemic, KS generally affected elderly men and was rarely fatal. In AIDS patients, however, the disease is much more aggressive and disseminates rapidly. The median age of patients affected by KS is now 35 years and almost all are homosexual men. KS causes many clinical problems, but the most evident is the rapid progression of pigmented skin tumors affecting any part of the body. Patients usually do not die directly from KS, although this does occur in about 10 percent of patients with pulmonary involvement. More often, patients with KS die of a wasting illness or from secondary opportunistic infections such as pneumocystis pneumonia.

AIDS leads to numerous infections. These are classified as opportunistic infections because they are caused by organisms in the environment which only affect persons with damaged immune systems. These include parasitic, viral, fungal and bacterial organisms. The most common infection seen in AIDS patients is pneumocystis pneumonia, which is caused by a parasite present in the lungs and is reactivated in AIDS. Pneumocystis pneumonia does not affect healthy individuals. Before AIDS, the majority of the cases of this pulmonary infection were in children with acute leukemia undergoing chemotherapy or in patients following kidney transplantation.

Another clinical problem caused by AIDS is a diffuse enlargement of the lymph glands. AIDS experts estimate that this problem is ten to twenty times more common than CDC-defined AIDS. We have studied a number of patients in our clinics with diffuse lymphadenopathy. Dr. Donald Abrams, working in my clinic, has estimated that approximately 5 percent of these patients will progress to AIDS within two years.

8. Since July, 1981, the number of patients with AIDS and AIDS-related diseases at the UCSF and SFGH clinics has escalated alarmingly. At the end of 1982, we were seeing approximately ten patients per week for follow-up; by the end of 1983, we were seeing approximately 150 per week. We currently record nearly 300 patient contacts per week, including patients with AIDS, patients with AIDS-related conditions, and risk-group members who are concerned that they might have AIDS. At present, approximately two new cases of AIDS are being diagnosed in San Francisco each day. To date, over 700 male homosexuals in San Francisco have been diagnosed with AIDS, with a mortality to date of nearly 50 percent. The number of persons with AIDS-related conditions is estimated to be ten to twenty times higher.

The existence of an AIDS epidemic in San Francisco has been confirmed by a study conducted in 1984 by the CDC and released on October 4, 1984. It is now possible to test persons for exposure to the AIDS virus. This testing is performed on serum and detects antibodies which confirm prior infection. The proportion of homosexual men tested in San Francisco who have antibody to

the AIDS virus is alarming. Serum collected from homosexual men visting San Francisco's Venereal Disease Clinic show as many as 66 percent with AIDS virus antibody. In contrast, a study in 1978 on the same individuals showed less than 1 percent had been infected by the virus.

9. I personally have been involved in the care of well over 50 percent of the AIDS patients in San Francisco and have participated in the care of at least 300 patients with AIDS. Of these patients, greater than 97 percent have been sexually active homosexual men. The exceptions include one person with AIDS acquired as a result of hemophilia, two patients who were exposed to AIDS as a result of intravenous drug abuse, and one person for whom risk factors could not be identified. In the case of homosexual males, AIDS is transmitted through contaminated semen or other body fluids such as blood or saliva. Homosexual men are more commonly affected by AIDS because of direct innoculation of the AIDS virus into the bloodstream facilitated by trauma incurred during rectal intercourse.

10. In my opinion, AIDS represents a major health problem to the country and especially to the cities most affected by the epidemic, including New York, Miami, Los Angeles, and San Francisco. San Francisco, with the highest per capita rate of AIDS in the country, has been especially affected by this disease. AIDS is almost uniformly fatal and is always irreversible. Although some patients have survived several years, the majority of patients die within the first two years

following the diagnosis. I know of no patient who, once diagnosed with AIDS virus, has experienced spontaneous remission. One patient that I treated told me that as a result of successful treatment of his KS, he could return to a sexually active lifestyle because his partners would not realize he had AIDS. Several other patients of mine with AIDS have developed rectal gonorrhea. This, occurring months after the diagnosis of AIDS, is clear evidence of ongoing non-protected anal sexual intercourse. I recall that at a meeting in May, 1984 at the SFGH AIDS Clinic with owners of gay bathhouses, one owner commented: "Let's face it - we both make money from these guys; we make money from their sex, you make money when they're sick."

11. The care of patients with AIDS is difficult medically, emotionally and financially. These patients are generally in their 30's and highly educated about their illness. They usually face a rapidly progressing series of medical problems for which in many cases there is no effective therapy. Death occurs after a prolonged illness which requires multiple lengthy hospitalizations. The cost of such care is not precisely known, but I estimate it to be between $60,000 and $70,000 per patient from the time of diagnosis to death.

It is tempting to predict that with widespread publicity and public education concerning AIDS earlier diagnoses can be made at a time when treatment is more effective. However, this has not been the case. In fact, at the present time there is no effective therapy for the underlying immune deficiency and our

treatment of the associated problems has not progressed significantly during the past three years. AIDS patients today, as they did three years ago, face a relentlously progressing course in all but a small fraction of cases.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct

Executed on October 8, 1984, at San Francisco, California.

Paul Volberding

PAUL VOLBERDING, M.D.

4124D

APPENDIX G

CONSTANCE BELL WOFSY
CURRICULUM VITAE

NAME Constance Bell Steinkuller Wofsy, M.D.

Social Security No. 572 - 68 - 6633

Office Address
San Francisco General Hospital
995 Potrero Avenue | Building 80, Ward 84
San Francisco, CA. 94110
415 - 476 - 4082 ext 84606 | 415 - 476 - 6953 (fax)

Home Address
4266 Army Street
San Francisco, CA. 94131
415 - 282 - 5043

Marital Status Married, 2 children

EDUCATION
A.B. 1964, University of California, Berkeley
(Honors in Bacteriology)
M.A., 1966 Bacteriology and Immunology
M.D., 1971 University of Southern California

PRESENT POSITION

Professor of Clinical Medicine
University of California, San Francisco

Co-Director, AIDS Activities Division
San Francisco General Hospital

Infectious Diseases
San Francisco General Hospital
Acting Chief, 1991

OTHER PROFESSIONAL ACTIVITIES

Co - Principal Investigator: AWARE - Association for Women's AIDS Research and Education
Director: APEX - AIDS Provider Education and Experience
Chairperson: Pneumocystis carinii pneumonia Study Group, San Francisco General Hospital
Chairperson: Communications Committee; Sixth Int'l Conf. on AIDS, San Francisco, June, 1990
American Chair - Sino American Conference on HIV; Beijing, China, November 1990
Program Director - W.H.O. Eastern European HIV Training Program, SFGH - May, 1991
Delegation Leader - Management of HIV Disease in Eastern Europe. October, 1992

EDITORIAL BOARDS

BRS Saunders, Inc.; Textbook Editor & Section Editor
San Francisco General Hospital AIDS Knowledgebase
[Computer data base] 1987; Cohen PT, Sande MA, et al., Co-Editors
Journal of the Acquired Immunodeficiency Syndrome
Paul A. Volberding, M.D./James O. Kahn, M.D.- Co-Editors
AIDS - Gower Academic Journals; M.W. Adler, J.W.M. Gold, J.N. Weber - Editors
Symposium Chair - HIV Disease Management - Focus on the AIDS Treatment Team; World Health Communications 1989

CURRICULUM VITAE
Constance B. Wofsy, M.D.

HONORS

Alpha Omega Alpha
Phi Kappa Phi - All University of So. Calif. Honor Society
Equal Rights Advocates -- 12th Anniversary Honoree, 1986
Harvey Milk Lesbian and Gay Democratic Club -- Annual Dinner Honoree - 1987
Plenary Speaker - IV International Conference on AIDS; June, 1988, Stockholm, Sweden
Annual Leadership Award - 1990; San Francisco AIDS Foundation

RESEARCH INTERESTS

Acquired Immunodeficiency Syndrome
Treatment of Opportunistic Infections
Transmission of AIDS in Women and prostitutes
Physician Education

CURRENT FUNDING SOURCES

Centers for Disease Control
National Institutes of Health (NIDA and NIAID)
Infectious Diseases Society of America
Community Provider AIDS Training Project

PAST FUNDING SOURCES

Universitywide Task Force on AIDS (State of California)
Federal Drug Administration
World Health Organization

TRAINING AND EXPERIENCE

1966-67	Harvard Medical School, Boston, MA. Dept. of Bacteriology, Research Assistant
June-Sept 1967	University of California, Berkeley Dept. of Bacteriology, Research Assistant
June-Sept 1968	State of California, Dept. of Public Health Epidemiology Research Training Program Research Assistant, Berkeley, Ca.

UNIVERSITY OF CALIFORNIA, SAN DIEGO

1971	Intern
1972-74	Resident, Department of Medicine
1974	Diplomate, American Board of Internal Medicine

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

1975-76	Clinical Instructor of Medicine
1976-83	Assistant Clinical Instructor of Medicine
1983-1989	Associate Clinical Professor of Medicine
1989	Professor of Clinical Medicine

SAN FRANCISCO GENERAL HOSPITAL

1974-76	Staff Physician for Emergency Unit
July, 1976-80	Associate Director, Emergency Services
July, 1976-80	Director, Emergency Ambulatory Care
1980-82	Preceptorship, Division of Infectious Diseases

LICENSURE State of California, G 24125

HOSPITAL COMMITTEES

SAN FRANCISCO GENERAL HOSPITAL

1981-Present	Infection Control
1982-1985	Pharmacy and Therapeutics
1978-1980	Credentials Committee
1984-1989	Quality Assurance
985-Present	Antibiotic Subcommittee

UNIVERSITY COMMITTEES

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

1976-80	Intern Selection Committee (Internal Medicine)
1985-Present	Clinical Faculty Promotion
1987-1989	Chancellor's Technical Advisory Committee on AIDS University of California Infection Control Task Force on AIDS

ADVISORY BOARDS|BOARDS OF DIRECTORS

1991-1993	San Francisco AIDS Foundation Board of Directors
1990 - 1992	County Community Consortium -- Board of Directors

CITY OF SAN FRANCISCO

1985-1988	Mayor's Advisory Committee on AIDS (Mayor Dianne Feinstein)
1987-Present	Perinatal and Pediatric AIDS Advisory
1990	Hoover Middle School Science Partnership Committee; San Francisco Public Schools

STATE, NATIONAL, AND INTERNATIONAL

1985-1988	National AIDS Network; Washington, D.C. -- Board of Directors
1987-1990	VI International Conference on AIDS/San Francisco,1990; Steering Committee; Chairperson, Communications Committee
1988	San Francisco AIDS Research Council
1988	Technical Advisory Committee - Cal. Museum of Sci.& Industry, Los Angeles, CA.
1988	National Advisory Board - Center for Women Policy Studies, Washington, D.C. National Resource Center on Women and AIDS
1988	National Academy of Sciences - Contributor to "Confronting AIDS", a national summary
1988	Lawrence Hall of Science Advisory Committee, Berkeley, CA.
1986-Present	KPIX (Channel 5,SF) AIDS LifeLine Advisory Committee
1987-Present	WGBH Boston; National Public Television, The AIDS Project
1990	World AIDS Day Advisory Council - Amer. Assn for World Health; Washington, D.C.
1990-1993	Acquired Immunodeficiency Syndrome Program; AIDS Program Advisory Committee (APAC) of the NIH, Bethesda, MD.(Appt by Louis Sullivan,M.D. - Sec., HHS)
1991-1992	Chair, Women's Core Committee, AIDS Clinical Trials Group, NIH
1993	Executive Committee, AIDS Clinical Trials Group, NIH

CURRICULUM VITAE
Constance B. Wofsy, M.D.

MEMBERSHIPS IN PROFESSIONAL ORGANIZATIONS

1980 American Society for Microbiology
1984 Infectious Disease Society of America
1988 Clinicians for Health Care Equality
1989 International AIDS Society
1989 Fellow - Infectious Disease Society of America

INVITED REVIEWER FOR MEDICAL JOURNALS

New England Journal of Medicine
Journal of the American Medical Association
Journal of Clinical Investigation
Antimicrobial Agents and Chemotherapy
American Journal of Medicine
Gastroenterology
Archives of Internal Medicine
Consultant - 7th edition, AMA Drug Evaluations

EDITORIAL BOARDS

AIDS
Journal of the Acquired Immunodeficiency Syndrome

PUBLICATIONS

Journal Articles

1. **Steinkuller C** and Burton D. Immunology of spontaneous mammary tumors in mice. Mode of action of a tumor protective fraction of tubercle bacilli (MER). Proc Am Assoc Cancer Res 1968; 7:68.

2. **Steinkuller CB**, Krigbaum LG, and Weiss DW. Studies on the mode of action of the heterologous immunogenicity of a methanol-insoluble fraction of attenuated tubercle bacilli (BCG). Immunology 1969; 16:255-275.

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4. Brant-Zawadzki M, **Wofsy CB**, Schechter G: CT evidence of subarachnoid hemorrhage due to presumed gnathostomiasis. West J Med 1982; 137:65.

5. Follansbee SE, Busch DF, **Wofsy CB**, et al: An outbreak of Pneumocystis carinii pneumonia in homosexual men. Ann Intern Med 1982; 96:705-713.

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9. **Wofsy CB**, Mills J. The acquired immune deficiency syndrome: an international health problem of increasing importance. Klin Wochenschr 1984; 62:512-22.

10. **Wofsy CB**: Pneumocystis carinii pneumonia. Front Radiat Ther Onc 1984; 19:74-81.

11. Haverkos HW, with **Wofsy CB** and the PCP Therapy Project Group. Assessment of therapy for Pneumocystis carinii pneumonia. Am J Med 1984; 76:501-508.

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13. Drotman DP, Masur H, **Wofsy CB**. AIDS update: what all your patients should know. Mod Med; Nov 1985:15-4-160.

14. Gordin F, **Wofsy CB**, Mills J. Once daily ceftriaxone for skin and soft tissue infections. Antimicrob Agents Chemother 1985; 27:648-649.

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16. Nyberg DA, Federle MP, Jeffrey RB, Bottles K, **Wofsy CB**. Abdominal CT findings of disseminated Mycobacterium avium-intracellulare in AIDS. AJR 1985; 145:297-299.

17. Leoung GS, Mills J, Hopewell PC, Hughes W, **Wofsy CB**. Dapsone-trimethoprim for Pneumocystis carinii pneumonia the acquired immunodeficiency syndrome. Ann Intern Med 1986; 105(1):45-48.

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2. **Wofsy CB**: Gynecology. In: Diamond N, et al (eds). Ambulatory Care for the House Officer; Baltimore, MD: Williams & Wilkins, 1982.

3. **Wofsy CB**: Respiratory disease. In: Diamond N, et al (eds). Ambulatory Care for the House Officer; Baltimore, MD: Williams & Wilkins, 1982.

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9. Cohen, J, **Wofsy CB**. Heterosexual transmission of AIDS. In: Levy J (ed). AIDS:Pathogenesis and Treatment. New York; Marcel Dekker, 1989.

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12. Wofsy CB. Isospora belli In: Cohen PT, Sande MA, Volberding P, et al, (eds). San Francisco General Hospital AIDS Knowledgebase [computer data base]. Latham, New York BRS 1987; n.p.

13. **Wofsy CB**. Pneumocystis carinii pneumonia. In: Mills J, Leoung G. (eds):Opportunistic Infections in the AIDS Patient. Marcel Dekker, Inc., New York, 1989.

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15. Mills J, Leoung G, Medina I, Hopewell PC, Hughes WT, **Wofsy CB**. Dapsone treatment of Pneumocystis carinii pneumonia in the Acquired Immunodeficiency Syndrome. Antimicrob Agents Chemother; July, 1988. P. 1057-1060.

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17. **Wofsy CB**. Preface to Madaras L, Lynda Madaras Talks to Teens About AIDS. Newmarket Press 1988. pp xi-xii.

18. **Wofsy CB**. Clinical Aspects of AIDS and Related Disorders. In: Human Retroviruses and Diseases They Cause. Allain J-P, Gallo R, Montagnier L - Eds. Excerpta Medica/Elsevier 1988.

19. **Wofsy CB**. HIV Disease Management:Focus on the AIDS Management Team. Symposia Chair. World Health Communications (New York) 1989.

20. **Wofsy CB**. Prevention of Human Immunodeficiency Virus Transmission. in Infectious Diseases (1991), Gorbach, Bartlett, Blacklow - eds. W.B. Saunders CO - 1991.

21. **Wofsy CB**. Prevention of HIV Transmission in The Medical Management of the Patient with AIDS. Sande MA, Volberding PA (eds); ID Clin of North Amer. WB Saunders, 1992.

22. **Wofsy CB**, Padian N, Cohen J, Greenblatt R., Coleman R, Korvick J, Management of HIV Disease in Women. in AIDS Clinical Review, Jacobson M, Volberding P (eds). M Dekker 1992.

23. Chaisson R, **Wofsy C**, Acquired Immunodeficiency Syndrome (AIDS) in Principles and Practice of Emergency Medicine. Schwartz et al (eds). Lea & Febiger 1992

Abstracts

1. Gordin F, Simon G, **Wofsy CB**, Mills J. Comparative toxicity of Pneumocystis (PCP) therapy in patients with acquired immunodeficiency (AIDS). In: Programs and Abstracts of the 23rd Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society for Microbiology; October 24-26, 1983:198, Abstract No. 631.

2. Gordin F, **Wofsy CB**, Mills J. Once daily ceftriaxone (CTX) compared with cefazolin (CZN) for therapy of skin and soft tissue infections. In: Programs and Abstracts of the 23rd Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society for Microbiology; October 24-26, 1983:101, Abstract No. 118.

3. Leoung GS, Mills J, Hughes W, Hopewell P, **Wofsy CB**. Treatment of first episode Pneumocystis carinii pneumonia in AIDS patients with dapsone and trimethoprim (DS/TMP). Presented at the First International Conference on AIDS, Atlanta, Georgia; April 14-17, 1985 page 43.

4. Leoung GS, Mills J, Hadley WK, Remington J, **Wofsy CB**. Cerebral toxoplasmosis in AIDS patients: Clinical presentation with laboratory, radiographic and histologic correlations. Presented at the First International Conference on AIDS. Atlanta, Georgia, April 14-17, 1985, page 76.

5. Mess TP, Hadley WK, **Wofsy CB**. Bacteremia due to Mycobacterium tuberculosis and Mycobacterium avium intracellulare in homosexual males. Presented at the First International Conference on AIDS. Atlanta, Georgia; April 14-17, 1985, page 47.

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Constance B. Wofsy

Connie appreciated life with an intensity and enthusiasm known only to those who do not take life for granted. As a child, Connie was told that she had a severe, unexplained hematological disorder that would probably prevent her from reaching adulthood. True to form even in her earliest years, Connie resisted the notion that her horizons might be limited and focused instead on enjoying her childhood. Raised in a family of art lovers and craftsmen, she developed a special fondness for art and architecture that remained a lifelong source of pleasure for her. When medical advances led to her accurate diagnosis and successful treatment at age 17, Connie moved West, from Pennsylvania to California, where she attended Berkeley and chose to pursue science rather than art as her life's work. Against the advice of well-meaning but short-sighted male friends and mentors, she embarked on a career in medicine. She was at the leading edge of that historic wave of women medical students of the past generation who, by the force of their will and their excellence, transformed a profession that had long denied women an equal chance. She rode that wave to its crest and lived to feel its strength and to appreciate its beauty.

Connie's pioneering spirit was never so important as when, at the start of her career, she was among the first physicians to see the emergence of a devastating new disease. At a time when many found it convenient to follow safer paths, Connie faced the new epidemic and riveted her energy against it. She joined forces with other pioneers at San Francisco General Hospital and in the surrounding community to develop an AIDS program in San Francisco that immediately, and from that time forward, set the standards for AIDS care and AIDS education throughout the world.

AIDS has occupied more than a decade of my professional life, and was superimposed on the very heart of the upbringing of two children, the most productive personal as well as professional years, those very high activity years. Things seem like the norm if you and the people closest to you are doing those things. I think I'm now able to reflect that this hasn't been the norm, and that we lived through a period of history that's not unparalleled, but is unique within the academic and medical world. Only when you step back from it do you say, "Oh, so that wasn't normal, everyday life after all." It's been a lot and it's been hard, but it would be tough to give up almost any of the experiences. If I had to go through and say, "Put a red line through that one," it would be hard to know what to put the red line through.

-Constance B. Wofsy

Excerpt from the UC AIDS Oral History

San Francisco General Hospital

Phil Donahue Show

When the need was to keep a human face on the AIDS epidemic, Connie sounded the call at the International AIDS meeting in Stockholm. When the need was to develop AIDS expertise in developing countries, Connie created a new educational model that brought AIDS health care providers from around the world to San Francisco for advanced training. When the need was to secure equal status for women on the national AIDS agenda, Connie became founding Chair of the Women's Health Committee of the AIDS Clinical Trials Group at the NIH. Connie never rested on her laurels, meeting each new challenge with equal determination.

Connie did not think of herself as a political person in the traditional sense. However, by virtue of her actions, she was a leader in the women's movement, a leader in the fight for gay and lesbian rights, and a leader in the struggle to deliver medical services to the poor. She remained committed to these ideals throughout the final decade of her life, choosing not to shift her efforts to activities more directly related to her own personal battle.

Connie, above all her other accomplishments, felt her greatest pride in her children, Kevin and Susan. She considered herself fortunate to have lived to see this part of her life's work so well done, although characteristically she took little credit herself. It was all the comfort she needed in her final days to know that her spirit was safe in their custody. She also knew how much her memory would be cherished by her husband David, her mother Ruth, and the other members of her family. It is doubtful, however, that she could ever have fully grasped how vividly she will remain in the hearts and lives of her colleagues, students, and many friends.

Connie - we love you and miss you, and we will always remember you with great happiness for all that you have given us.

Age 2

Age 5

Age 14

July 16, 1970

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Sally Smith Hughes

Graduated from the University of California, Berkeley, in 1963 with an A.B. degree in zoology, and from the University of California, San Francisco, in 1966 with an M.A. degree in anatomy. She received a Ph.D. degree in the history of medicine from the Royal Postgraduate Medical School, University of London, in 1972.

Postgraduate Research Histologist, the Cardiovascular Research Institute, University of California, San Francisco, 1966-1969; science historian for the History of Science and Technology Program, The Bancroft Library, 1978-1980.

Presently Senior Editor on medical and scientific topics for the Regional Oral History Office, and Research Historian in the Department of History of Health Sciences, University of California, San Francisco. Author of *The Virus: A History of the Concept*, Sally Smith Hughes is currently interviewing in the fields of AIDS and molecular biology/biotechnology.